perature which renders the procedure impractical except for small-scale runs.

An alternative approach to the syntheses of **6a** via **10a** employs a new reagent, the [(trimethylsilyl)ethynyl]dithiane **12**, for synthesizing an acetylenic ketone as suggested in Scheme II. The thioacetal **12**[11] was readily prepared in 59% overall yield[8c,d] by condensation ($BF_3 \cdot Et_2O$ in HOAc, 15 min, 15 °C) of 1,3-propanedithiol with 3-(trimethylsilyl)propynal[11a] which was formed,[8d] in turn, by pyridinium chlorochromate oxidation[12] of the corresponding alcohol.[13]

The thioacetal (0.99 mmol) **12** was converted (1.05 mmol of *n*-BuLi, 5 mL of THF, 1 h, −40 to −20 °C) into its lithium salt, which was alkylated with the known[14] allylic chloride **13** (0.92 mmol, 1 mL of THF, −20 to −15 °C, 4 h) to give the thioketal **14**[8c,d,11] in 84% yield. A variety of known methods were tried for the hydrolysis of **14**, but the only satisfactory procedure[15] was the treatment of **14** (0.279 mmol in 2 mL of THF) with thallium(III) nitrate trihydrate (0.443 mmol in 5 mL of MeOH) for 5 min at 23 °C, followed by further treatment (5 min, 23 °C) with 2 mL of 5% HCl. Thus the known ketone **15**[2] was obtained[8c,d] in 86% yield. Reduction of **15** (0.13 mmol) was effected by the method of Midland,[16] using the complex from (+)-α-pinene[17] (0.617 mmol) and 9-BBN (0.5 mmol) in THF (43 h, ~20 °C). The product **9**[8c] (75% yield) was desilylated (see above) and purified,[8a,c] giving **10**, $[\alpha]^{20}_D$ +72.4° (*c* 0.71, $CHCl_3$). The composition of the diastereomeric MTPA esters[9] derived from this +72.4° specimen of **10** was shown by GC[10] to be 98.5:1.5 **11a**/**11b**, corresponding to an optical yield of 97%. The Midland reduction of **15** has been repeated successfully several times; thus on a 2.74-mmol scale a 71% yield of **9**, having 96% ee of **9a**, was obtained.

The new approach to the cyclization substrate **1** via the sequence described in Scheme II has the following novel features: (1) the overall process is more convergent than the original scheme; (2) the process gives very high optical yields; (3) a new reagent, namely, **12**, for producing the acetylenic ketone **15** has been developed; (4) finally, the process (as in Scheme II) involving alkylation of the reagent **12**, followed by deketalization, asymmetric reduction, and then further alkylation should be useful for synthesizing a variety of optically pure alcohols.

Acknowledgment. We thank the National Institutes of Health and the National Science Foundation for support of this research. B.F. is indebted to the Swiss National Science Foundation for financial aid. We want to express our appreciation also to Dr. Tsung-Tee Li for helpful discussions and to Professor H. S. Mosher for supplying us with optically pure (+)-α-pinene.

Registry No. 3, 58403-88-6; **6a** (R^1 = H; R^2 = OH), 76704-56-8; **6b** (R^1 = H; R^2 = H), 76704-57-9; **8**, 54655-07-1; **9a** (R^1 = H; R^2 = OH), 76649-00-8; **9b** (R^1 = OH; R^2 = H), 76649-01-9; **10a** (R^1 = H; R^2 = OH), 76704-58-0; **10b** (R^1 = OH; R^2 = H), 76704-59-1; **11a** (R^1 = H; R^2 = MTPA-O), 76684-07-6; **11b** (R^1 = MTPA-O; R^2 = H), 76649-02-0; **12**, 76649-03-1; **12** Li, 76665-49-1; **13**, 58403-77-3; **14**, 76649-04-2; **15**, 76649-05-3; 1,3-propanedithiol, 109-80-8; 3-(trimethylsilyl)propynal, 6224-91-5; (2*S*,2′*S*)-2-(hydroxymethyl)-1-[(1-methylpyrrolidin-2-yl)methyl]pyrrolidine, 66283-23-6; (+)-α-pinene-9-BBN, 64106-79-2.

William S. Johnson,* Bruno Frei
Aravamudan S. Gopalan
Department of Chemistry
Stanford University
Stanford, California 94305

Received December 29, 1980

---

[11] (a) The NMR and IR spectra were consistent with the assigned structures. (b) A satisfactory combustion analysis was obtained for this compound.

[12] Corey, E. J.; Suggs, W. *Tetrahedron Lett.* **1975**, 2647.

[13] Jäger, V. *Methoden Org. Chem. (Houben-Weyl)* **1977**, *V/2a*, 329.

[14] Johnson, W. S.; Escher, S.; Metcalf, B. W. *J. Am. Chem. Soc.* **1976**, *98*, 1039.

[15] Smith, R. A. J.; Hannah, D. J. *Synth. Commun.* **1979**, *9*, 301.

[16] Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867.

[17] Optically pure (+)-α-pinene, $[\alpha]^{20}_D$ +51.6° (neat), that had been isolated from a sample of Port Orford cedar oil was used.

Reaction of Organic Molecules on Solid Surfaces. 1. Facile Deuteration of Active Methylene Compounds with D_2O-Treated Alumina

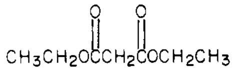
Summary: A procedure has been developed for the preparation of deuterated alumina. Treatment of ketones, active methylene compounds, and acidic hydrocarbons with this solid resulted in the deuteration of the compounds at acidic sites. Deuterated molecular sieves are also effective in these deuterations.

Sir: We report the development of a new, facile, and convenient method by which organic molecules can be deuterated at acidic sites. The procedure involves treatment of acidic organic molecule with deuterated alumina either on a column or as a slurry. The combination of speed, efficiency, convenience, and other factors to be described below should make this method competitive with more traditional methods of deuteration and offers substantial synthetic potential.

Chromatography alumina (Fisher adsorption, 80–200 mesh)[1] has both physisorbed and chemisorbed H_2O, and all such proton sources must be removed and replaced by deuterium before the material can be used for deuteration. Unfortunately, this is not accomplished by simply heating alumina followed by treatment with D_2O.[2] However, we observed that seven to nine sequential heatings (315 °C, 18 h) followed by treatment with D_2O (3 wt %) afforded material which quantitatively deuterated phenylacetylene (**1**) upon passage through a 10-g column (100 mg of **1** in pentane).[3]

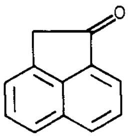
$$\underset{\mathbf{1}}{C_6H_5C{\equiv}CH} \xrightarrow{Al_2O_3/D_2O} \underset{\mathbf{1}\text{-}d}{C_6H_5C{\equiv}CD}$$

Several compound types bearing acidic hydrogens were found to be effectively deuterated by deuterated alumina. For example, diethyl malonate (**2**), was >96% deuterated



$$CH_3CH_2O\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$$

2



3

at the methylene site when treated as a slurry with the

---

[1] (a) For a review of the use of alumina in organic synthesis see: Posner, G. H. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 487. (b) One group has reported on the tritiation of a keto steroid by chromatography on Al_2O_3/T_2O. See: Klein, P. D.; Knight, J. C. *J. Am. Chem. Soc.* **1965**, *87*, 2657; Klein, P. D.; Erenrich, E. H. *Anal. Chem.* **1966**, *38*, 480.

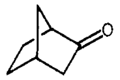
[2] Peri, J. B. *J. Phys. Chem.* **1960**, *64*, 1526.

[3] The deuterated alumina could be prepared by treating the dehydrated solid with D_2O in dry tetrahydrofuran. It took, however, several additional cycles before a phenylacetylene sample could be completely deuterated.

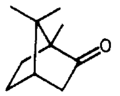
0022-3263/81/1946-1513$01.25/0

reagent for 5 min.[4] Likewise, acenaphthenone (**3**) was almost completely deuterated.[5,6] Although this type of exchange may also be accomplished under other conditions (with *t*-BuOD/*t*-BuOK, for example), the ease and short reaction time with the alumina reagent strongly recommend it for such conversion.

Norbornanone (**4**) and camphor (**5**) were both found to exchange when treated as a slurry with deuterated alumina in 1:1 ether–pentane but at substantially slower rates than for **1**–**3**. After 72 h, for example, **4** was 44% deuterated (based on two exchangeable sites), and **5** was only 5% deuterated.[7] The difference in reactivity of **4** and **5** is attributed to a steric effect of the 7-*syn*-methyl group in the latter compound since the stereochemistry of exchange in norbornanone was demonstrated to involve the exo proton by 400-MHz NMR.[8] Interestingly, the stereoselectivity observed here is exactly the same, and of the same magnitude, as that observed in solution.[9]

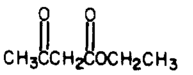


4



5

Ethyl acetoacetate (**6**) represents an interesting example[10] since two sites are available for exchange which differ greatly in acidity. In homogeneous solution, the methylene hydrogens exchange much more rapidly than the methyl protons as predicted by the greatly enhanced acidity of the former.[11] The results were quite different with deuterated alumina. Thus, treatment of **6** slurried with deuterated alumina (1:1 ether–pentane, 5 min) gave material in which the methyl–methylene ratio of deuteration was ca. 40:60. Over a longer period, the methylene site reaches an asymptotic value of 70% exchange while the methyl site is completely deuterated. The regiochemistry of the exchange on the alumina is thus time dependent and quite different than that observed in homogeneous solution. Although the reasons for this phenomna are obscure, the differences may be synthetically useful.



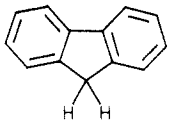
$CH_3\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3$

6

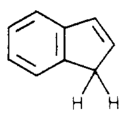
It was also of interest to determine if hydrocarbons other than **1** could be deuterated on alumina and the compounds triphenylmethane (**7**), fluorene (**8**), and indene (**9**) were chosen for investigation. Under conditions where 100-mg samples of **1** were completely deuterated, comparable samples of **7**–**9** were 20%, 15%, and 44% deuterated, respectively, at the acidic positions.[12] Because **8** and **9** have solution acidities similar to that of phenylacetylene,[13] these differences may be attributed to a steric effect.[14] Linear, unhindered phenylacetylene should experience no difficulty in locating a basic site on the surface, whereas **8** and **9**, being relatively planar, cannot penetrate the surface as readily as **1** and locate the active sites. Finally, although the three hydrocarbons did not exchange as completely as **1**, recycling the compounds through the alumina should enable complete deuteration to be achieved.

$(C_6H_5)_3CH$

7



8



9

We also compared the ability of molecular sieves[15] and silica gel[16] to exchange acidic hydrogen on organic molecules. The sieves and silica gel were deuterated in the same manner as the alumina (several cycles) and the resulting solids analyzed by treatment with **1** as previously described. The experiments demonstrated that molecular sieves deuterate phenylacetylene (**1**) readily, whereas silica gel does not. Thus, molecular sieves should also be useful for the deuteration of acidic organic molecules.

We examined, in a preliminary manner, the exchange capacity of the alumina by sequential treatment of 10 g of the alumina reagent with 100-mg portions of phenylacetylene. The results demonstrated that ca. 200–300 mg of **1** was completely exchanged and ca. 4 g could be deuterated to greater than 50%. Although this represents only a modest efficiency of deuterium incorporation,[17] the ease and convenience of utilizing a solid reagent recommends it for synthesis. We are continuing our investigation to increase the efficiency and scope of the process.

Acknowledgment. P.B. and E.W. were NSF undergraduate research participants at the University of Tennessee during the summer of 1980. The authors thank the NSF-sponsored NMR facility at the University of South Carolina (Grant CHE78-18723) for running the 400-MHz ^1H NMR spectra. H.M.H. thanks the Egyptian government for support.

Registry No. 1, 536-74-3; **2**, 105-53-3; **3**, 2235-15-6; **4**, 497-38-1; **5**, 76-22-2; **6**, 141-97-9; **7**, 519-73-3; **8**, 86-73-7; **9**, 95-13-6; Al_2O_3, 1344-28-1; D_2O, 7789-20-0.

---

[4] A 100-mg sample of **2** was treated with 10-g, cycle-9 alumina with 1:1 diethyl ether–pentane as solvent.

[5] The bulk of the ketone in fact was completely deuterated, while the "tailings" off the column were substantially less than 100% deuterated.

[6] In a similar experiment, 69% deuteration at all three active sites was found by mass spectrometry for 2-methylcyclohexanone. These results, in conjunction with NMR studies, suggest that the α-hydrogen next to the methyl group exchanges somewhat faster than the other two α-hydrogens.

[7] For norbornanone (**4**), mass spectrometry showed 17.1% d_0, 78.8% d_1, and 4.1% d_2 and for camphor (**5**), 90.3% d_0 and 9.7% d_1.

[8] There are, of course, two processes to consider. One is the removal of an *exo*- or *endo*-H, and the second is the addition of an *exo*- or *endo*-D. These experiments cannot unravel these processes unambiguously.

[9] See, for example: Jefford, C. W.; Boschung, A. F. *Helv. Chim. Acta* **1974**, *57*, 2242.

[10] In addition to **3** and **6**, we also looked at the behavior of dimedone. It, unfortunately, underwent a chemical transformation when treated with alumina.

[11] Dugnay, G.; Metayer, C.; Quiniou, H. *Bull. Chim. Soc. Fr.* **1974**, 2853.

[12] (a) Indene (**9**) was 50% deuterated at the methylene position and 33% at the vinyl position next to the benzene ring. This works out to 44% total deuteration. (b) The results in 12a demonstrate that the exchange proceeds via the uncomplexed indenyl anion.

[13] Cram, D. J. "Fundamentals of Carbanion Chemistry"; Academic Press: New York, 1965; p 19.

[14] Of course, acidities (pK_a's) measure thermodynamic quantities while rates of exchange measure kinetic quantities. One would expect for these similar compounds that the rates of exchange should parallel the pK_a's.

[15] Davison Type 4A (8–12-mesh) sieves were used.

[16] Davison silica gel (grade 922) (220–325 mesh) was used.

[17] A simple calculation shows that in the 4 g of 50% deuterated material 7% of *all* the deuterium put on the solid has been used.

George W. Kabalka,* Richard M. Pagni*
Paula Bridwell, Elaine Walsh, Hamdi M. Hassaneen
Department of Chemistry
University of Tennessee
Knoxville, Tennessee 37916

Received January 28, 1981