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Organic Photochemistry. III.[1] Photo-reductive Cleavage of *p*-Toluenesulfonamides[2]

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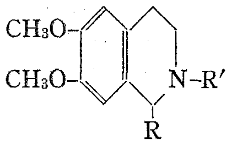
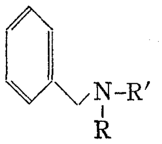
Photolysis of an aqueous ethanolic solution of *p*-toluenesulfonamide (IId—f, IIIe—h, IVc—d and Vd—f) and Na_2CO_3 in the presence of $NaBH_4$ was found to give the corresponding free amine (IIa—c, IIIa—d, IVa—b and Va—c) in moderate yield. The mechanistic pathway of this reaction was deduced.

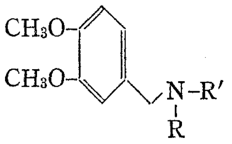
In a previous paper,[1] photolysis of N-tosyl-1-substituted-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolines (Ie-h) in the presence of $NaBH_4$ (basic medium) has shown to give smoothly the corresponding amines (Ia-d) in excellent yields and this observation appeared to imply ready elimination[4] of the tosyl group in usual *p*-toluenesulfonamides. Thereupon, in order to explore the scope of this reaction, ultraviolet irradiation on 12 kinds of *p*-toluenesulfonamides IId-f, IIIe-h, IVc-d and Vd-f) was attempted under the same condition as previously reported,[1] and the following results were obtained.



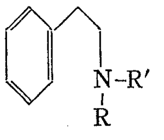
Ia : $R=R'=H$
Ib : $R=CH_3$, $R'=H$
Ic : $R=Ph$, $R'=H$
Id : $R=CH_2Ph$, $R'=H$
Ie : $R=H$, $R'=Ts$
If : $R=CH_3$, $R'=Ts$
Ig : $R=Ph$, $R'=Ts$
Ih : $R=CH_2Ph$, $R'=Ts$



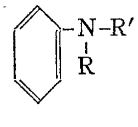
IIa : $R=R'=H$
IIb : $R=CH_3$, $R'=H$
IIc : $R=C_2H_5$, $R'=H$
IId : $R=H$, $R'=Ts$
IIe : $R=CH_3$, $R'=Ts$
IIf : $R=C_2H_5$, $R'=Ts$



IIIa : $R=R'=H$
IIIb : $R=CH_3$, $R'=H$
IIIc : $R=C_2H_5$, $R'=H$
IIId : $R=CH_2CH_2OH$, $R'=H$
IIIe : $R=H$, $R'=Ts$
IIIf : $R=CH_3$, $R'=Ts$
IIIg : $R=C_2H_5$, $R'=Ts$
IIIh : $R=CH_2CH_2OH$, $R'=Ts$



IVa : $R=R'=H$
IVb : $R=CH_3$, $R'=H$
IVc : $R=H$, $R'=Ts$
IVd : $R=CH_3$, $R'=Ts$



Va : $R=R'=H$
Vb : $R=CH_3$, $R'=H$
Vc : $R=C_2H_5$, $R'=H$
Vd : $R=H$, $R'=Ts$
Ve : $R=CH_3$, $R'=Ts$
Vf : $R=C_2H_5$, $R'=Ts$

Chart 1

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[1] Part II: B. Umezawa, O. Hoshino and S. Sawaki, *Chem. Pharm. Bull.* (Tokyo), **17**, 1120 (1969).

[2] A part of this work was presented at the 89th Annual Meeting of the Pharmaceutical Society of Japan, Nagoya, April 1969. To avoid unnecessary confusion, the name of N-tosylate in Part I and II or this series should be altered to that of *p*-toluenesulfonamide.

[3] Location: *12, Ichigayafunagawara-machi, Shinjuku-ku, Tokyo.*

[4] *cf.* S. Searles and S. Nukina, *Chem. Revs.*, **59**, 1077 (1959).

The starting materials (IId-f, IIIe-h, IVc-d and Vd-f), *p*-toluenesulfonamides of benzylamine (IIa), N-benzylmethylamine (IIb), N-benzylethylamine (IIc), veratrylamine (IIIa), N-veratrylmethylamine (IIIb), N-veratrylethylamine (IIIc), N-veratrylethanolamine (IIId), pheenethylamine (IVa), N-phenethylmethylamine (IVb), aniline (Va), N-methylaniline (Vb), and N-ethylaniline (Vc), were prepared from the corresponding amines and *p*-tosyl chloride by Schotten-Baumann method. Melting points and analyses of each compound were summarized in Table I.

Table I

Compound	mp (°C)	Formula	Analysis (%) Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
IId	112—114°[a]							
IIe	94—95°	$C_{15}H_{17}O_2NS$	65.42	6.22	5.09	65.59	6.26	5.01
IIf	48—49°	$C_{16}H_{19}O_2NS$	66.37	6.27	4.84	66.35	6.64	4.79
IIIe	123—125°[b]							
IIIf	104—105°	$C_{17}H_{21}O_4NS$	60.88	6.31	4.18	60.77	6.28	4.18
IIIg	75—76°	$C_{18}H_{23}O_4NS$	61.88	6.64	4.01	61.68	6.69	4.24
IIIh	122—123°[c]							
IVc	62—64°[d]							
IVd	55.5—56°	$C_{16}H_{19}O_2NS$	66.37	6.27	4.84	66.60	6.71	4.89
Vd	98—101°[e]							
Ve	90—93°[f]							
Vf	66—68°[g]							

a) mp 116° [F.D. Chattaway, *J. Chem. Soc.*, **87**, 159 (1905)]
b) mp 122° (G.R. Proctor and R.H. Thomson, *J. Chem. Soc.*,**1957**, 2308)
c) B. Umezawa, O. Hoshino, H. Hara and J. Sakakibara, *Chem. Pharm. Bull.* (Tokyo), **18**, 177 (1968)
d) mp 66° (G.R. Proctor and R.H. Thomson, *J. Chem. Soc.*, **1957**, 2311)
e) mp 103° [I. Remsen and A.G. Palmer, *Am. Chem. J.*, **8**, 242 (1886)]
f) mp 94—95° [R. Otto, *J. Pr. Chem.*, **47**, 371 (1893)]
g) mp 87—88° [R. Otto, *J. Pr. Chem.*, **47**, 373 (1893)]

Irradiation of an aqueous ethanolic solution of each *p*-toluenesulfonamide (IId-f) or (IIIe-h) in the presence of $NaBH_4$ and Na_2CO_3 with 200 W mercury lamp under nitrogen stream was run and completion of the reaction was checked by thin-layer chromatography (TLC). The reaction mixtures from IId-f were treated with 10% HCl or 20% H_2SO_4 and the solvent was removed under reduced pressure, while those from IIIe-h were subjected to direct removal of the solvent without acid treatment. Then usual work-up of each reaction mixture gave basic and neutral fractions. Each of the former was converted into its picrate or oxalate and expectedly characterized as follows: benzylamine (IIa) [picrate, mp 196—199° (lit,[5] mp 195—199°)]; N-benzylmethylamine (IIb) (oxalate, mp 192—194°); N-benzylethylamine (IIc) (oxalate, mp 215—216°); veratrylamine (IIIa) (oxalate, mp 189—191°); N-veratrylmethylamine (IIIb) (oxalate, mp 189—190.5°); N-veratrylethylamine (IIIc) (oxalate, mp 211—212.5°); N-veratrylethanolamine (IIId) [picrate, mp 145—148° (lit.[6] mp 155—156°)]. The latter, upon chromatographic purification, was found to be the same compound irrespective of the starting materials [comparison was made on infrared (IR) spectrum ($CHCl_3$) and TLC]. However, its structure was still uncertain and in each case the starting material was not obtained. Results were given in Table II.

From the above observation, it was found that elimination of *p*-tosyl group took place readily regardless of the presence or the length of N-alkyl group or of the presence or absence

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[5] G. Jerusalem, *J. Chem. Soc.*, **95**, 1283 (1909).
[6] R. Baltzly and O. Kauder, *J. Org. Chem.*, **16**, 176 (1951).

Table II

Compound (mg)		Condition					Product	
		NaBH$_4$ (mg)	Na$_2$CO$_3$ (mg)	H$_2$O (ml)	C$_2$H$_5$OH (ml)	Reaction Time (hr)	Picrate or Oxalate of Base	mg (%)
IId	261	190	159	24	120	3	IIa	72.6 (21.6)[a)]
IIe	275	190	159	24	120	3	IIb	62.5 (29.6)[b)]
IIf	289	190	159	24	120	3	IIc	125.4 (55.8)[b)]
IIIe	321	190	159	24	120	3	IIIa	67.1 (26.1)[b)]
IIIf	335	190	159	24	120	3	IIIb	161.8 (59.7)[b)]
IIIg	349	190	159	24	120	3	IIIc	183.7 (64.5)[b)]
IIIh	365	190	159	24	120	3	IIId	183.1 (41.6)[a)]

a) picrate b)oxalate

of *p*-methoxyl group. Considering that all the starting materials (IIe-f or IIIe-h) had a reactive benzylic site, however, the finding noted above might be specific, that is, the presence of activated hydrogen on carbon attached to N-tosyl group seemed to be necessary requirement.

Therefore, in order to settle the aforementioned problem, photolysis of N-tosyl-phenethylamines or -anilines (IVc-d or Vd-f) was performed under the same condition as described above.

Irradiation of the former and usual treatment of the reaction mixtures afforded phenethylamine (IVa) [picrate, mp 168—170° (lit.[7] mp 170°)] and N-phenethylmethylamine (IVb) [picrate, mp 149—151° (lit.[8] mp 140—141°)], respectively. Furthermore, in the case of the latter, aniline (Va) [picrate, mp 185—188° (lit.[9] mp 181°)], N-methylaniline (Vb) [picrate, mp 117—119° (lit.[10] mp 134°)], and N-ethylaniline (Vc) [picrate, mp 133—134.5° (lit.[11] mp 137.5—138°)] were obtained, though in lower yield. The similar reaction[12] of Vd in the absence of NaBH$_4$, however, was unsuccessful. In each case, the neutral product which was identical with the unknown compound as noted above was also formed and the starting material was not isolated. Results were given in Table III.

Table III

Compound (mg)		Condition					Product picrate of base mg (%)	
		NaBH$_4$ (mg)	Na$_2$CO$_3$ (mg)	H$_2$O (ml)	C$_2$H$_5$OH (ml)	Reaction time (hr)		
IVc	275	190	159	24	120	3	IVa	127.7 (36.5)
IVd	289	190	159	24	120	3	IVb	141.9 (38.7)
Vd	247	190	159	24	120	3	Va	38.1 (11.9)
Ve	261	190	159	24	120	3	Vb	57.9 (17.2)
Vf	275	190	159	24	120	3	Vc	120.6 (34.4)

In conclusion, the reaction could be recommended in some cases as a useful cleavage method of *p*-toluenesulfonamides because of mild condition and simple procedure. In view of the fact that Va from Vd was produced under the condition, the presence of a reactive hydrogen on carbon alpha to N-tosyl group was proved not always to be essential. Therefore, this detosylation took place probably by way of direct photo-reductive cleavage of *p*-toluenesulfon-

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[7] H. Decker and W. Kropp, *Ber.*, **42**, 2078 (1909).

[8] R. Wegler and G. Pieper, *Chem. Ber.*, **83**, 1 (1950).

[9] O. Silberrad and G. Rotter, *J. Chem. Soc.*, **89**, 169 (1906).

[10] L. Vignon and E. Evieux, *Bull. Soc. Chim. France*, **3**, 1024 (1908).

[11] J. Meisenheimer, L. Angermann, O. Finn and E. Vieweg, *Ber.*, **57**, 1750 (1924).

[12] As an analogous example, Nozaki and his co-workers have already shown that photolysis of Vd in neutral or acidic medium affords aniline (16% or 68%) besides 4-amino-4′-methyldiphenylsulfone (25% or 25%) (recovery of Vd; 81% or 72%) [H. Nozaki, T. Okada and M. Kawanishi, *Tetrahedron*, **22**, 2177 1966)].

amide with $NaBH_4$ rather than $NaBH_4$ reduction of the corresponding Schiff base as an intermediate.

Experimental[13]

Preparation of N-Benzyl-methylamine (IIb) and -ethylamine (IIc)——i) N-Benzylmethylamine (IIb) was prepared by $NaBH_4$ reduction of the corresponding Schiff base (1.6 g) in CH_3OH which was formed by refluxing a mixture of benzaldehyde (2 g), $CH_3NH_2 \cdot HCl$ (2.1 g) and K_2CO_3 (4 g) in abs. benzene (14 ml) under stirring for 11 hr. IIb obtained above was directly transformed into its oxalate, mp 192—194° (CH_3OH), colorless plate. *Anal.* Calcd. for $C_8H_{11}N \cdot C_2H_2O_4$: C, 56.86; H, 6.20; N, 6.63. Found: C, 56.59; H, 6.22; N, 6.60.

ii) N-benzylethylamine (IIc) was obtained by the same method as described above except using $C_2H_5NH_2 \cdot HCl$ instead of $CH_3NH_2 \cdot HCl$. Oxalate, mp 215—216° (CH_3OH), colorless prisms. *Anal.* Calcd. for $C_9H_{13}N \cdot C_2H_2O_4$: C, 58.65; H, 6.71; N, 6.22. Found: C, 58.48; H, 6.70; N, 6.07.

Preparation of Veratrylamine (IIIa), and N-Veratrylmethylamine (IIIb) and -ethylamine (IIIc)——i) Veratrylamine (IIIa) was obtained by the method of Kametani and Nomura.[14] Oxalate, mp 203—205° (CH_3OH), colorless prisms. *Anal.* Calcd. for $C_9H_{13}O_2N\frac{1}{2}C_2H_2O_4\frac{1}{4}H_2O$: C, 55.42; H, 6.74; N, 6.46. Found: C, 56.05, 55.60; H, 6.76, 6.70; N, 6.60, 6.33.

ii) N-Veratrylmethylamine (IIIb) was prepared from veratraldehyde and $CH_3NH_2 \cdot HCl$ by the similar method as described in preparation of IIa. Oxalate, mp 189—190.5° (CH_3OH), colorless prisms. *Anal.* Calcd. for $C_{10}H_{15}O_2N \cdot C_2H_2O_4$: C, 53.13; H, 6.32; N, 5.16. Found: C, 53.40; H, 6.36; N, 5.25.

iii) N-Veratrylethylamine (IIIc) was obtained by the same method as noted above. Oxalate, mp 212—213° (CH_3OH), colorless needles. *Anal.* Calcd. for $C_{11}H_{17}O_2N \cdot C_2H_2O_4$: C, 54.73; H, 6.71; N, 4.91. Found: C, 54.40; H, 6.70; N, 4.94.

Preparation of N-Phenethylmethylamine (IVb)——N-Phenethylmethylamine (IVb) was obtained by $LiAlH_4$ reduction of N-formylphenethylamine (5 g) which was formed by heating phenethylamine·HCOOH (5.9 g) at 150—160° for 3 hr. Picrate, mp 149—151° (CH_3OH), yellow prisms, (lit.[8] mp 140—141°).

Preparation of *p*-Toluenesulfonamides (IId—f, IIIe—h, IVc—d and Vd—f)——Reaction of amines and *p*-tosyl chloride was carried out by Schotten–Baumann method to give the corresponding *p*-toluenesulfonamides in yield of 60—80%.

General Procedure of Photolysis——i) To a solution of *p*-toluenesulfonamide (IId—f, IVc—d and Vd—f) (1 mmole) in ethanol[15] (60 ml), Na_2CO_3 (1.5 mmole) in water (24 ml) and $NaBH_4$ (6 mmole) were added and the whole was diluted with ethanol (60 ml). After irradiation of the ethanolic solution, the reaction mixture was treated with 10% HCl (in the case of IIe—f and IVc—d) or 20% H_2SO_4 (in the case of IId and Vd—f) and the solvent was removed under reduced pressure. To the resultant residue, water was added and the solution was extracted with ether. The acidic solution was basified with Na_2CO_3 (powder) and the product was taken up in ether. The former ether extract, upon evaporation of the solvent, gave neutral substance which was not identical with the starting material by comparison of each IR spectrum ($CHCl_3$) and TLC. Its chromatographic purification on silicic acid (Mallinckrodt) gave an oil which was not examined further. Usual work-up of the latter ether extract gave the corresponding free amine which was converted into its picrate or oxalate. Its characterization was carried out by comparison of each IR spectrum (KBr) and by mixed fusion. Results were shown in Table II and III.

ii) On irradiation of the ethanolic solution of *p*-toluenesulfonamide (IIIe—h) prepared as noted above, the solvent was removed under reduced pressure. To the resultant residue, water was added and the reaction mixture was treated with 10% HCl. After the acidic solution was extracted with ether and basified with Na_2CO_3 (powder), the product was taken up in ether. The similar treatment of each ether extract as described above gave results shown in Table II.

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13) All melting points were uncorrected and measured on a Yanagimoto micro melting point measuring apparatus. Identification of products was performed by thin-layer chromatography (TLC) run on silica gel G (Merck) with $CHCl_3$–CH_3OH (4:1) (as developing solvent) and infrared (IR) spectroscopy ($CHCl_3$ or KBr) using a Hitachi Model EPI-S_2. Irradiation was carried out at 10—15° with high pressure mercury lamp (Osawa UV-HT, 200 W) under nitrogen which was purified through sodium β-anthraquinonesulfonate solution and concd. H_2SO_4.

14) T. Kametani and Y. Nomura, *Yakugaku Zasshi,* 74, 413 (1954).

15) Absolute ethanol (commercial grade).