A Convenient Method for Sulphonamide Cleavage

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Summary It has been found that 40% (by volume) sulphuric acid in acetic acid is a mild and selective (time and temperature dependent) reagent for the cleavage of aryl sulphonamides.

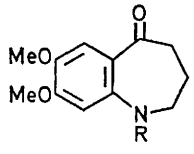
A MIXTURE of 40% (by volume) concentrated sulphuric acid in glacial acetic acid has been found to be a very clean and effective general reagent for the cleavage of sulphonamides. Even though sulphuric acid in various forms has been extensively used to cleave sulphonamides,[1] to our knowledge no detailed experimental procedures have appeared describing it being used in acetic acid.

The reagent is of general applicability to aryl sulphonamides, cyclic or acyclic and unsubstituted or substituted in the benzene ring, although it was not applicable to the two alkyl amine sulphonamides we used.

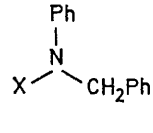
N-Tosylmethyl anthranilate (2 g) was stirred (50°, 7 h) in 40% sulphuric acid in acetic acid (25 ml). The mixture was diluted to 150 ml with water, adjusted to pH 8 with solid sodium hydroxide, and extracted with chloroform to give pure methyl anthranilate (84%). No other products were detected in the chloroform extract. The reaction is both time and temperature dependent.

Attempts to remove the tosyl group from (I; R = tosyl)‡ using hydrobromic acid in acetic acid[2] or sodium in liquid ammonia,[3] caused numerous complications. However, heating (I; R = tosyl) (50° for 4 h) with 40% sulphuric acetic acid gave pure (I; R = H) (90%); heating for a further 4 h at 100° caused a demethylation of the methoxy group *para* to the nitrogen and sustained heating at 100° produced the corresponding catechol. If the previous reaction is carried out at 100° concurrent hydrolysis of the ester group occurs.

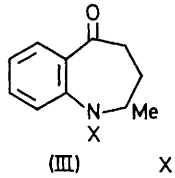
Compound (II) can be detosylated with the reagent with no benzyl cleavage products being detected. It has been reported that concentrated sulphuric acid causes cleavage of the benzyl but not the tosyl group in compounds related to (II).[4]



(I)

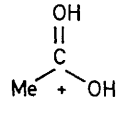


(II)



(III)

X = tosyl



(IV)

Compound (III) has also been detosylated whereas other procedures[2,3] only resulted in the recovery of starting material.[5]

It is felt that the reactive component of the medium is (IV), the protonated form of acetic acid, which is $>10^3$ times stronger than H_3O^+, the acidic species of aqueous sulphuric acid.[6] This pronounced increase in acid strength could facilitate the attack on the tosylated nitrogen under milder conditions than with aqueous acids of the same

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‡ All new compounds gave correct elemental analyses and spectral data.

concentration. These milder conditions as well as the lower concentration of sulphuric acid thus needed could also account for the absence of complications encountered using other sulphuric acids.[1]

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[4] A. F. Pozharskii, E. A. Zvezlina, V. M. Maryanovskii, A. M. Sumonov, and S. F. Popova, *Zhur. org. Khim.*, 1969, **5**, 106.
[5] Unpublished results from this laboratory.
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