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Organic Photochemistry. II.[1,2] Tetrahydroisoquinolines from Their N-Tosylates

Bunsuke Umezawa, Osamu Hoshino, and Shohei Sawaki

Faculty of Pharmaceutical Sciences, Science University of Tokyo[3]

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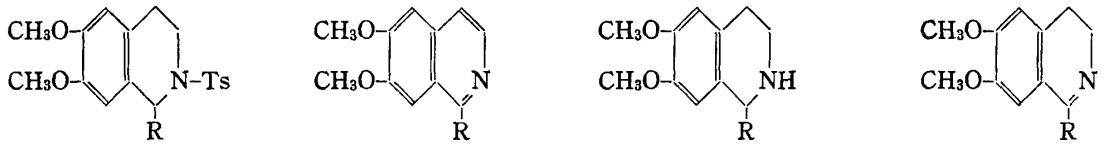
Photolysis (high pressure mercury lamps, 100W and 400W) of 1-substituted-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline N-tosylates (Ia—d) in a basic medium [80% (v/v)EtOH–Na_2CO_3] in the presence of $NaBH_4$ was carried out to give the corresponding amines (IIIa—d) in good yields.

In a preceding paper,[1] photolysis of 1-substituted 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline N-tosylates (Ia—d) was shown to give 3,4-dihydroisoquinolines (IVa—c) together with isoquinolines (IIa—d) and/or tetrahydroisoquinolines (IIIc—d).

At this stage, if suitable conditions were chosen, it seemed possible to expect that amines were smoothly formed photochemically from the corresponding N-tosylates, hydrolysis of which generally met some difficulties.

Expectedly amines (IIIa—d) were produced from the above N-tosylates (Ia—d) in high yields under ultraviolet irradiation (100 W or 400 W) in the presence of $NaBH_4$ (basic medium).



Ia : R=H
Ib : R=CH_3
Ic : R=Ph
Id : R=CH_2Ph

IIa—d

IIIa—d

IVa—d

Chart 1

Irradiation (high pressure mercury lamp, 100 W) of Ia—d with $NaBH_4$ and Na_2CO_3 in 80% (v/v) EtOH solution was continued (bath temperature 15—20°, under N_2), until spots due to the starting materials disappeared on thin-layer chromatography (TLC).

Usual treatment of the reaction mixture followed by silicic acid chromatography, if necessary, gave the corresponding amines as major products: IIIa[4] (82.8%, picrate, mp 201—205°) from Ia, IIIb[5] (76.6%, picrate, mp 200—203°) from Ib, IIIc[6] (70.5%, mp 109—110°) from Ic, and IIId[7] [98.6%, oxalate, mp 228—231° (decomp.)] from Id, respectively. And in every cases isoquinolines (IIa—d) were not isolated.

On the other hand, employment of 400 W lamp gave better results (reaction times were shortened appreciably and amines formed in excellent yields (over 80%)) as shown in Table I.

1) Part I: B. Umezawa, O. Hoshino, and S. Sawaki, *Chem. Pharm. Bull.* (Tokyo), **17**, 1115 (1969).
2) A part of this work was presented at the 88th Annual Meeting of the Pharmaceutical Society of Japan, Tokyo, April 6, 1968.
3) Location: *12, Ichigayafunagawara-machi, Shinjuku-ku, Tokyo.*
4) R. Forsth, C.I. Kelly, and F.L. Pyman, *J. Chem. Soc.*, **127**, 1666 (1925).
5) E. Späth and F. Dengel, *Ber.*, **71**, 113 (1938).
6) M. Levy, *Farmatsiya* (Sofia), **1961**, No.4, 25 [*C.A.*, **56**, 11569*c* (1962)].
7) J. Niimi, *Yakugaku Zasshi*, **80**, 1005 (1960).

Table I

Compound (mg)		Condition	Reaction time (hr)	Yield of III mg (%)
Ia	200.0	A	10.0	92.0 (82.8)
	347.0	B	2.5	166.8 (86.4)
Ib	200.0	A	9.0	87.5 (76.6)
	500.0	B	3.0	237.1 (82.8)
Ic	200.0	A	7.0	89.4 (70.5)
	362.5	B	4.5	125.3 (85.7)
Id	100.0	A	6.5	63.8 (98.6)
	433.8	B	2.0	227.3 (80.9)

A) irradiation by 100 W mercury lamp B) irradiation by 400 W mercury lamp

Thus, the present method for hydrolysis of sulfonamides was proved to be recommendable in the following two points, namely conditions used were rather mild and yields high enough.

The fact that no isoquinolines were obtained might be ascribable to the inhibitory effect of $NaBH_4$ for photo-oxidation.

As to the reaction mechanisms, the following two pathways seemed probable: 1) $NaBH_4$ reduction of 3,4-dihydro compounds (IVa—d) as intermediates and 2) direct photo-reductive cleavage of N-tosyl group.

On this point, reasonable assumption could not yet be made and further investigations should be performed.

Experimental[8]

Irradiation of N-Tosyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (Ia)[1]——a) A solution of Ia (200 mg), Na_2CO_3 (86.2 mg), and $NaBH_4$ (182 mg) in 80% (v/v)EtOH (140 ml) was irradiated for 10 hr. After removal of the solvent and addition of brine to the residue, the product was taken up in $CHCl_3$. The $CHCl_3$ layer was extracted with 10% HCl and the acidic solution was basified with K_2CO_3 (powder). After extraction of the alkaline solution with $CHCl_3$, the $CHCl_3$ layer was rinsed with brine and dried (K_2CO_3). Removal of the solvent gave a crystalline mass [92 mg (82.8%), single spot on TLC; picrate (135.7 mg), mp 198—200.5° (MeOH)], which was identified with 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (IIIa) (lit.[4] picrate, mp 202—203°) by comparison of their infrared (IR) spectra and by mixed fusion of each picrate. A minor neutral oil obtained was not examined further.

b) A solution of Ia (347 mg), Na_2CO_3 (106 mg), and $NaBH_4$ (152 mg) in 80% (v/v)EtOH (280 ml) was irradiated for 2.5 hr. The same treatment of the reaction mixture as described above gave IIIa [166.8 mg (86.4%)].

Irradiation of N-Tosyl-1-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (Ib)[1]——a) A solution of Ib (200 mg), Na_2CO_3 (92 mg), and $NaBH_4$ (164 mg) in 80% (v/v)EtOH (140 ml) was irradiated for 9 hr. The similar work-up of the reaction mixture as shown above gave a basic oil [87.5 mg (76.6%), single spot on TLC; picrate, mp 200—202° (MeOH)], which was identical with 1-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (IIIb) (lit.[5] picrate, mp 201—201.5°) by comparison of their IR spectra and by melting point determination of each picrate and a neutral oil (52.4 mg; not identical with Ib).

b) Irradiation of a solution of Ib (500 mg), Na_2CO_3 (147 mg), and $NaBH_4$ (210 mg) in 80% (v/v)EtOH (280 ml) was carried out for 3 hr to give IIIb [237.1 mg (82.8%)].

Irradiation of N-Tosyl-1-phenyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (Ic)[1]——a) A solution of Ic (200 mg), Na_2CO_3 (50 mg), and $NaBH_4$ (104 mg) in 80% (v/v)EtOH (140 ml) was irradiated for 7 hr. A usual work-up gave an oil (130 mg), which was chromatographed on silicic acid (Mallinckrodt) (6.5 g) to furnish crystals[89.4 mg (70.5%), single spot on TLC, mp 109—110° (pet. benzine)], from eluate with $CHCl_3$

8) All melting points were uncorrected and measured on a Yanagimoto micro melting point measuring apparatus. Characterization of products was performed by thin-layer chromatography (TLC) run on silicagel G (Merck) with benzene–MeOH (3:1) as developping solvent and IR spectroscopy ($CHCl_3$ as solvent) using a Hitachi Model EPI-S_2. Irradiation was carried out at 15—20° with the following two high pressure mercury lamps (Ôsawa UV-HT) under N_2 which was purified through sodium β-anthraquinone sulfonate solution and conc. H_2SO_4; a) 100W and b) 400W.

and $CHCl_3$–MeOH (100:4), which were identified with 1-phenyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (IIIc) (lit.[6] mp 124—125°) by comparison of their IR spectra and by mixed fusion.

b) A solution of Ic (362.5 mg), Na_2CO_3 (91 mg), and $NaBH_4$ (130 mg) in 80% (v/v)EtOH (240 ml) was irradiated for 4.5 hr. The same treatment as described above gave an oil (230.7 mg) which was purified by silicic acid chromatography to afford IIIc [125.3 mg (85.7%)] from eluate with $CHCl_3$ and $CHCl_3$–MeOH (100:2).

Irradiation of N-Tosyl-1-benzyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (Id)[1]——a) Photolysis of a solution of Id (100 mg), Na_2CO_3 (25 mg), and $NaBH_4$ (54 mg) in 80% (v/v)EtOH (70 ml) for 6.5 hr and usual treatment gave an oil [63.8 mg (98.6%), single spot on TLC; oxalate, mp 228—231° (decomp.) (MeOH)], which was identified with 1-benzyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline (IIId) (lit.[7] oxalate, mp 231—232°) by their IR spectral comparison and by mixed fusion of each oxalate.

b) Photolysis of a solution of Id (433.8 mg), Na_2CO_3 (110 mg), and $NaBH_4$ (236 mg) in 80% (v/v)EtOH (260 ml) was carried out for 2 hr to afford on oil (269.6 mg), which was chromatographed on silicic acid (14.0 g) to furnish IIId [227.3 mg (80.9%)] from eluate with $CHCl_3$–MeOH (100:2).

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