MIGRATION OF THE TOSYL GROUP IN 7-O-TOSYLESCULETINS

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Khimiya Geterotsiklicheskikh Soedinenii, Vol. 6, No. 3, pp. 309–310, 1970

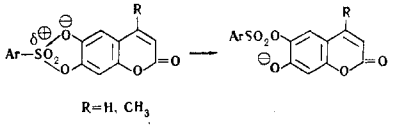
UDC 547.812.5'814.1

The action of sodium hydride in dimethyl sulfoxide on 7-O-tosylesculetin and 4-methyl-7-O-tosylesculetin leads to the migration of the tosyl group into position 6, with the formation of 6-O-tosylesculetin and 4-methyl-6-O-tosylesculetin, respectively.

While intramolecular migrations of acyl residues (O → N, N → O, O → O, etc) have been widely studied (see, for example, a review on this question [1]), the similar migrations of arenesulfonyl groups have been inadequately examined. O-Arenesulfonyl and O-alkanesulfonyl protection is used very frequently in the performance of very diverse syntheses [2,3]. The idea has been maintained that the sulfonyl group is stable to the action of numerous reagents and does not migrate to neighboring hydroxyl groups (see, for example, [2]).

In one of our papers [4], we have mentioned the possibility of the rearrangement of 7-O-tosylesculetin (I) into 6-O-tosylesculetin (II) under the action of sodium hydride in the dimethylformamide (DMF) or of potassium carbonate in boiling acetone. Since in these experiments the formation of the product of tosyl group migration was established only by chromatography in a thin layer of Al_2O_3, in the present paper we describe the rearrangement of both 7-O-tosylesculetin and 4-methyl-7-O-tosylesculetin (III) in dimethyl sulfoxide (DMSO) with isolation and characterization of the reaction products, II and 4-methyl-6-O-tosylesculetin (IV). The rearrangements of I and III into II and IV were carried out in anhydrous DMSO in the presence of sodium hydride with yields of rearrangement products of 86 and 95%, respectively. The structures of compounds I–IV have already been shown conclusively [4].

It is usual to consider [1] that the migration of O-acyl groups to neighboring hydroxyl groups takes place by the same mechanism as the hydrolysis of esters, i.e., through intermediate products of hydroxyl addition at the position of the double bond of carbonyl. Because such a mechanism is less probable for sulfonates, the migration of the tosyl groups in O-tosylesculetins possibly takes place by an S_N1 or S_N2 mechanism. Since phenol sulfonates are fairly stable to alkaline intermolecular hydrolysis and the 7-O-tosylesculetins rearrange into the 6-O-tosyl derivatives in an alkaline medium very readily, it must be assumed that the second mechanism is the more likely.



R=H, CH_3

There is no doubt that polar aprotic solvents of the DMF and DMSO type greatly accelerate the rearrangement since they weakly solvate the anion. It has been mentioned previously [4] that in aqueous alkali the 7-O-tosylate undergoes no change during a day.

The relative ease of O → O migration of a tosyl group in the esculetin system, which, from the mutual position of the OH groups, may be regarded as a dihydrophenol like catechol, requires the protection of hydroxyl groups in the form of sulfonates to be used with some caution, especially when neighboring nucleophilic groups are present.

EXPERIMENTAL

The initial 7-O-tosylates were obtained as described previously [4]. The substances were chromatographed in a thin layer of Al_2O_3 of activity grade IV in anhydrous ethyl acetate.

Rearrangement of 7-O-tosylesculetin (I). A solution of 0.42 g (0.00125 mole) of I (mp 207.5–208.5° C) in 2.5 ml of anhydrous DMSO was treated with 0.06 g of powdered sodium hydride containing 76% active hydrogen (a slight rise in temperature was observed), and the mixture was stirred for 3 hr and left to stand for 16 hr. Then it was poured into 35 ml of 2 N HCl, and the precipitate that deposited was filtered off, washed with water, and dried in vacuo over P_2O_5

at 90° C for 2 hr, giving 0.36 g (86%) of II with mp 219–220.5° C. After crystallization from ethanol, 0.25 g of pure substance with mp 223.5–224.5° C was obtained. Compound II was identical with respect to melting point (mixture) and R_f with an authentic sample and showed a clear depression of the melting point in admixture with I.

Rearrangement of 4-methyl-7-O-tosylesculetin (III). A solution of 0.43 g (0.00125 mole) of III (mp 226–227° C; according to chromatography in Al_2O_3, the substance contained not more than 4% of the possible impurity IV) in 2.5 ml of anhydrous DMSO was treated with 0.03 g of 76% NaH (no appreciable rise in temperature took place), and the mixture was stirred for 6 hr and left to stand for 16 hr. Then it was treated as described above, giving 0.41 g (95%) of IV, mp 216–218° C. Recrystallization from ethanol yielded 0.25 g of pure IV with mp 221.5–222.5° C. The substance was identical with respect to melting point (mixture) and R_f value with a sample of known structure and showed a clear depression of the melting point in admixture with III.

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5 September 1968

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