

Microwave Assisted Selective Cleavage of Sulfonates and Sulfonamides in Dry Media

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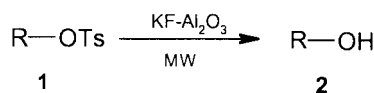
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Abstract: A simple and efficient method for the cleavage of Sulfonates and Sulfonamides has been achieved for the first time under microwave irradiation conditions using $\text{KF}\cdot\text{Al}_2\text{O}_3$.

Key words: sulfonates, sulfonamides, $\text{KF}\cdot\text{Al}_2\text{O}_3$, microwave irradiation

Microwave promoted reactions are advantageous in many ways over conventional approaches because of short reaction time, cleaner reactions with easier work up and solvent free conditions¹. Recently, use of inorganic solid supports as catalysts has been developed for dry media reactions² resulting in higher selectivity, milder conditions and ease of handling. Toluenesulfonyl groups are widely used as protecting agents for hydroxyl group³ and amines⁴. These groups are highly stable and require drastic deprotection conditions. In the literature a limited number of methods is available for the cleavage of sulfonates and sulfonamides, for example reduction with sodium in liquid ammonia⁵, sodium naphthylidene⁶, $\text{Mg}\cdot\text{MeOH}$ ⁷ and hydrogenolysis with Nickel⁸. Furthermore aryl toluenesulfonates are more stable than alkyl toluenesulfonate and refluxing with aqueous alcoholic KOH is required to deprotect them, giving moderate yields.

We now wish to report a simple and efficient cleavage method for sulfonates and sulfonamides using $\text{KF}\cdot\text{Al}_2\text{O}_3$ ⁹ in dry media under microwave irradiation conditions. This method is general and applicable for the cleavage of alkyl as well as aryl toluenesulfonates and sulfonamides. Sulfonates were selectively cleaved in presence of benzyl, N-Boc and allyl groups indicating the tolerance of other functionalities in the substrate. Reductive cleavage of sulfonamides with Pd/C, SmI_2 , Mg/MeOH , Na in liquid NH_3 and sodium naphthylidene results in the reduction of other functional groups such as halides, nitro, azide, carbonyl, and α,β -unsaturated system. HBr/AcOH system is highly acidic and it does not tolerate acid sensitive functionalities like Boc, Cbz and various ethers. Na in liquid NH_3 affords low yields associated with cumbersome experimental and tedious isolation procedures. Present reaction conditions are compatible with above functional groups and tolerate aliphatic acetates, acetals and sulfides whereas epoxides are not stable. Although, the benzoic halide exchange by dried KF under PTC conditions was reported, we have not observed such type of halogen exchange using commercial grade KF under our reaction conditions. It has been observed that sulfonates are cleaved faster than sulfonamides. The cleavage of sulfonates and sulfona-



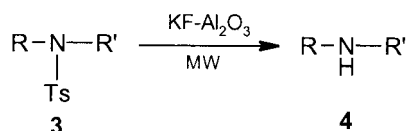
Scheme 1

Table 1 Cleavage of Sulfonates to alcohols using $\text{KF}\cdot\text{Al}_2\text{O}_3$

entry	Substrate	Alcohol	microwave irradiation time(min) ^a	Yield(%) ^b
a)			3	88
b)			4	85
c)			3	90
d)			6	86
e)			5	84
f)			4	85
g)			4	83
h)			3	87
i)			3	85
j)			2	87
k)			3	83
l)			3	85
m)			4	88
n)			3	86

^a) Pulsed irradiation with an output of 600 watts

^b) Isolated yields after column chromatography



Scheme 2

Table 2 Cleavage of Sulfonamides to amines using KF-Al₂O₃

entry	Substrate	amine	microwave irradiation time(min) ^a	yield(%) ^b
a)			5	80
b)			6	76
c)			6	78
d)			5	77
e)			4	84
f)			4	82
g)			6	85
h)			5	83
i)			6	80
j)			5	78
k)			5	76

a) Pulsed irradiation with an output of 600 watts.

b) Isolated yields after column chromatography.

midates was not successful either with non supported KF or basic Al₂O₃ alone. A strong microwave effect on the rate of the reaction was observed as the yield fell to 40-50% under conventional conditions instead of 80-90% under microwave irradiations.

In conclusion the present procedure is a better alternative to the existing ones for the cleavage of sulfonates and sulfonamides due to its simplicity, comparable yields, shorter times and solvent free conditions.

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- a) Typical procedure for the cleavage of sulfonates: Piperonyl-toluenesulfonate (**1a**, 2.92g, 10mmol) and 37% KF on Al₂O₃¹⁰ (3 weight equivalents of sulfonate) were admixed in a pyrex test tube and subjected to microwave irradiation for 3min. After cooling down to room temperature, the solid mass was extracted with ethyl acetate and concentrated *in vacuo*. The crude product was subsequently purified by column chromatography on silica gel (100-200 mesh, ethyl acetate-hexane 2:8) to afford sesmol (**2a**, 1.22g, 88% yield) as white solid.
b) Typical procedure for the cleavage of sulfonamides: Indole sulfonamide (**3a**, 2.71g, 10mmol) and 37% KF on Al₂O₃ (3 weight equivalents of sulfonate) were admixed in a pyrex test tube and subjected to microwave irradiation for 5min. The solid mass was allowed to cool to room temperature, and was extracted with ethyl acetate (2 x 15ml). The organic layer was concentrated *in vacuo* and was purified by column chromatography on silica gel (100-200 mesh, ethyl acetate-hexane 2:8) to afford indole (**4a**, 1.03g, 88% yield) as a white solid.
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