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ORGANIC REACTIONS AT ALUMINA SURFACES. DISPLACEMENT REACTIONS EFFECTED BY ALCOHOLS, THIOLS, AND ACETIC ACID ON DEHYDRATED ALUMINA.[1]

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Organic compounds containing one or more heteroatoms usually adsorb to alumina. When the heteroatom carries a hydrogen atom (RZ-H), adsorption to alumina sometimes involves heterolytic cleavage of the heteroatom-hydrogen bond ($RZ^- + H^+$).[2] We reasoned that adsorption of organic electrophiles (e.g. sulfonate esters, epoxides) to RZH-doped alumina might bring electrophile and nucleophile into proximity; the juxtaposition of electrophile and nucleophile and the enhanced nucleophilicity (and basicity) of the nucleophile might work synergistically to produce a chemical reaction under unusually mild conditions. We report here that methanol on dehydrated Woelm W-200 (Brockmann activity super I)[3], neutral, alumina displaces sulfonate and sulfamate ester groups to form methyl ethers and that alcohols, thiols, and acetic acid on this alumina open epoxides to the corresponding 2-hydroxyethyl ethers, 2-hydroxyethyl thioethers and 2-hydroxyethyl acetates.

When ℓ-2-octyl p-toluenesulfonate[4] in diethyl ether was stirred for 24 hr at 25° over W-200, neutral alumina which had been impregnated with 2% methanol by weight, 1- and 2-octenes (40%) and d-2-methoxyoctane (40%) were formed. In separate experiments, the rotation of the d-2-methoxyoctane varied between α_D^{24} 2.25-2.47° (90-95% net inversion of configuration).[5] Likewise cyclohexylmethyl N,N-dimethylsulfamate (**1**) was converted by methanol-doped W-200, neutral, dehydrated (W-200-N-D) alumina to a 1:6 ratio of methylenecyclohexane and cyclohexylmethyl methyl ether (eq. 1). Because these two displacement reactions effected by methanol on dehydrated alumina proceed with such high stereoselectivity and so little rearrangement (e.g. no tertiary ether **2** was detected), respectively, carbonium ion intermediates seem unlikely; these displacements resemble more S_N2 than S_N1 reactions.

Cyclohexene oxide reacted with alcohol-doped, thiol-doped, and acetic acid-doped dehydrated W-200 alumina to form the corresponding trans-2-alkoxy-, trans-2-alkylthio-, and trans-2-acetoxycyclohexanols in good, isolated yields (eq. 2). These reactions are rapid and mild, proceeding to completion within 1 hr at 25°; in most cases, 1 mmol of substrate and 7.5 g of W-200-N-D alumina were used. Because these reactions are heterogeneous, taking place at the alumina surface, some were repeated several times; reproducible results were obtained to within ± 5%. Although some of these epoxide openings can be achieved homogeneously, via either acid or base promoted reactions, formation of trans-2-acetoxycyclohexanol and especially trans-2-benzyloxycyclohexanol is very difficult to achieve homogeneously in good yield;[6] cyclohexene oxide in refluxing acetic acid gave mainly trans-1,2-diacetoxycyclohexane, and trans-2-benzyloxylcyclohexanol was not formed when cyclohexene oxide was treated with benzyl alcohol and hydrochloric acid, with sodium benzyloxide in tetrahydrofuran, or with lithium benzyloxide even in presence of hexamethylphosphoramide. Reaction 2 was run also with 0.75 g (7.5 mmol) of cyclohexene oxide to illustrate the effectiveness of benzyl alcohol on dehydrated alumina to produce gram quantities of trans-2-benzyloxycyclohexanol; even on this scale, the reaction proceeded smoothly to give trans-2-benzyloxycyclohexanol in 37% distilled yield. This mono-protected, 1,2-disubstituted glycol allows selective chemical operation at the free hydroxyl center and then hydrogenolytic removal of the benzyl group to release the second hydroxyl functionality. The trisubstituted epoxide methylcyclohexene oxide reacted with methanol on dehydrated alumina to form a regiochemical mixture of trans-2-methoxycyclohexanols; in ether as solvent, the mixture was nearly 1:1, and in carbon tetrachloride the mixture was nearly 2:1 in favor of the product of typical S_N2 opening as shown in eq. 3. Interestingly, the only product isolated from reaction of methylcyclohexene oxide with acetic acid-doped alumina was trans-2-acetoxy-1-methylcyclohexanol (eq. 4). The acyclic trans-epoxide derived from trans-3-hexene also reacted with methanol-doped dehydrated alumina to produce erythro-2-hydroxyethyl ether **3** stereospecifically (eq. 5).

Several control experiments were performed to determine the stability of variously functionalized compounds stirring in ether for a prolonged time (18 hr) at 25° over (a) methanol-doped and (b) acetic acid-doped W-200 alumina. 3-Hydroxypropionitrile is recovered in 67% (a) and 75% (b) yields; 2-octanone is recovered in 70% (a) yield; 1,2-bis(chloromethyl)benzene is recovered in 75% yield (b); and 1,3-diiodopropane is recovered in 48% (a) and 54% (b) yields.

These easily worked-up displacement reactions effected by alcohols, thiols, and acetic acid on dehydrated alumina constitute a new, unusually mild, selective synthetic method.[7] This work is being extended to other doping agents,[8] other electrophiles, and other metal oxides.

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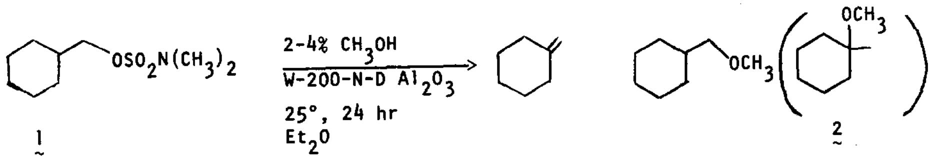
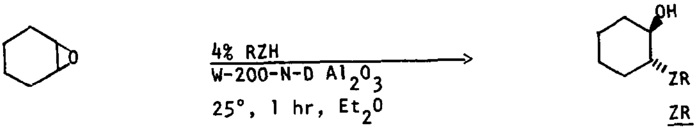
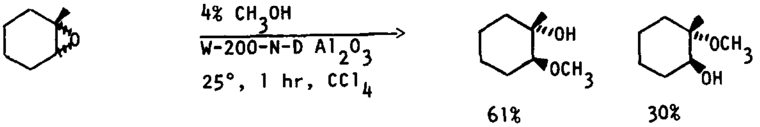


(1)

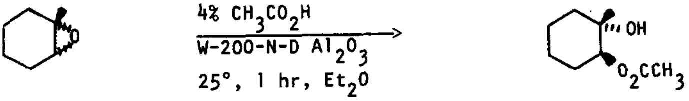


(2)

ZR	
OCH$_3$	66%
OCH$_2$C$_6$H$_5$	40%
SC$_2$H$_5$	78%
SC$_6$H$_5$	78%
O$_2$CCH$_3$	74%

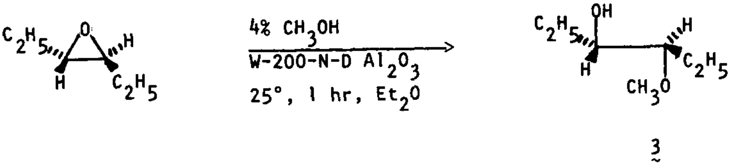


(3)



52%

(4)



74%

(5)

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