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ALUMINA CATALYZED TRANSFORMATIONS OF O-(3-OXOBUTYL) URETHANES

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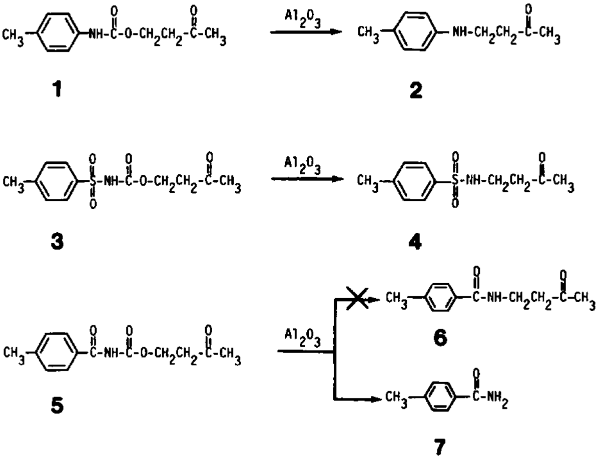
Abstract. The alumina-catalyzed transformations of a urethane to a secondary amine and a sulfonyl urethane to a sulfonamide are described Alumina is also shown to catalyze the conjugate addition of p-toluenesulfonamide to methyl vinyl ketone.

The use of alumina in organic synthesis as a catalyst for a variety of reactions has increased in recent years[1,2] Alumina promotes the elimination of certain groups (e.g ROH, RCO_2H) if an α,β-unsaturated carbonyl compound will result[1] It has also been found to catalyze the intramolecular 1,4-addition of alcohols to α,β-unsaturated carbonyls to form cyclic ethers, and the Michael addition of secondary amines to exocyclic α,β-unsaturated ketones.[2] In the course of our studies we prepared the keto-urethane **1** which was synthesized from p-tolyl isocyanate and 4-hydroxy-2-butanone. Upon silica gel chromatography of **1** in $CHCl_3$ we observed the formation of the secondary amine **2** We have since found that alumina (neutral, activity I) is most active in catalyzing the transformation Compound **1** can be purified without rearrangement by recrystallization from EtOAc/hexanes.[3] Pure **1** is converted to **2** in 73% yield by heating a 1 1 w/w mixture of **1** and alumina in a minimum volume of $CHCl_3$ or CH_3CN at 35°C for 24 hours followed by vacuum distillation.

The sulfonyl urethane **3**, prepared from tosyl isocyanate and 4-hydroxy-2-butanone, is converted to sulfonamide **4** in 58% yield by refluxing a 1.1 mixture of **3** and alumina in a minimum volume of $CHCl_3$ for 18 hrs followed by preparative TLC We found that the acyl urethane, **5**, prepared from p-toloyl isocyanate[4] and 4-hydroxy-2-butanone, does not form **6** with alumina but cleaves to p-toluamide **7**

The transformation of **1** to **2** most probably occurs via the alumina-assisted cleavage of **1** to p-toluidine, carbon dioxide, and methyl vinyl ketone p-Toluidine then adds to methyl vinyl ketone by a well-established, conjugate addition reaction to yield the secondary amine **2** (the



presence of alumina is not required). This speculation is supported by the observation that p-toluidine is present in the reaction mixture (as established by TLC) and is a side-product upon termination of the reaction. Without alumina 1 is stable in refluxing $CHCl_3$ for at least 2 days

The conversion of sulfonyl urethane 3 to sulfonamide 4 may proceed similarly through an alumina-assisted cleavage of the urethane to give p-toluenesulfonamide, which could then add to methyl vinyl ketone yielding 4. We have found that p-toluenesulfonamide will add to methyl vinyl ketone under mild conditions in the presence of alumina (1.1 w/w p-toluenesulfonamide/Al_2O_3, 1.2 eq. methyl vinyl ketone, min vol $CHCl_3$, 45°C, 2-3 days, 60-75% yield). In the absence of alumina, p-toluenesulfonamide does not add to methyl vinyl ketone under the same conditions

On the other hand, p-toluamide does not add to methyl vinyl ketone in the presence of alumina which explains the inability of 5 to be converted to 6 under the same conditions as the transformation of 3 to 4 The difference in reactivity towards methyl vinyl ketone of the sulfonamide and the carboxamide probably results from the greater acidity of the sulfonamide protons. We are currently expanding our investigations into the scope and limitations of these interesting reactions

Acknowledgment

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Reference and Notes

1. G Posner, Angew Chem Int Ed Engl , 17, 487 (1978), and references therein.
2. S.W Pelletier, A Venkov, J. Finer-Moore and N. Mody, Tet. Lett , 1980, 809
3. Compounds 1 to 5 were characterized by IR, ^1H NMR (360 MHz), and elemental analysis (C, H, N ± 0.2% and S ± 0 2% 3 and 4). Melting points 1, 109-110.5°C, 2, 38-40°, 3, 103-105°, 4, 69-71°, 5, 80-83°
4. p-Toloyl isocyanate was prepared from p-toluamide by the procedure of A. Speziale and L Smith, J Org Chem., 27, 3742 (1962)

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