Hydroquinone as a Reducing Agent for Conversion of Aryldiazonium Salts into Arenes

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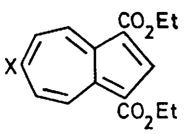
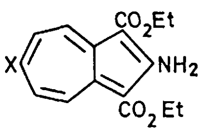
Summary A convenient, *in situ* method is described for reductive removal of an aromatic amino-group in high yield: hydroquinone is used to reduce intermediate diazonium salts and the method has been applied to certain azulenylamines.

IN a study of possible synthetic routes leading to 5-substituted azulenes, it became necessary to carry out reductive deamination of diethyl 6-aminoazulene-1,3-dicarboxylate[1] (**1**). Diethyl 2-aminoazulene-1,3-dicarboxylate[2] (**2**) and its 6-bromo-derivative[3] (**3**) are readily converted into blue-purple diazonium salts, which can be reduced to the diesters (**4**) and (**5**), respectively. Since substituents at the 2- and 6-positions of azulene have similar effects on the visible absorption,[4] we expected a blue-purple diazonium salt also to be produced from (**1**). However, the yellow solution of (**1**) darkened only slightly during the diazotization reaction [conditions as for (**3**) → (**5**)], never giving even a fleeting blue-purple colouration, and the product isolated was the 6-hydroxy-compound (**6**) (35%). Diazotization with mineral acid and isopentyl nitrite in ethanol, which was effective for the conversion (**2**) → (**4**) gave a 55% yield of the 6-ethoxy-derivative (**7**). Use of nitrosyl sulphate in acetic acid, a reagent frequently employed for the preparation of less accessible diazonium salts, gave the 6-acetoxy-compound (**8**) in 61% yield. Reaction of (**1**), anhydrous hydrogen chloride, and isopentyl nitrite in benzene gave the 6-chloro-derivative (**9**) in 38% (83% net) yield.[5]



(**1**) X = NH_2
(**4**) X = H
(**5**) X = Br
(**6**) X = OH
(**7**) X = OEt
(**8**) X = OAc
(**9**) X = Cl



(**2**) X = H
(**3**) X = Br

It thus appeared that the diazonium salt from (**1**) was being produced, although in insufficient concentration to be observed visually, and was reacting extremely rapidly with nucleophiles in the reaction medium. We therefore required an *in situ*, soluble reducing agent which would perform its function in a non-aqueous and non-nucleophilic solvent. Hydroquinone proved suitable, although it has received only scant attention in this role.[6]

The procedure used was as follows. To a stirred solution of (**1**) (0·26 mmol), hydroquinone (3·6 mmol), and conc. H_2SO_4 (1 drop) in dry dioxan (40 ml) at room temperature was added isopentyl nitrite (1·7 mmol) in dry dioxan (10 ml) during 20 min. After stirring for 2·5 h, work-up gave (**4**) in 92% yield. For larger-scale runs (2—10 g of amine), it is best to start with the amine, 1 equiv. of H_2SO_4, and 2 equiv. of hydroquinone in dioxan and to add to this separate solutions of 15—20 equiv. of the nitrite and hydroquinone in equal volumes of dioxan at approximately equal rates during 30 min. The reason for using the nitrite and hydroquine in large excess is that the amine and hydroquinone compete for the oxidizing agent. Quinone is removed from organic extracts by washing with aqueous $NaHSO_3$.

Reductive deaminations of azulenylamines

Reagent:	Yield (%)			
Conversion	$C_6H_4(OH)_2$ *in situ*	H_3PO_2	$NaBH_4$[7]	EtOH
(**2**) → (**4**)	100	33[2a] (53 net)		35 (53 net)
(**3**) → (**5**)	93	50[2a]	26[2a]	
(**1**) → (**4**)	92	0		0
5-Bromo-(**1**) → 5-Bromo-(**4**)	84 (100 net)			
2,5-Dibromo-(**1**) → 2,5-dibromo-(**4**)	80			
2,5,7-Tribromo-(**1**) → 2,5,7-Tribromo-(**4**)	0			

The procedure applied to (**2**) (100 mg) produced a quantitative yield of (**4**); (**3**) (2 g) gave (**5**) in 93—98% yield; on a 10 g scale the yield of (**5**) from (**3**) was *ca.* 93%. In neither of these reactions was there observed any sign of the colour of the intermediate diazonium salts. If these are in fact produced, hydroquinone must be an efficient and highly reactive reducing agent in these deaminations. No coupling products were observed.

This method has also been applied to the mono-, di- and tri-bromo-derivatives of (**1**) (see Table). No product was observed with 2,5,7-tribromo-(**1**) and only *ca.* 50% of the starting amine was recovered. This may indicate that this method will not be useful for sterically hindered aromatic amines.

In test-tube reactions, the suitability of various solvents for the diazotisation of (**2**) with isopentyl nitrate has been compared by observing the generation of the blue-purple colour of the diazonium salt. With dioxan, ethyl acetate, 1,2-dimethoxyethane, and acetonitrile colour production is instantaneous, whereas chloroform, methylene chloride, ether, and tetrahydrofuran are poor. Of these solvents, 1,2-dimethoxyethane appears to be the best substitute for dioxan.

Orton and Everatt[6a] have reported that hydroquinone is a good reducing agent for preformed diazonium salts, although without experimental details. The low solubility of hydroquinone in water suggests that its usefulness in this capacity may be greatest in non-aqueous media. We have obtained a 30% yield of biphenyl by diazotization of benzidine dihydrochloride in dioxan with sodium nitrite (dissolved in a minimal amount of water) followed by addition of hydroquinone;† no effort was made to optimize these conditions.

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† This result was obtained by Ronald E. Kittle.

[1] T. Nozoe, K. Takase, and M. Tada, *Bull. Chem. Soc. Japan*, 1965, **38**, 247.

[2] (*a*) H. E. Petty, Ph.D. Thesis, Kansas State University, 1971; (*b*) T. Nozoe, S. Seto, S. Matsumura, and T. Murase (*Bull. Chem. Soc. Japan*, 1962, **35**, 1179) report that reduction of the diazonium salt from (**2**) with H_3PO_2 gave a 42% yield of (**4**).

[3] T. Nozoe, S. Seto, and S. Matsumura, *Bull. Chem. Soc. Japan*, 1962, **35**, 1990.

[4] E. Heilbronner in 'Non-Benzenoid Aromatic Compounds,' ed. D. Ginsburg, Interscience, New York, 1959.

[5] These reaction conditions with (**2**) gave a 95% yield of diethyl 2-chloroazulene-1,3-dicarboxylate.

[6] (*a*) K. J. P. Orton and R. W. Everatt, *J. Chem. Soc.*, 1908, **93**, 1021; (*b*) for reviews on reductive deamination see K. H. Saunders, 'The Aromatic Diazo-Compounds and Their Technical Applications,' 2nd edn., Edward Arnold, London, 1949, and N. Kornblum, *Org. Reactions*, 1944, **2**, 262.

[7] J. B. Hendrickson (*J. Amer. Chem. Soc.*, 1961, **83**, 1251) examined the use of $NaBH_4$ with aryldiazonium fluoroborates.