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Cyclodextrin-Promoted Radical Cyclization of o-(2-Propenyloxy)- and o-(2-Propynyloxy)benzenediazonium Ions

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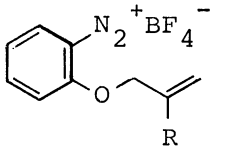
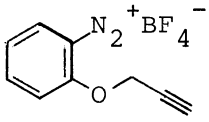
Radical dediazoniation of o-(2-propenyloxy)- and o-(2-propynyloxy)benzenediazonium ions in the presence of β-cyclodextrin gives selectively dihydrobenzofurans under N_2, while hydroxymethylated dihydrobenzofurans and 3-hydroxymethyl-benzofuran under air, respectively.

In the early papers,1) we reported the effective generation of aryl radicals from aromatic diazonium ions in the aqueous solution by binding with cyclodextrins (CDs) and their specific hydrodediazoniation. Beckwith et al. have described that aromatic diazonium ions with ortho substituents containing double or triple bond in the 5,6 positions to the diazonio group undergo regioselective intramolecular cyclization via aryl radicals.2) These radical cyclizations have been limited in the polar aprotic solvents such as dimethyl sulfoxide and acetone. Recently, free radicals and reactive oxygen intermediates are suggested as the main cause of aging and various diseases.3) The reaction of radicals with organic substrates or oxygen molecule in such hydrophobic surroundings as CD, micelle, and vesicle is of interest from the viewpoint of deterioration of organic materials and adipose tissues in the aqueous solution. We now wish to report the CD-promoted radical cyclization of o-(2-propenyloxy)benzenediazonium ions (1a and 1b) and o-(2-propynyloxy)benzenediazonium ion (1c) in the absence or in the presence of O_2, leading to reduction or oxidation products.



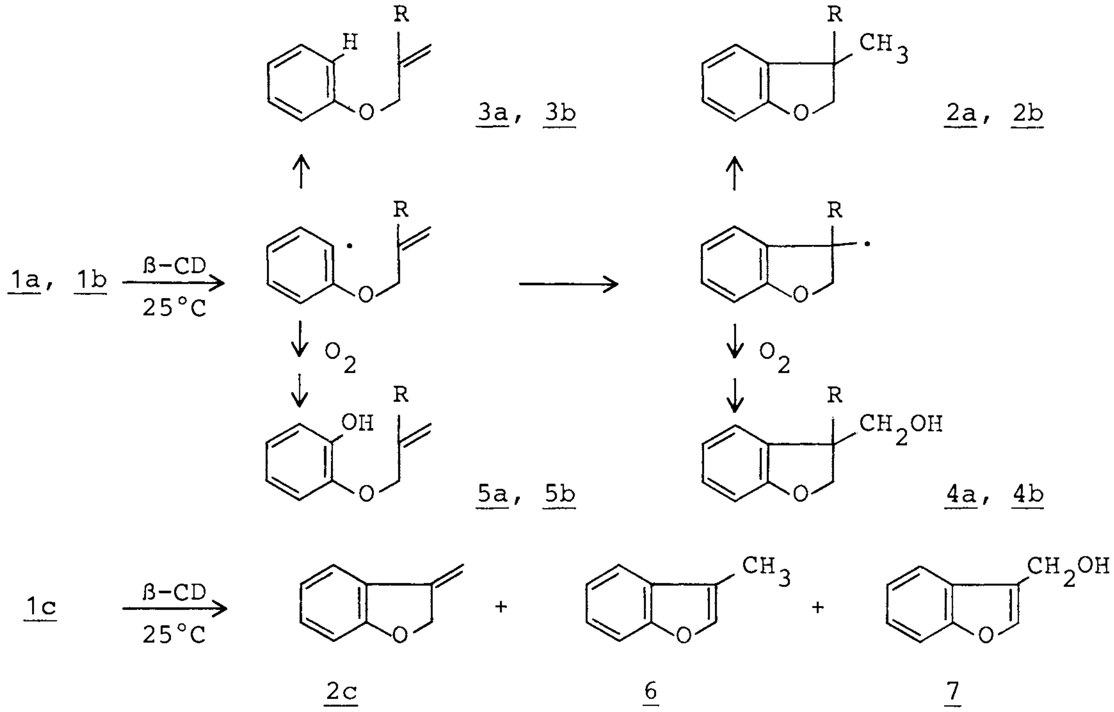
1a R=H
1b R=CH_3



1c

Table 1. Dediazoniation Products of Diazonium Ions 1a, 1b, and 1c in the Presence of β-CD

Diazonium ion	Atmosphere	Product yield/%			
		2a	3a	4a	5a
1a	N_2	47	1	0	0
	air	0	0	37	6
		2b	3b	4b	5b
1b	N_2	25	0	8	0
	air	9	0	16	0
		2c + 6		7	
1c	N_2	23		0	
	air	23		17	



Dediazoniation of o-(2-propenyloxy)-benzenediazonium tetrafluoroborate (1a) (1.30 mM) in pH 7.4-buffer solution was carried out in the presence of β-CD (13.0 mM) at 25 °C. After extraction of a reaction mixture with diethyl ether, the products were analyzed by GLC (frame ionization detector, OV-1 column), GC-mass (Shimazu QP- 1000), and NMR (Varian XL-200), and their structures were determined by comparing with those of authentic samples.

The decomposition of 1a in the absence of β-CD was extremely slow ($t_{1/2}$: over a week) and gave many intractable tarry products, while the reaction in the presence of β-CD was markedly accelerated ($t_{1/2}$: about 3 hours in ten times excess of β-CD) and the rate was saturated at about a fifty-fold excess of β-CD. Cyclohexanol, a good guest of β-CD, effectively suppressed the reaction. This result suggests the formation of an inclusion complex between β-CD and the diazonium ion in this reaction. CD-promoted dediazoniation of 1a yielded a cyclized compound, 3-methyl-2,3-dihydrobenzofuran (2a), in the moderate yield (47%) under N_2 atmosphere.

The hydrodediazoniation product, 2-propenyloxybenzene (3a), was minor (1%). Similar results were obtained in the reaction of 1b. The dediazoniation of 1c in the presence of β-CD under N_2 atmosphere gave the reduction products, 3-methylene-2,3-dihydrobenzofuran (2c) and 3-methylbenzofuran (6). In this case, 2c was readily converted to 6 by heating. The dediazoniation of the diazonium ions leads to more preferential intramolecular cyclization, rather than the hydrogen atom abstraction of the phenyl radicals from surroundings (CD), and it is different from exclusive hydrodediazoniation of p-substituted benzenediazonium ions.1) The high regioselectivity of the diazonium ions to the five-membered ring compounds is consistent with that reported for the intramolecular cyclization of the corresponding aryl radical.4)

In contrast with the predominance of 2 under N_2 atmosphere, the dediazoniation of 1 under air had a dramatic effect on the products: 1a gave oxidized products, 3-hydroxymethyl-2,3-dihydrobenzofuran (4a) and o-(2-propenyloxy)phenol (5a) in the yields of 37% and 6%, respectively, and 1c gave also 3-hydroxymethylbenzofuran (7, 17%) in addition to 2c and 6. The results for dediazoniation of 1 in the presence of β-CD are shown in the Table 1.

Uv-irradiated dediazoniation of 1a in the aqueous solution under air yielded also 4a and 5a in 5% and 51%, respectively. Direct photolysis of the diazonium salt results in the formation of the aryl cation,5) which may bring about cyclization and hydroxylation when 1 is used. However, the mechanism for CD-promoted dediazoniation under air has remained obscure, especially with regard to intermediate species. To shed light on this question, we studied the dediazoniation of 1a in ^{18}O labelled water ($H_2{}^{18}O$ 20%, Cambridge Isotope Laboratory). Photo-induced dediazoniation in ^{18}O labelled water gave ^{18}O labelled 4a and 5a, of which molecular ion peaks showed intensity ratios of 4:1 at the respective M^+ and M^++2. These results are to expect from the cation intermediate which reacts with water. On the contrary, gc mass fragmentation patterns for 4a and 5a obtained from CD-promoted dediazoniation in ^{18}O labelled water were the same as those obtained in normal water. The conclusion can be drawn that the CD-promoted dediazoniation under air (O_2) proceeds by a mechanism involving the formation of free radical species and the addition of the radical to oxygen molecule. The nature of initiation is, also, less clear. With regard to the mechanism of initiation of CD-promoted radical dediazoniation of benzenediazonium ions, it has been proposed that complex formation of the diazonium ion with β-CD leads to preferential formation of the unstable syn-arylazo ether rather than the anti-arylazo ether.1) This, subsequently, undergoes homolytic scission without conversion into the more stable anti-arylazo ether to form an aryl radical which enters propagation cycles. This mechanism of initiation is supported by stabilization of the diazonium ion by 2,3,6-tri-O-methyl-β-cyclodextrin complexation, contrary to the case of β-CD.6)

When CD is used as an asymmetric reaction vessel, we might expect that the environment surrounding the diazonium ions will bring about an asymmetric cyclyzation of the o-(2-propenyloxy)phenyl radical. When the diazonium ion 1b and β-CD were used in the molar ratio of 1:10, the kinetic selection of 3-methyl-3-hydroxymethyl-2,3-dihydrobenzofuran (4b) was observed. Enantiomer excess of 4b was 8%.7) Although the efficiency of the kinetic selection by β-CD has not been satisfied, the enantioselectivity suggests that β-CD has fairly strong binding ability for the diazonium ion or the corresponding phenyl radical.

According to the CPK model consideration, the selective hydroxylation for dediazoniation of the diazonium ions under air is assumed to result from a shallow binding with β-CD. The resulting radicals are sufficiently exposed to oxygen molecule dissolved in water. Since the reaction rate of aryl or alkyl radicals with oxygen molecule should be close to the diffusion-controlled limit, it is reasonable to consider that the reaction of these radicals with oxygen molecule precedes the hydrogen abstraction. This is a marked contrast with the high selective hydrodediazoniation of p-substituted benzenediazonium ions owing to the deep binding, irrespective of N_2 or O_2 atmosphere.1)

The CD promoted radical dediazoniation is much influenced with the size and the concentration of CD used. Details of these reactions will be discussed in the coming paper.

References

1) K. Fukunishi, H. Kazumura, H. Yamanaka, M. Nomura, and S. Kojo, J. Chem. Soc., Chem. Commun., 1982, 799; K. Fukunishi, J. Hira, H. Yamanaka, and M. Nomura, J. Chem. Soc., Perkin Trans. 1, 1985, 991.
2) A. L. J. Beckwith and G. F. Meijs, J. Chem. Soc., Chem. Commun., 1981, 136; G. F. Meijs and A. L. J. Beckwith, J. Am. Chem. Soc., 108, 5890(1986); A. L. J. Bechwith and G. F. Meijs, J. Org. Chem., 52, 1922(1987); A. N. Abeywickrema and A. L. J. Beckwith, ibid., 52, 2568(1987).
3) B. N. Ames, Sciences, 221, 1256(1983).
4) A. N. Abeywickrema and A. L. J. Beckwith, J. Chem. Soc., Chem. Commun., 1986, 464.
5) J. C. Scalano, N. Kim-Thuan and W. J. Leigh, J. Photochem., 24, 79(1984).
6) K. Fukunishi, T. Yoshioka, H. Yamanaka, and M. Nomura, Chem. Express, 1. 161(1986).
7) E.e. of 4b was determined by NMR analysis for the diastereomers, which were formed in the reaction of 4b with (+)-α-Methoxy-α-trifluoromethylphenylacethyl chloride: the intensity ratio for methyl signals of the 4b-portion (δ: 1.392 and 1.385) was 1.18. This result agreed with very closely with that obtained by NMR analysis, using a shift reagent tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato] Europium (III) derivative, $Eu(hfc)_3$.

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