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ORGANIC REACTIONS AT ALUMINA SURFACES II.
2-PROPANOL ON DEHYDRATED ALUMINA AS A REAGENT FOR SELECTIVE REDUCTION OF ALDEHYDES[1]

Gary H. Posner* and Alfonse W. Runquist

Department of Chemistry, The Johns Hopkins University, Baltimore, Maryland 21218

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Alumina is widely used as an adsorbent for chromatographic purification of organic compounds. Water, present even in the most active aluminas available commercially, often promotes undesired side reactions, such as hydrolyses, eliminations, and rearrangements of adsorbed substances.[2,3] We reasoned that dehydration of aluminas and then introduction of alcohols, thiols, or amines in place of the removed water would produce novel aluminas which might serve as useful reagents for organic synthesis. Indeed, alcohol-doped dehydrated aluminas promote several useful organic transformations;[4] we report here that 2-propanol on dehydrated Woelm chromatographic alumina at room temperature[5] reduces structurally diverse aldehydes cleanly and rapidly (<2 hrs) into the corresponding alcohols which are isolated easily in pure form in 65-88% yields. Furthermore, with a limited amount of 2-propanol on dehydrated alumina, aldehydes, but not most ketones, are reduced, and $(CH_3)_2CDOH$ on alumina converts aldehydes into the corresponding 1-deutero-alcohols

The general procedure involves dehydration of commercial aluminas by heating in a quartz vessel at 400° and 0.06 torr for 24 hr.[6,7] About 5 g of the dehydrated alumina is transferred inside a nitrogen-filled glove bag to an oven-dried tared 25 ml round bottom flask containing a magnetic stirring bar. The flask is stoppered and removed from the glove bag. About 5 ml of inert solvent (e.g. diethyl ether, chloroform, carbon tetrachloride, or hexane) and ~500 mg of 2-propanol are added. After stirring for 0.5 hr at 25°, ~1 mmol of aldehyde in ~1 ml of solvent is added and stirring is continued for 2 hr at 25°. The reaction is quenched by addition of 5 ml of methanol and stirring for 15 min. Vacuum filtration through Celite, washing the Celite with ~35 ml of methanol, and rotary evaporation of solvent gives crude alcohols which are either distilled or recrystallized. The results of this procedure using aldehydes of various structural types and 2-propanol-doped dehydrated Woelm W-200 (Brockmann activity super 1) neutral alumina are shown in equations 1-8; yields are of isolated, purified products.

$$\underline{n}\text{-}C_9H_{19}CHO \xrightarrow{84\%} \underline{n}\text{-}C_9H_{19}CH_2OH \tag{1}$$

$$C_6H_5CH_2CHO \xrightarrow{65\%} C_6H_5CH_2CH_2OH \tag{2}$$

$$C_6H_5CH(CH_3)CHO \xrightarrow{77\%} C_6H_5CH(CH_3)CH_2OH \tag{3}$$

$$C_6H_5CH\overset{t}{=}CHCHO \xrightarrow{82\%} C_6H_5CH\overset{t}{=}CHCH_2OH \tag{4}$$

$$(CH_3)_2CH{=}CH(CH_2)_2CH{=}CHCHO \xrightarrow{88\%} (CH_3)_2CH{=}CH(CH_2)_2CH{=}CHCH_2OH \tag{5}$$

$$C_6H_5CHO \xrightarrow{77\%} C_6H_5CH_2OH \tag{6}$$

$$\underline{p}\text{-}O_2NC_6H_4CHO \xrightarrow{84\%} \underline{p}\text{-}O_2NC_6H_4CH_2OH \tag{7}$$

$$\underline{p}\text{-}CH_3CONHC_6H_4CHO \xrightarrow{76\%} \underline{p}\text{-}CH_3CONHC_6H_4CH_2OH \tag{8}$$

Several aspects of conversions 1-8 merit emphasis. Infrared analysis of the crude alcohol products (before purification) indicates a very small amount of conjugated carbonyl absorption due presumably to aldol condensations;[8] the Meerwein-Ponndorf-Verley reduction of aldehydes with aluminum isopropoxide often gives significant amounts of aldol, Tishchenko, and Cannizzaro products, and special precautions must be taken to minimize these side reactions.[9] Because transformations 1-8 are heterogeneous reactions which take place at the alumina-solvent phase boundary, they were each repeated several times to establish their reproducibility; in all cases, reproducible results were obtained to within ± 5%. 2-Propanol on dehydrated Woelm W-200 basic and acidic and Alcoa F-20 aluminas was found to reduce <u>n</u>-decanal about as effectively as 2-propanol on dehydrated Woelm W-200 neutral alumina. Transformation 1 was performed also on a ~10 mmol (~2 g) scale to illustrate application of this method to preparation of gram quantities of alcohols; the yield of pure 1-decanol after distillation was 81%. Conversions 2 and 3 demonstrate the effectiveness of the 2-propanol-doped alumina reduction procedure even for aldehydes having especially acidic α-protons, and equation 5 indicates that even highly sensitive α,β-ethylenic aldehydes having γ-protons are reduced effectively (88%) to the corresponding allylic alcohols;[10] citral (35% <u>cis</u>, 65% <u>trans</u>) was used in conversion 5, and the geraniol formed had the same isomeric composition as the reactant citral.[11]

Although aldehydes are reduced by 2-propanol on dehydrated aluminas, various other functional groups are inert. Using the general procedure described above, we recover 1-iodooctane, 3-hydroxpropionitrile, p-nitrobenzamide, 1,2-bis(chloromethyl)benzene, and dimethyl 1,10-decanedioate in 80, 83, 79, 84 and 96% yields, respectively. Furthermore, although 4-*t*-butylcyclohexanone is completely reduced under standard conditions,[12] cycloheptanone, 2-octanone, 5-nonanone, acetophenone and 2-cyclohexenone are reduced only to the extent of 10-40%. When 1 mmol of decanal and 1 mmol of 2-octanone are mixed together and then added to 2.5 g (half the usual amount) of dehydrated Woelm W-200 neutral alumina containing a small amount (125 mg, 5%, ~2 mmol) of 2-propanol, glpc analysis after 2 hrs at 25° indicates 5% decanal, 95% 1-decanol, 95% 2-octanone, and 5% 2-octanol. Likewise, 10-oxoundecanal,[13] a keto aldehyde, is converted to 10-oxoundecanol[14] in 70% recrystallized yield (eq. 9). 2-Propanol on dehydrated alumina is then the first effective reagent for selective reduction of aldehyde in presence of most ketone carbonyl groups.

$$CH_3CO(CH_2)_8CHO \xrightarrow{70\%} CH_3CO(CH_2)_8CH_2OH \qquad (9)$$

That the hydride ion which reduces the carbonyl substrates arises from the carbinol carbon atom of 2-propanol (and not from the methanol used to quench the reaction, for example[15]) is unambiguously shown by doping dehydrated alumina with $(CH_3)_2CDOH$; benzaldehyde is converted in 80% distilled yield into $C_6H_5CH(D)OH$ having essentially the same spectral properties as those of the product of $LiAlD_4$ reduction of benzaldehyde.

The full scope and limitations of this carbonyl reduction process promoted by 2-propanol on dehydrated alumina and reactions of organic compounds at other metal oxide surfaces are being examined.

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