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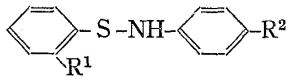
Anodic Oxidation of 2- and 4'-Substituted Benzenesulfenanilides. A New Method of Synthesis of 2,7-Disubstituted Phenazines

Anodic oxidations of benzenesulfenanilides (4'-OMe (I), 4'-Me (II), 4'-Cl (III), 4'-H (IV)) and 2-nitrobenzenesulfenanilides (4'-OMe (V), 4'-Me (VI), 4'-Cl (VII), 4'-H (VIII)) were carried out in acetonitrile containing 0.1 M $NaClO_4$. Electrolyses of I, II, V, VI, and VII gave the corresponding 2,7-disubstituted phenazines, whereas those of III, IV, and VIII did not. The R–$\dot{\underset{\cdot\cdot}{N}}$· intermediates are suggested for the formation of the phenazines.

Keywords——benzenesulfenanilides; anodic oxidation; oxidation of sulfenamides; anodic dimerization; synthesis of phenazines; nitrene; imido intermediate; 2,7-disubstituted phenazines

We wish to report the results on the controlled potential electrolyses of benzenesulfenanilides (4'–OMe (I), 4'–Me (II), 4'–Cl (III), 4'–H (IV)) and 2-nitrobenzenesulfenanilides (4'–OMe (V), 4'–Me (VI), 4'–Cl (VII), 4'–H (VIII)). The electrolyses were carried out in acetonitrile containing 0.1 M $NaClO_4$ at the peak potentials of their voltammetric first waves. The results are shown in Table I.

Table I. Results of Controlled Potential Electrolysis of 2- and 4'-Substituted Benzenesulfenanilides in acetonitrile containing 0.1M $NaClO_4$,



Compd. No.	R^1	R^2	Conc. mM (mg/ml)	Applied potential V *vs.* SCE.	*n*-Value	λ_{max}[a] nm	Products identified	Yield mg
I	H	OMe	10(231/100)	0.75	0.67	263, 343, 406, 424	2, 7-dimethoxyphenazine	47.2
							diphenyldisulfide	108.2
							p-anisidine	*ca.* 1
II	H	Me	10(215/100)	0.90	0.69	255, 362, 376,[b] 397[b]	2, 7-dimethylphenazine	43.7
							diphenyldisulfide	107.4
III	H	Cl	2 (19/ 40)	1.00	0.82	247	*c*)	
IV	H	H	2 (16/ 40)	0.97	0.63	240, 550	*c*)	
V	NO_2	OMe	30(332/ 40)	0.85	0.67	264, 350, 410,[b] 424	2, 7-dimethoxyphenazine	44.4
							2, 2'-dinitrodiphenyldisulfide	41.3
							p-anisidine	16.0
VI	NO_2	Me	30(312/ 40)	1.03	0.88	255, 365, 378,[b] 398[b]	2, 7-dimethylphenazine	37.1
							2, 2'-dinitrodiphenyldisulfide	23.4
VII	NO_2	Cl	30(337/ 40)	1.18	0.99	256, 362,[b] 380, 394	2, 7-dichlorophenazine	24.4
VIII	NO_2	H	30(296/ 40)	1.13	1.08	443	*c*)	

a) after addition of a small amount of solid Na_2CO_3 to the solution from electrolysis
b) shoulder
c) Products were not identified.

Electrolysis of I (10 mM) at the anode potential of 0.75 V gave a coulometric *n*-value (number of Faradays passed per mole of I) of 0.67. The voltammogram of the resulting deep purple solution showed a single anodic peak at 1.46 V *vs.* S.C.E., which is in good agreement with that of diphenyldisulfide under the same condition. The ultraviolet (UV) spectrum of the resulting solution had absorption maxima at 263, 384, 429, and 486 nm. On addition of solid sodium carbonate to the solution, the maxima shifted to 263, 343, 406, and 424 nm, which were very

close to those reported on 2,7-dimethoxyphenazine.[1] From the resulting solution 2,7-dimethoxyphenazine (XII), diphenyldisulfide, and *p*-anisidine were obtained. XII was identified from its UV and infrared (IR) spectra in comparison with those of authentic sample prepared by the method of Yoshioka.[2]

Although electrolysis of II similarly gave 2,7-dimethylphenazine and diphenyldisulfide, electrolyses of III and IV did not gave the corresponding phenazines. On the other hand, electrolyses of V, VI, and VII gave the corresponding phenazines, whereas electrolysis of VIII did not.

The following schemes are suggested for the anodic oxidation of I.

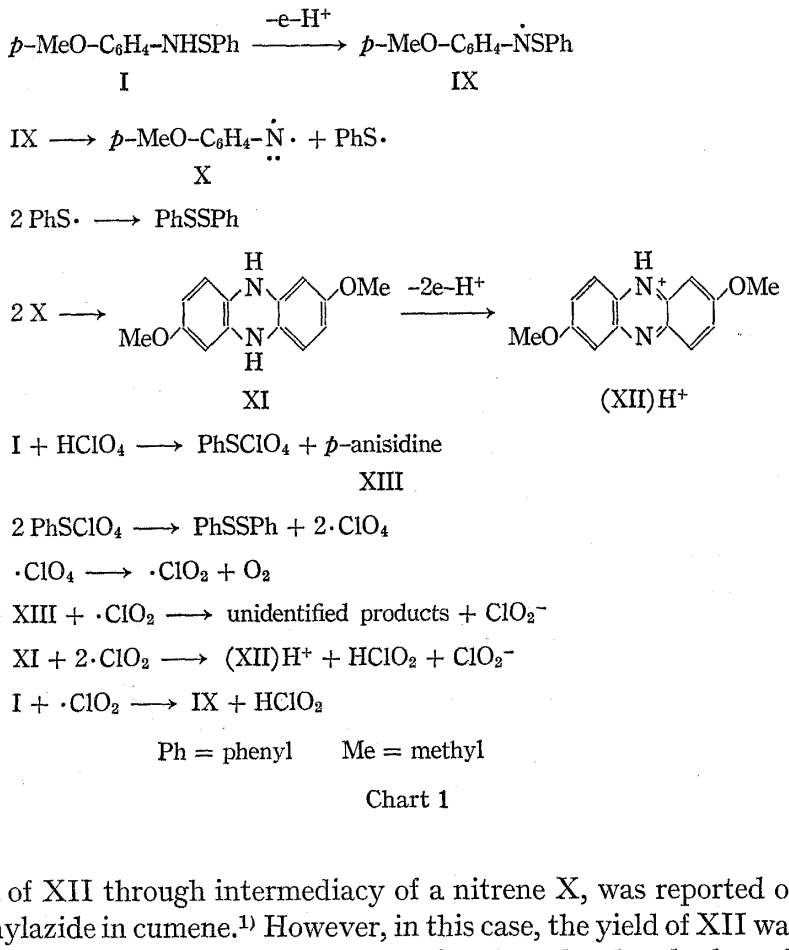


Chart 1

Formation of XII through intermediacy of a nitrene X, was reported on the pyrolysis of *p*-methoxyphenylazide in cumene.[1] However, in this case, the yield of XII was very low and the main product was 4,4′-dimethoxyazobenzene. On the other hand, electrolysis of I gave no indication of the formation of 4,4′-dimethoxyazobenzene, and the yield of XII was 39.4 mole %. Since I is very labile in acidic media[3] and the anolyte becomes acidic with a progress of electrolysis, about 60% of starting I was considered to decompose to diphenyldisulfide, *p*-anisidine, and perchlorate radical without being oxidized at the anode. Perchlorate radical is reported to decompose very rapidly to produce other chlorine-oxygen compounds, including chlorine dioxide, which are capable of serving as strong oxidizing agents.[4] These can react with I, XI, and *p*-anisidine to produce XII and unidentified resinous colored compounds. Thus overall stoichiometry is very complicated. However, the nitrene formed is assumed to

1) P. Walker and W.A. Waters, *J. Chem. Soc.*, **1962**, 1632.
2) I. Yoshioka, *Pharm. Bull.* (Japan), **1**, 66 (1953).
3) N. Kharasch, S.J. Potempa, and H.L. Wehrmeister, *Chem. Rev.*, **39**, 269 (1946).
4) C.K. Mann and K.K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, Inc., New York, 1970, p. 509.

be quantitatively converted into XII, contrary to the results of the pyrolysis of *p*-methoxyphenylazide. The reason why electrolyses of III, IV, and VIII do not give the corresponding phenazines is not clear at present. Detailed studies are now in progress.

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The Enzymatic Conversion of (−)-Lupinine to (−)-(*trans*-4′-Hydroxycinnamoyl) lupinine by Extracts of *Lupinus* Seedlings

(−)-(*trans*-4′-Hydroxycinnamoyl) lupinine (III) was found to be synthesized from (−)-lupinine (I) and *trans*-4-hydroxycinnamic acid (II) by enzymes in *Lupinus* seedlings in the presence of adenosine triphosphate and co-enzyme A as cofactors. The conversion of *trans*-cinnamic acid (IV) to (−)-(*trans*-cinnamoyl) lupinine (V) by the enzyme systems was negligible although the cinnamoyl-CoA ligase activity was clearly observed.

Keywords——enzymatic synthesis; *Lupinus luteus* seedlings; leguminosae; lupin alkaloid; lupinine; cinnamic acid derivatives; cinnamoyl lupinine derivatives; CoA; ATP

In the course of our investigations on the lupin alkaloids in the family leguminosae, we have established the presence of a new alkaloid, (−)-(*trans*-4′-hydroxycinnamoyl) lupinine (III), in the extracts of young seedlings of *Lupinus luteus*.[1] No detectable amount of III was found in the mature and immature seeds, and in the later stages of the plant growth.

However, its concentration increased rapidly during the first 4—8 days growth of *Lupinus* seedlings grown in both the dark and the daylight at 25—30°; during further growth of the plant the concentration of III fell gradually to a very low level.

Cinnamic acid and a variety of closely related hydroxycinnamic acids have been postulated for a long time to be involved in a great variety of important metabolic pathway in higher plants, including the formation of flavonoids, lignin, chlorogenic acid and many other plant products.

This communication reports new enzymatic systems in *Lupinus* seedlings capable of forming III from (−)-lupinine (I) and *trans*-4-hydroxycinnamic acid(II) in the presence of ATP and CoA as cofactors, as shown in Fig. 1.

Enzyme preparations were obtained from the hypocotyls of seedlings of *Lupinus luteus* grown in the dark for 5—6 days at 30° essentially as described in previous papers[2—4]: the hypocotyls were homogenized in a mortar with Si sand and 0.1 M K-phosphate buffer, pH 7.5,

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2) I. Murakoshi, H. Kuramoto, J. Haginiwa, and L. Fowden, *Phytochemistry*, **11**, 177 (1972).
3) I. Murakoshi, F. Kato, and J. Haginiwa, *Chem. Pharm. Bull.* (Tokyo), **22**, 473 (1974); *ibid.*, **22**, 480 (1974); *ibid.*, **21**, 918 (1973).
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