MECHANISM OF PHOTODETOSYLATION OF N-TOSYL-1,2,3,4-TETRAHYDROISOQUINOLINES INVOLVING ELECTRON TRANSFER IN THE EXCITED STATE

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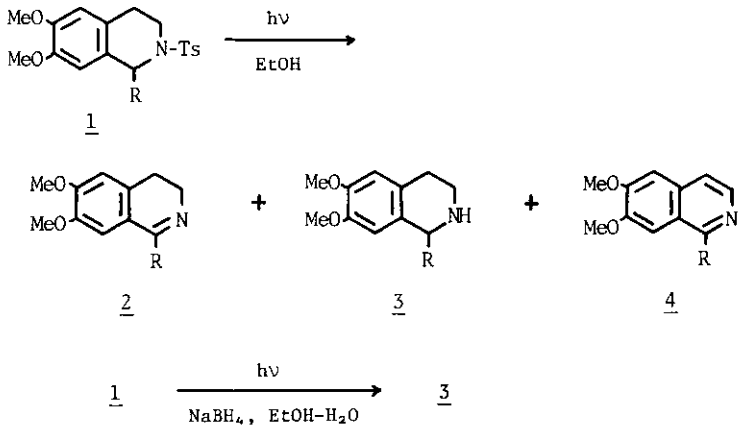
Abstract —— Umezawa and Hoshino reported that on irradiation N-tosyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolines (1) gave the detosylated, 3,4-dihydroisoquinolines (2) accompanied by the corresponding 1,2,3,4-tetrahydroisoquinolines (3) and aromatized isoquinolines (4), while in the presence of $NaBH_4$ only 3 was isolated in high yield. The mechanism of this photodetosylation has now been elucidated. Thus, the reaction was initiated by the formation of exciplex or the electron transfer between the excited dimethoxybenzene group and the tosyl group followed by the formation of a biradical (7) and an N-radical (9), which readily changed to 2. Oxidation-reduction of 7 and 9 probably gave 3 and 4. In the presence of $NaBH_4$, both 7 and 9 were reduced to 3. Experiments using deuterated compounds revealed that the routes via 7 and 9 acted almost equally in the photodetosylation.

In recent years there have been many reports describing the photoreaction of excited electron donor-acceptor pairs, exciplexes, which are formed by electron transfer from the donor to the acceptor in the excited state of either compound.[1] The photocyclization of N-chloroacetylphenethylamines is one of the most typical photoreactions involving intramolecular exciplex of electron transfer[2] and has been extended to the intermolecular photoreaction between electron-rich aromatics (donor; phenols, methoxybenzenes, anilines, indoles) and electron-deficient acceptors (chloroacetamide, chloroacetic esters, chloroform, carbon tetrachloride).[3]

In 1969, the photochemical detosylation of N-tosyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolines (1) was reported by Umezawa and Hoshino,[4] though its mechanism has remained equivocal. On irradiation with a medium pressure mercury lamp in EtOH, 1 gave three detosylated products, 2 (main product). 3, and 4, while in the presence of $NaBH_4$ only 3 was isolated in a high yield. Since 1 has both the electron-donative dimethoxybenzene group and the electron-attracting sulfonamide



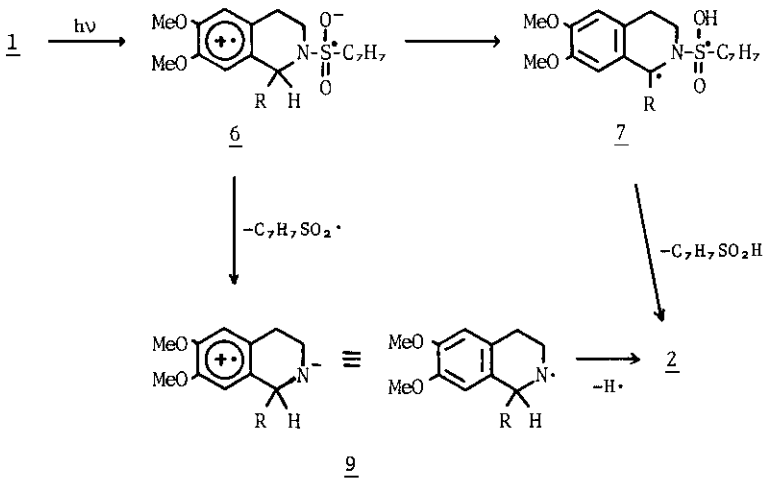
group, the intramolecular electron transfer must have occurred in the initial step of the photodetosylation. We have now reexamined this photodetosylation in detail to establish its mechanism.

Results and Discussion

The N-acetyl derivative (5), which is stable under the above photochemical conditions, has a strong fluorescence (E_{max} 312 nm, excitation at 283 nm in EtOH) identical to that of 1,2-dimethoxybenzene, but in the corresponding N-tosyl derivative (1a) the fluorescence completely disappears.[5]

This quenching can be explained in terms of the exciplex formation or the electron transfer between the dimethoxybenzene and the tosyl group to give 6.[6] Since benzylic protons of aromatic radical cations such as 6 are quite acidic, an intramolecular proton transfer in 6 then probably occur to give a biradical (7),[7] which readily lose toluenesulfinic acid to yield 2, the main product of this photodetosylation in the absence of $NaBH_4$. As another possible intermediate to 2, we can presume 9 from the mechanism of the anion radical cleavage of sulfonamides.[8] The N-radical (9) lose hydrogen also to yield 2.

In order to account for the formation of 3 and 4 the time-course of this photodetosylation was next examined (Figure 1). Both compounds were apparently formed in the same rate from the beginning of this photoreaction[9] and not the secondary products via 2, because no photodisproportionation of 2 was observed when isolated 2 was reirradiated under the same conditions. Compound 8 is also not present as an intermediate, because the deuterium of the 3-dideutero derivative (1b)



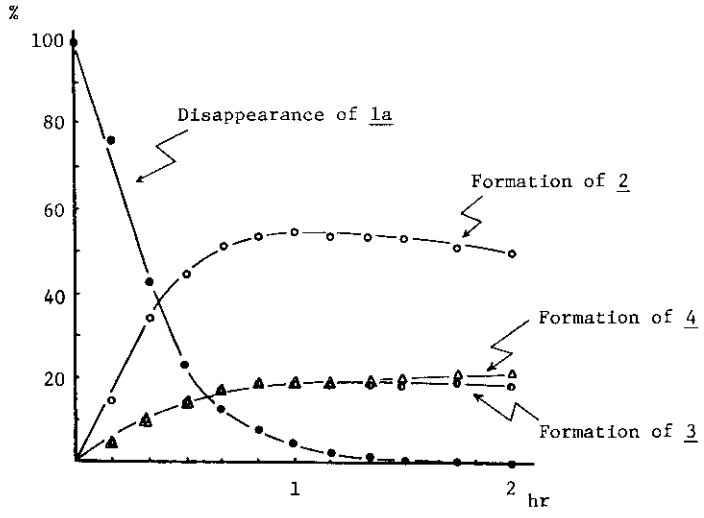
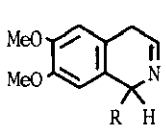


Figure 1. Time-course of the photolysis of 1a in EtOH with a 100W medium pressure mercury lamp (immersion well).



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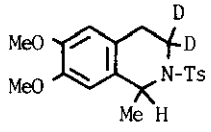


1b

were remained unchanged in the photoproducts (2, 3) after irradiation in the absence and presence of $NaBH_4$, and no 3-deutero product was observed when 1a was irradiated in the presence of $NaBD_4$. Therefore, oxidation-reduction of 7 and 9 is probably the main route for the formation of 3 and 4. If this is the case, the product formation may be depressed with decreasing the concentration of 7 and 9, which is proportional to light intensity as well as concentration of the starting material. The results in Table I show clearly these light intensity and concentration dependence. The relatively high yield of 3 and 4 was obtained under irradiation of a concentrated solution with intense light, but the yield dercresed with decreasing light intensity and concentration, and finally 2 became almost the sole product.

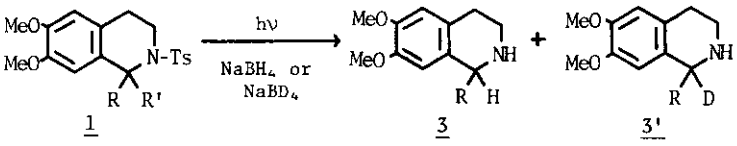
$$7 \quad + \quad 9 \longrightarrow 3 \quad + \quad 4$$

Table I. Photolysis of 1a under various light intensities and concentrations.

Lamp[1]	Mode of irradiation	Concentration (mM)	Yield (%)[2] 2	3	4	3+4/2
500 W	Internal (immersion well)	3.8	33.3	9.3	21.8	0.93
100 W	Internal (immersion well)	6.3	39.5	9.9	14.7	0.62
		6.3	(54.0)	(18.5)	(18.2)	0.68
		0.6	(58.8)	(11.6)	(14.1)	0.44
100 W	External (merry-go-round)	6.3	53.7	7.6	5.4	0.24
		0.6	(65.0)	trace	(0.8)	0.013

[1] Medium pressure mercury lamp. [2] Isolation yield (Yields in parentheses are determined by GC analysis).

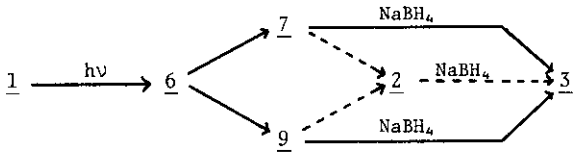
Table II. Photolysis of 1 in the presence of $NaBH_4$ or $NaBD_4$.



1 3 3'

	R	R'		Yield (%) 3(1-H)	3'(1-D)	Ratio 3/3'
1a	Me	H	$NaBD_4$	45.4	41.0	1.1
1c	C_6H_5	H	$NaBD_4$	43.0	44.0	0.97
1d	C_6H_5	D	$NaBH_4$	33.0	67.0	0.49

On irradiation in the presence of $NaBH_4$, 1 gave 3 as the sole product in a high yield probably via both 7 and 9.[10] These two routes can be differentiated as follows (Table II). When irradiated in the presence of $NaBD_4$, 1a gave almost 1 : 1 mixture of 3a (1-H) and 3a' (1-D) indicating that the both routes proceeded almost equally. Compound 1c also gave a similar result, while retardation of the route via 7 was observed probably owing to the deuterium isotope effect when the 1-deuterated analog (1d) was irradiated in the presence of $NaBH_4$. These results support the proposed mechanism of this photodetosylation.



Extension of this type of intramolecular photoreactions to intermolecular reactions, which may provide a potentially useful method for detosylation of usual sulfonamides including lysine peptides protected by N-tosylation, is now in progress.

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5. The N-mesyl derivative has again the strong fluorescence and no detosylation occurs on irradiation.
6. Cf. M. T. McCall, G. S. Hammond, O. Yonemitsu, and B. Witkop, J. Am. Chem. Soc., 1970, 92, 6991.

7. Cf. S. G. Cohen, A. Parola, and G. H. Parsons, Jr., Chem. Rev., 1973, 73, 147.

8. W. D. Closson, S. Ji, and S. Schulenberg, J. Am. Chem. Soc., 1970, 92, 650.

9. Decomposition of a small amount of 2 and additional formation of 4 in the last stage of this photoreaction is due to the photodehydrogenation of 2.

10. For an example of the $NaBH_4$ reduction of radicals, see L. A. Barltrop and D. Bradbury, J. Am. Chem. Soc., 1973, 95, 5085.

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