

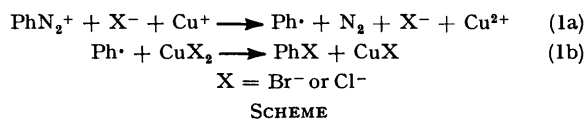
An Investigation of the Two-step Nature of the Sandmeyer Reaction

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The roles of the reductant and of the ligand transfer agent in the Sandmeyer reaction are examined. Several new reducing agents, namely Sn^{2+} , Fe^{2+} , ferrocene, $\text{Fe}(\text{CN})_6^{4-}$, and ascorbic acid are shown to be able to stimulate bromo- and chloro-dediazoni-ation. The procedure is of potential synthetic interest in that the reaction occurs smoothly at room temperature. The efficiency of the process depends on the redox potential of the reductant and the presence of a potential threshold of *ca.* 1 V is detected, above which the reaction does not occur. Evidence for the non-catalytic role of the reductant are presented. Comparison with the iodide stimulation case is also discussed.

THE conversion of arenediazonium salts into aryl halides is of great synthetic value. Though considerable attention has consequently been devoted to this reaction,^{1,2a} the mechanism has not been completely elucidated. There is now general agreement³ that in the thermolysis of a diazonium salt an aryl cation is produced by a heterolytic decomposition. In competition with this route it is held that a radical process can occur under appropriate conditions,^{2a} but several aspects of radical initiation and the presence of radical intermediates are still debated.

This work was undertaken with the aim of contributing to a better understanding of the radical mechanism of the halogenodediazoni-ation. According to Kochi,⁴ the Sandmeyer reaction occurs by a two-step mechanism (Scheme). In the first step the substrate is reduced by



copper(I) ion and the second step is a ligand transfer process leading to the product. We can therefore ask what is unique in the copper(I) salt reducing action and if there are other agents able to give step (1a).

The results reported here show that reductants other than the copper(I) cation can act as efficient promoters of the reaction.

RESULTS AND DISCUSSION

Several reducing species have been examined and some peculiar features emerge from the results shown in the Table. Tin(II) chloride whose reducing power is comparable to that of a copper(I) salt is unable to assist chlorodediazoni-ation. However it is remarkable that fairly good yields of chlorobenzene are obtained by adding a Cu^{2+} salt (experiment 2), which, on the other hand, is ineffective by itself (experiment 4). Hence, we may infer the need for both a reducing species (Sn^{2+}) and a ligand transfer agent (Cu^{2+}) in this process.⁵ Similar behaviour is shown for the bromodediazoni-ation (experiment 3), while under the same conditions F^- and NO_2^- are not reactive at all.

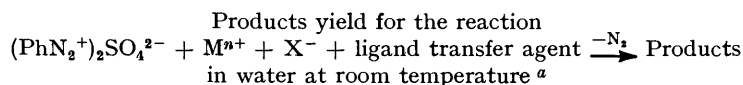
Other tested reductants, Fe^{2+} , ferrocene, $\text{Fe}(\text{CN})_6^{4-}$, and ascorbic acid,⁵ stimulate the Cl^- and Br^- reaction in the presence of a Cu^{2+} salt. This can be either copper(II)

halide or nitrate or sulphate indifferently, being able to pick up from the water solution the added halide ion employed in step (1b). It gives the best results when supplied in stoichiometric amounts; larger amounts no longer increase the product yield (experiments 16 and 17). Whenever tested (experiments 13 and 14) the bromide proved to be better transferred than the chloride.⁵

The presence of small percentages of benzene or biphenyl supports the radical nature of the reaction.^{2a,4} The formation of radical reduction (benzene) or radical coupling (biphenyl) products soars when the conditions for the radical halogenodediazoni-ation are either unfavourable (experiment 7) or not met at all (experiments 1, 5, and 6). Moreover, radical induced phenol formation, as already reported by Cohen,⁶ occurs significantly under the conditions of experiments 1 and 15, while it disappears in the absence of radical initiator (experiment 4). Trace amounts of azobenzene, halogenobiphenyl, and terphenyl were also detected by g.l.c.-m.s. analysis of the reaction.

The results of the Table widen Kochi's mechanism: the electron transfer step (1a) can be assisted by several agents M^{n+} . The ligand transfer process (1b) is performed specifically by a Cu^{2+} complex (a Fe^{3+} salt is far less reactive, experiment 7). The two-fold role of the copper salt in the Sandmeyer reaction was ambiguous up to now since copper had to act both as reductant (Cu^+) and as ligand transfer agent [Cu^{2+} , formed in step (1a) under typical Sandmeyer conditions]. The use here of other stimulants allows a clear separation of the two roles. To have the two functions fulfilled by two different species, both present since the start of the reaction, may lead to an optimization of the process. Indeed, it occurs easily at room temperature, according to a previous report,⁵ and does not require heating, as is the case for classical Sandmeyer conditions, while still affording better yields. When Cu^+ is used along with Cu^{2+} an increase of halogenobenzene yield is observed (*cf.* experiments 11 and 12), which confirms the previous finding.^{1c}

The following evidence clarifies the function of the stimulant. Increasing amounts of the one-electron reductant ascorbic acid cause a regular increase of the yield of PhBr from zero up to a plateau (Figure 1) which is reached when the stimulant : substrate molar ratio is



Expt. no.	Stimulant	X ⁻ (0.50M)	Ligand transfer agent (0.25M)	Products (%) ^b			
				PhX	PhH	Ph ₂	PhOH
1 ^c	SnCl ₂ , 0.13M	Cl ⁻	None	<0.1	7	3	5
2	SnCl ₂ , 0.13M	Cl ⁻	Cu ²⁺	67	Trace	0.2	
3	SnCl ₂ , 0.13M	Br ⁻	Cu ²⁺	58		0.2	
4	None	Cl ⁻	Cu ²⁺	(+14% PhCl) ^d			
5	SnCl ₂ , 0.13M	NO ₂ ⁻	Cu ²⁺	<0.1	13	7	3
6	SnCl ₂ , 0.13M	F ⁻	Cu ²⁺	(+13% PhCl) ^d			
7	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	<0.1	2	0.4	2
8	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	(+16% PhCl) ^d			
9	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	12	13	7	0.5
10	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	31	8	3	1
11	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	51	3	1	
12	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	19	2	1	2
13	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	45		0.7	Trace
14	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	63		Trace	Trace
15	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	28		1	
16	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	64	1		
17	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	8		3.5	26
18	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	48 ^f	7	2	0.4
19	SnCl ₂ , 0.13M	Cl ⁻	Fe ³⁺	65 ^g			

^a Employing $[\text{PhN}_2^+] 0.25\text{M}$. ^b Determined by g.l.c. analysis after 30 min reaction; maximum error *ca.* 4%. ^c Phenylhydrazine is among the observed products, in agreement with ref. 2. ^d Due to the Cl⁻ added as SnCl₂. ^e Ferrocene, dissolved in dioxan. ^f The Cu²⁺ salt was present in only half the molar amount of the substrate. ^g The Cu²⁺ salt was 2.9 times the molar amount of the substrate.

unity. For the two-electron reductant Sn²⁺ the plateau is reached for a 0.5 : 1 stimulant : substrate molar ratio

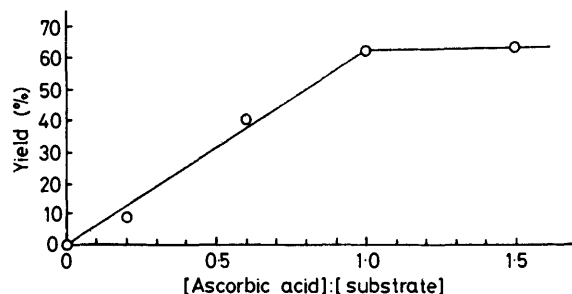


FIGURE 1 Yield (%) of bromobenzene as a function of the ascorbic acid : substrate molar ratio

(Figure 2). Hence, the reductant is required in stoichiometric amount. It is implied in these observations that steps (1a and b) are distinctly separated and that the copper(I) ion possibly produced in step (1b) does not compete with the reductant in step (1a). Were this

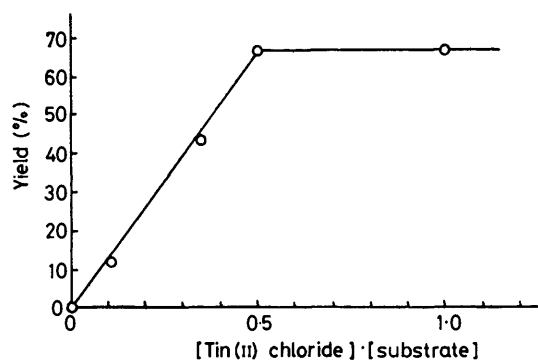


FIGURE 2 Yield (%) of chlorobenzene as a function of tin(II) chloride : substrate molar ratio

not the case, catalytic amounts of reductant would be able to promote a radical chain reaction.

The yield data reported in the Table were determined after 30 min for all the stimulants under the same conditions. Hence the yields are likely to reflect the

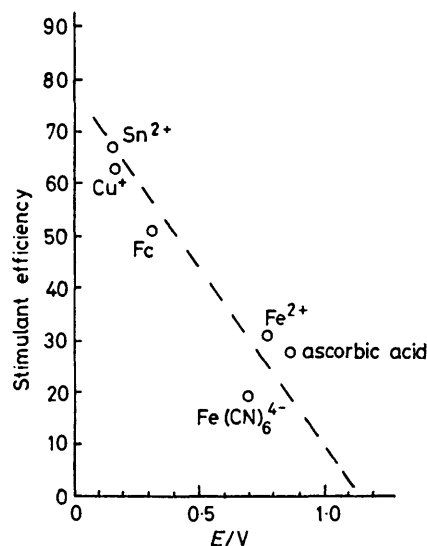


FIGURE 3 Dependence of the stimulant efficiency on the redox potential E_0

relative efficiencies of the different reductants* and are related in gross terms to their redox potential.⁷ A potential threshold of *ca.* 1 V can be inferred by the steep drop of the PhCl yield when the E_0 of the stimulant approaches this value (Figure 3).

* It is reasonable that in the case of the less efficient stimulants larger amounts of unreacted diazonium salt are left within the reaction time adopted.

Hence, from the data at hand the electron transfer step involves the reductive interaction of the substrate with reductants having a redox potential of at least 1 V and the efficiency of the overall process markedly depends on the reducing power of the stimulant.

The potential requirement for a reductant (Figure 3) could explain an up to now puzzling difference in behaviour between I^- , which is known to lead to halogenodiazonation without the need for any copper salt, and the other two halides. We observe that iodide ion (E_0 0.5 V) is a fairly good reductant by itself, while Br^- and Cl^- (E_0 1.1 and 1.4 V, respectively) are less good and hence the electron transfer step must be carried out on their behalf by a better reductant. Actually, Br^- seems to be in a borderline situation. It has been reported⁸ that in dimethyl sulphoxide solution or in water but with a strong electron-withdrawing substituent on the diazonium salt, a slow but detectable formation of aryl bromide triggered by Br^- can be observed without any Cu^+ stimulation.⁹

However, if this can explain why I^- is able to perform step (1a), in what way can it give step (1b) without the presence of the ligand transfer agent Cu^{2+} ?

The reaction of iodide ion with diazonium salts has been previously suggested by Singh and Kumar¹⁰ to occur according to a radical chain $S_{RN}1$ mechanism.¹¹ They propose an electron transfer step due to I^- ($ArN_2^+ + I^- \rightarrow Ar\cdot + N_2 + I\cdot$), as we have stated previously. However, in a further step, they postulate the formation of a iodobenzene radical anion from I^- and $Ar\cdot$, which should then act as an electron donor to the diazonium salt, giving rise to a chain process. This seems quite odd in that the radical anion of a halogenobenzene, most particularly iodobenzene, is known to have a high tendency to fragment, as soon as it is formed, into aryl radical and halide ion.^{11,12} Instead, a more likely proposal could be (i) combination of the $Ar\cdot$ and $I\cdot$ radicals produced in the electron transfer step or (ii) atom abstraction by the $Ar\cdot$ radical from I_2 (formed from $I\cdot$ coupling) or both proposals. These reactions should occur with I^- only among the halides, since it is the only one able to give the reductive electron transfer step (1a).

The experiments reported in this paper indicate the significance of the two different functions of steps (1a and b) on the overall reactivity of a halogenodiazonation of the Sandmeyer kind.

EXPERIMENTAL

Reagent grade commercially available compounds were used throughout the study.

The arenediazonium salts (sulphate mainly) were prepared in water under the usual conditions,¹³ the temperature not exceeding 5 °C, at 0.25M initial concentration. An equivalent amount of Cu^{2+} salt (generally nitrate) and the halide salt were then added. When they were dissolved, the cooling bath was removed and a concentrated solution (ca. 2M) of the reductant was added all at once. The amount of halide ion sometimes introduced as the counterion of the stimulant was taken into account; an overall amount of halide twice that of the substrate was always used. The resulting mixture was stirred at room temperature for 30 min, quickly quenched by dilution with water, and, after addition of the internal standard, extracted with ether, washed with water, and dried (Na_2SO_4).

The yields were determined by g.l.c. analysis performed on a Hewlett-Packard 5830A flame ionization instrument, fitted with a 186 cm \times 4 mm column of 2% OV-17 on 80–100 mesh Chromosorb GAW-DMCS. Molar response factors were determined and used in the evaluation of g.l.c. results.

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REFERENCES

- (a) W. A. Waters, 'Physical Aspects of Organic Chemistry', Van Nostrand, New York, 1950, 4th edn.; (b) L. Friedman, in 'Carbonyl Ions', eds. G. A. Olah and P. von R. Schleyer, Wiley, New York, 1970, vol. 2, ch. 16; (c) D. C. Nonhebel and W. A. Waters, *Proc. Roy. Soc.*, 1957, **242**, 16.
- (a) H. Zollinger, 'Azo and Diazo Chemistry', Interscience, New York, 1961; (b) R. M. Eloffson, *Can. J. Chem.*, 1958, **36**, 1207.
- (a) H. Zollinger, *Angew. Chem. Int. Ed. Engl.*, 1978, **17**, 141; (b) H. B. Ambroz and T. J. Kemp, *Chem. Soc. Rev.*, 1979, **8**, 353; (c) C. G. Swain, J. E. Sheats, and K. G. Harbison, *J. Am. Chem. Soc.*, 1975, **97**, 783 and following papers.
- J. K. Kochi, *J. Am. Chem. Soc.*, 1957, **79**, 2942; *Tetrahedron*, 1962, 483.
- C. Galli, *Tetrahedron Lett.*, 1980, 4515.
- T. Cohen, A. G. Dietz, and J. R. Miser, *J. Org. Chem.*, 1977, **42**, 2053.
- 'Handbook of Chemistry and Physics', CRC Press, Cleveland, 59th edn., 1978.
- H. Zollinger and B. L. Kaul, *Helv. Chim. Acta*, 1968, **51**, 2132; M. D. Johnson, *J. Chem. Soc.*, 1965, 805.
- E. S. Lewis, L. D. Hartung, and B. M. McKay, *J. Am. Chem. Soc.*, 1969, **91**, 419.
- P. R. Singh and R. Kumar, *Aust. J. Chem.*, 1972, **25**, 2133.
- J. F. Bunnett, *Acc. Chem. Res.*, 1978, **11**, 413.
- C. P. Andrieux, C. Blocman, J. M. Dumas-Bouchiat, and J. M. Savéant, *J. Am. Chem. Soc.*, 1979, **101**, 3431.
- A. Vogel, 'Textbook of Practical Organic Chemistry', Longman, Harlow, 1978, 4th edn., p. 694.