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THE REARRANGEMENT MECHANISMS OF N-TOSYLOXYISOCARBOSTYRIL AND N-TOSYLOXYCARBOSTYRIL (1)

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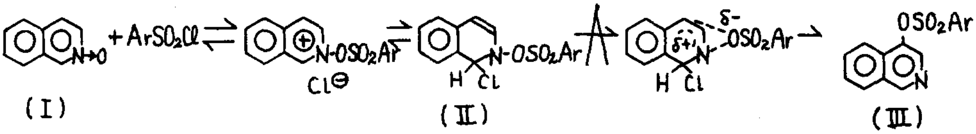
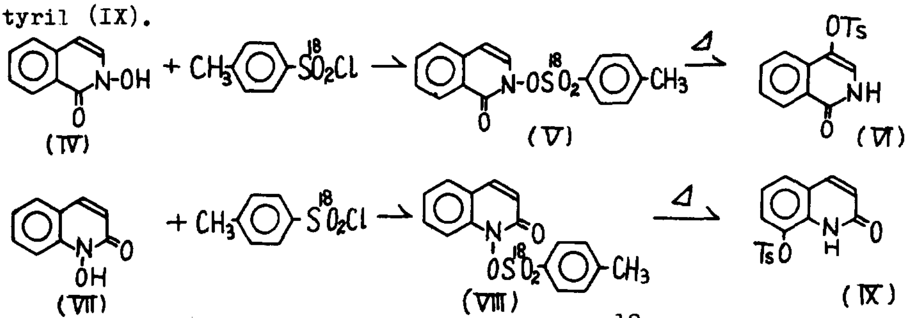
The reaction (2) between isoquinoline N-oxide and arenesulfonyl chloride to afford 4-arenesulfonyloxyisoquinoline has been suggested to proceed via the oxygen-bridged ion pair pathway that involves rate-determining N-O bond cleavage on the basis of ^{18}O tracer and kinetic experiments. However, N-arenesulfonyloxy derivatives (II), anhydrobases,



have never been isolated nor detected during the rearrangement, and hence the nature of α,γ-migrations cannot be studied independently. Meanwhile, N-tosyloxyisocarbostyril (V) (3) and N-tosyloxycarbostyril (VIII) (4) are known to be quite stable and can be isolated, and hence can serve as a model for either II or "anhydro bases", i.e., neutral species generally accepted as the key intermediates of the reaction (5) of 2-or 4-alkylpyridine N-oxides and many acylating agents, for studying the nature of the α,γ-migration of tosyloxy group. Therefore, the rearrangement reactions of these compounds (V) and (VII), have been studied through our usual ^{18}O-tracer experiments.

Upon treatments of N-hydroxyisocarbostyril (IV) and N-hydroxycarbostyril (VII) with uniformly ^{18}O-labeled tosyl chloride under usual Schotten-Baumann conditions, the respective N-tosyloxy derivatives (V) and (VIII) were obtained in fairly good yields. These N-tosyloxy compounds were then heated in nitromethane or acetonitrile to give the rearranged products, 4-tosyloxyisocarbostyril (VI) and 8-tosyloxycarbostyril (IX).



In order to improve the accuracy of the ^{18}O-tracer experiments the carbonyl group in the products was converted to chloro group. 1-Chloro-4-tosyloxyisoquinoline and 2-chloro-8-tosyloxyquinoline thus obtained were hydrolyzed in ethanol-potassium hydroxide, and 1-chloro-4-hydroxyisoquinoline and 2-chloro-8-hydroxyquinoline formed were subjected together with the tosylates to the routine ^{18}O-analysis to determine the ^{18}O content in the respective etheral oxygen. The ^{18}O analytical results of the starting material, the tosylates and hydrolyzed products are shown in Table 1 and 2.

TABLE 1.

^{18}O analytical results of the reaction of N-tosyloxyisocarbostyril

solvent, temp. Compound	CH_3NO_2, 80-90°C		CH_3CN, reflux Excess atom % ^{18}O (calc.)	
N-Tosyloxyisocarbostyril (V)	0.70	(0.72)	0.65	(0.67)
4-Tosyloxyisocarbostyril (VI)	0.73	(0.72)	0.64	(0.67)
1-Chloro-4-tosyloxyisoquinoline	*0.80	(0.95)	0.85	(0.89)
1-Chloro-4-hydroxyisoquinoline	0.74		0.66	
p-Tosyl chloride	1.43		1.33	

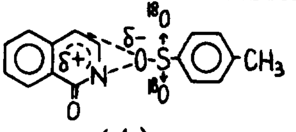
*Contaminated with a small amount of the original carbonyl compound.

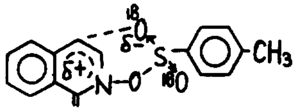
There are following four conceivable mechanisms for the rearrangement, (A) oxygen-bridged ion pair process, (B) six-membered ring transition complex, (C) solvent separated ion pair path and (D) nucleophilic

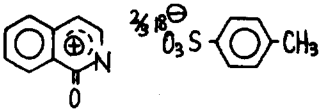
TABLE 2.

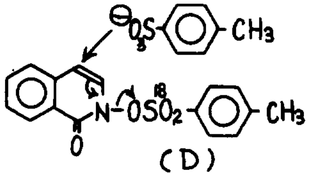
^{18}O analytical results of the reaction of N-tosyloxycarbostyril

Compound	solvent, temp. CH_3NO_2, 80-90°C Excess atom % ^{18}O (calc.)	
N-Tosyloxycarbostyril (VIII)	0.71	(0.72)
8-Tosyloxycarbostyril (IX)	0.69	(0.72)
2-Chloro-8-tosyloxyquinoline	0.90	(0.95)
2-Chloro-8-hydroxyquinoline	0.73	
p-Tosyl chloride	1.43	


(A)


(B)


(C)


(D)

attack of outer tosylate anion to the N-tosyloxy derivatives. Inspection of these ^{18}O analytical results seems to suggest that the main route of the migration of the tosyloxy group is via the solvent separated ion pair path (C) in both cases of V and VIII. In every case a small deviation of ^{18}O analytical value in the etheral oxygen of the product from the calculated value for the path (C) was observed. The deviation may be ascribed to the minor contribution of the process (A) in the reaction. While the mechanism (B) can be excluded, the contribution of the mechanism (D) cannot be ruled out, since the mechanism (D) would require the same ^{18}O destribution in the product with that expected by the process (C). In order to clarify this question the following experiment has been carried out. When the ^{18}O-labeled N-tosyloxyisocarbostyril (mean value 0.65 % of excess atom %^{18}O) was treated as usual in the presence of on equimolar amount of non-labeled tetra-n-butyl ammonium tosylate (0.00), the rearrangement product obtained was found to contain 0.52 % of excess ^{18}O. According to the mechanism (D), the excess atom % ^{18}O

of 4-tosyloxyisocarbostyril should be the mean avarage of the whole ^{18}O content of the tosylate group in the reaction system (ca. 0.3). Therefore the mechanism involving the path (D) can be ruled out. Based on these observations, the rearrangement is considered to proceed mainly via (C) with a minor portion passing the route via (A). This makes a clear contrast to that of the reaction of isoquinoline N-oxide with tosyl chloride. The contribution of the mechanism via (A) relative to that via (C) is considered to depend on the strength of solvation at the trasition states of these compounds, and probably also on the stability of the cationic partner of the rearranging intermediate. This α,γ-tosyloxy migration looks very much similar to the wellknown allylic rearrangement, and like in the allylic rearrangement the tosyloxy migrations may be so rapid after the N-O bond cleavage that one natural oxygen of N-O group and two sulfonyl oxygens could not be scrambled thoroughly before recombining and hence could result in a slightly less ^{18}O incorporation in the ethereal oxygen of the final product.

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