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Reductive Acylamination of Pyridine *N*-Oxide with Ethylenediamine and Phenylenediamines

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Abstract—Reactions of pyridine *N*-oxide with ethylenediamine and *o*- and *p*-phenylenediamines in the presence of *p*-toluenesulfonyl chloride in alkaline medium lead to the formation of the corresponding *N*,*N*′-bis(*p*-tolylsulfonyl)-*N*,*N*′-bis(pyridin-2-yl)diamines as a result of reductive acylamination.

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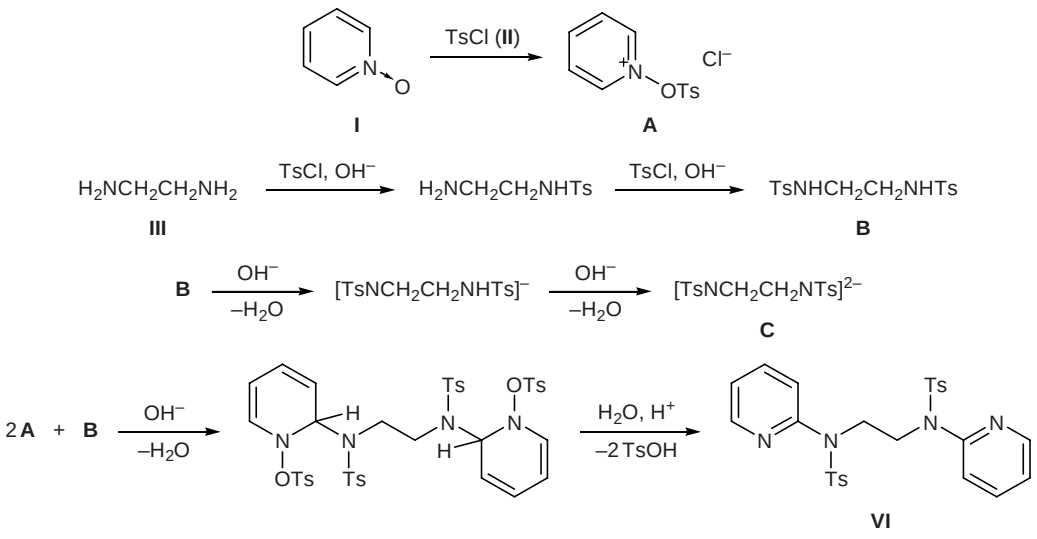
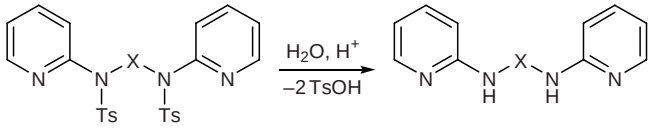
We previously reported on the reductive acylamination of pyridine *N*-oxide (**I**) with aromatic and heteroaromatic monoamines and their *N*-(*p*-tolylsulfonyl) derivatives [1, 2] in the presence of *p*-toluenesulfonyl chloride (**II**) as acylating agent. In continuation of these studies we examined reactions of pyridine *N*-oxide (**I**) with diamines, ethylenediamine (**III**) and *o*- and *p*-phenylenediamines **IV** and **V**, under analogous conditions. The reactions were carried out at room temperature in a two-phase system (chloroform–water) in the presence of *p*-toluenesulfonyl chloride (**II**) and various bases (potassium and sodium hydroxides and carbonates). The reaction of pyridine *N*-oxide (**I**) with diamine **III** gave *N*,*N*′-bis(*p*-tolylsulfonyl)-*N*,*N*′-bis(pyridin-2-yl)ethylenediamine (**VI**) in high yield (88%). The fact that we failed to detect the corresponding monosubstituted derivative suggests intermediacy of *N*,*N*′-bis(*p*-tolylsulfonyl)ethylenediamine dianion **C** in the process (Scheme 1). Thus the observed reaction may be regarded as a rare case of direct formation of disubstituted product without isolation of intermediate monosubstituted derivative.

Likewise, the reactions of pyridine *N*-oxide (**I**) with aromatic diamines **IV** and **V** produced *N*,*N*′-bis(*p*-tolylsulfonyl)-*N*,*N*′-bis(pyridin-2-yl)benzene-1,2- and -1,4-diamines **VII** and **VIII** in 65 and 66% yield, respectively (Scheme 2). The lower yields of compounds **VII** and **VIII** as compared to **VI** are likely to result from reduced nucleophilicity of the corresponding *N*-acyl anions, while similar reactivities of *o*- and *p*-phenylenediamines may be rationalized in terms of high reaction rate (reaction time 2 h). The structure of **VI**–**VIII** was proved by their acid hydrolysis to the corresponding *N*,*N*′-bis(pyridin-2-yl)diamines **IX**–**XI**.

Scheme 1.



Scheme 2.



VI, **IX**, X = $(CH_2)_2$; **VII**, **X**, X = *o*-C_6H_4; **VIII**, **XI**, X = *p*-C_6H_4.

The described reactions attract interest from the viewpoint of synthesis of substituted heteroaromatic diamines. Compound **IX** was shown to exhibit trypanocidal activity [3], while derivatives of **XI** possess bactericidal properties [4].

EXPERIMENTAL

The progress of reactions and the purity of products were monitored by paper chromatography (fast no. 2) using butan-1-ol–hydrochloric acid–water (50:7:14 by volume) as eluent; spots were detected by spraying with the Dragendorff reagent.

***N*,*N*′-Ethane-1,2-diylbis[*N*-(pyridin-2-yl)-4-toluenesulfonamide] (VI).** A solution of 0.95 g (10 mmol) of pyridine *N*-oxide (**I**), 0.25 g (5 mmol) of ethylenediamine (**III**), and 0.7 g (3.7 mmol) of *p*-toluenesulfonyl chloride in 25 ml of chloroform was mixed with 30 ml of 10% aqueous sodium hydroxide, and the mixture was stirred for 8 h at 20°C. Every 2 h, a sample was withdrawn from the mixture and analyzed by paper chromatography as indicated above. The mixture contained initial pyridine *N*-oxide **I** and final product **VI**. The aqueous phase was separated and repeatedly extracted with chloroform, the extracts were combined with the organic phase and dried over anhydrous sodium sulfate, the solvent was distilled off, and the residue was washed with hexane. Yield 2.1 g (88%), mp 175–177°C (from ethanol). Found, %: N 10.6. $C_{26}H_{26}N_4O_4S_2$. Calculated, %: N 10.7.

***N*,*N*′-Benzene-1,2-diylbis[*N*-(pyridin-2-yl)-4-toluenesulfonamide] (VII).** A solution of 0.95 g (10 mmol) of oxide **I**, 0.54 g (5 mmol) of diamine **IV**, and 3.8 g (20 mmol) of *p*-toluenesulfonyl chloride in 30 ml of chloroform was mixed with 30 ml of 10% aqueous sodium hydroxide, and the mixture was stirred for 2 h at 20°C. The mixture was treated as described above to isolate 1.8 g (66%) of compound **VII**, mp 171–172°C (from acetonitrile). Found, %: N 9.6. $C_{30}H_{26}N_4O_4S_2$. Calculated, %: N 9.82.

***N*,*N*′-Benzene-1,4-diylbis[*N*-(pyridin-2-yl)-4-toluenesulfonamide] (VIII).** A solution of 0.95 g (10 mmol) of oxide **I**, 0.54 g (5 mmol) of diamine **V**, and 5.7 g (30 mmol) of *p*-toluenesulfonyl chloride in 30 ml of chloroform was mixed with 30 ml of 10% aqueous sodium hydroxide, and the mixture was stirred for 2 h at 20°C. The mixture was treated as described above to isolate 2.1 g (65%) of compound **VIII**, mp 170°C (from ethanol). Found, %: N 9.7. $C_{30}H_{28}N_4S_2O_4$. Calculated, %: N 9.82.

Hydrolysis of amides VI–VIII. A solution of 1.7 mmol of compound **VI**–**VIII** in 5 ml of concentrated hydrochloric acid was heated for 21 h at the boiling point. The mixture was evaporated to dryness, the residue was washed with diethyl ether, and the solvent was distilled off to isolate *p*-toluenesulfonic acid; yield 88, 80, and 73%, respectively (mp 90–92°C; published data [5]: mp 92°C). The material insoluble in diethyl ether was dissolved in a minimal amount of water, the solution was made alkaline by adding potassium carbonate and extracted with chloroform, the extract was dried over anhydrous sodium sulfate, the solvent was distilled off, and the residue was recrystallized from petroleum ether (bp 70–110°C).

***N*,*N*′-Bis(pyridin-2-yl)ethane-1,2-diamine (IX).** Yield 97%, mp 132–133°C; published data [3]: mp 134–135°C.

***N*,*N*′-Bis(pyridin-2-yl)benzene-1,2-diamine (X).** Yield 80%, mp 164–165°C; published data [6]: mp 167°C.

***N*,*N*′-Bis(pyridin-2-yl)benzene-1,4-diamine (XI).** Yield 70%, mp 199–200°C; published data [6]: mp 200–201°C.

REFERENCES

1. Kurbatov, Yu.V. and Solekhova, M.A., *Zh. Org. Khim*., 1983, vol. 19, p. 663.
2. Kurbatov, Yu.V. and Solekhova, M.A., *Khim. Geterotsikl. Soedin*., 1986, p. 936.
3. Sharp, T.M., *J. Chem. Soc*., 1938, p. 1191.
4. Thomas, K. and Jerchel, D., FRG Patent Appl. no. 2606592, 1974; *Chem. Abstr*., 1977, vol. 87, no. 167891z.
5. *Dictionary of Organic Compounds*, Heilbron, J. and Bunbury, H.M., Eds., London: Eyre and Spottswoode, 1953, vol. 1.
6. Fischer, O., *Ber*., 1902, vol. 35, p. 3674.