The Inhibition of Autoxidation by Aromatic Amines[1]

K. ADAMIC, D. F. BOWMAN and K. U. INGOLD, Division of Chemistry,
National Research Council of Canada, Ottawa 7, Canada

Abstract

Recent work on the inhibition of autoxidation by aromatic amines is reviewed. The rate controlling step for the inhibition process is abstraction of the amino hydrogen by a peroxy radical. The rate of this reaction is increased by electron donating substituents attached to the aromatic ring. Nitroxide radicals may be produced in the reaction of peroxy radicals with secondary amino radicals. The efficiency of nitroxide formation is greater for tertiary than for secondary peroxy radicals because, in the latter case, the caged nitroxide and alkoxy radical may disproportionate to give a hydroxylamine and a carbonyl compound. Primary aromatic amines do not give nitroxides, presumably because the peroxy radical-amino radical reaction gives an alcohol and a nitroso aromatic. The tertiary amine, N,N,N′,N′-tetramethyl-*p*-phenylenediamine is shown to be a catalyst of autoxidation rather than an inhibitor, as has been previously reported. The products of the N-phenyl-2-naphthylamine-peroxy radical reaction have been identified.

The autoxidation of most organic substrates is a free radical chain process. The overall rate of oxidation depends on the rate of chain initiation, chain propagation and chain termination. The rate can generally be reduced or the length of the induction period increased by the addition of relatively low concentrations of compounds which contain certain specific functional groups. These compounds are called antioxidants.

Among the most widely used antioxidants are aromatic amines. These compounds fall into the group of antioxidants which reduce the rate of oxidation by interfering with the normal propagation process by reacting with the free radicals that carry the chain. Under ideal conditions the overall process can be represented by the following reaction scheme (1,2)

Initiator	$\rightarrow R\cdot$	[1]
$R\cdot + O_2$	$\rightarrow ROO\cdot$	[2]
$ROO\cdot + RH$	$\rightarrow ROOH + R\cdot$	[3]
$ROO\cdot + \diagdown NH$	$\rightarrow ROOH + \diagdown N\cdot$	[4]
$ROO\cdot + \diagup N\cdot$	$\rightarrow$ Nonradical products	[5]

RH represents the substrate being oxidized and $\diagdown NH$ the amine antioxidant. The rate of oxidation, $-d[O_2]/dt$, is proportional to the substrate concentration, to the rate of chain initiation, R_i, and is inversely proportional to $[\diagdown NH]$. That is $-d[O_2]/dt = k_2[RH]R_i/k_4[\diagdown NH]$.

By deuterating the amino hydrogen in several different amines we have shown that Reaction 4 has a deuterium isotope effect, $k_H/k_D \sim 3$ at 65 C (1,2), that is, peroxy radicals abstract an amino hydrogen three times as readily as they will abstract a deuterium from the same amine. This result provided one of the first positive pieces of evidence that the rate determining inhibition process with amines involved abstraction of the amino hydrogen and thus provided more rational grounds for a search for better amine antioxidants.

Of major importance to any understanding of the inhibition reaction is the effect on the rate of Reaction 4 of substituent groups added to the aromatic ring of the amine. Now within reaction series of *meta*- and *para*- substituted side chain derivatives of benzene the effect of structure on rates and equilibria is nearly always determined by a single basic factor, the polar effect of the substituent. The result of this simplification is the most general relationship known for correlating the effect of substituents on rates and equilibria, namely the Hammett equation,

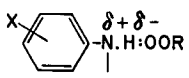
$$\log (k/k_o) = \rho\sigma$$

In this expression k_o refers to the unsubstituted benzene derivative and k to the substituted derivative; σ is a substituent constant which is independent of the nature of the reaction. It gives a quantitative measure of the polar effect of a particular *meta* or *para* substituent relative to a hydrogen atom. ρ is a proportionality constant which is dependent on the nature of the reaction.

For many reactions involving electrophilic aromatic substitution and side chain reactions the Hammett equation is not applicable to strongly electron donating groups such as a *para*-methoxy group. In these cases, it is common to use Brown's electrophilic substituent constants.

$$\log (k/k_o) = \rho\sigma^+$$

We have obtained an excellent correlation with σ^+ for the rate constants for inhibition by ring-substituted diphenylamines and N-methyl anilines (2) (Fig. 1). The rate constants for the attack of a peroxy radical on the amino hydrogen vary over three or four orders of magnitude but the individual values are well correlated by the σ^+ constants of the substituents. The fact that the rate constants are correlated by σ^+ indicates that there is considerable charge separation in the transition state. That is, the dipolar structure



contributes significantly to the transition state. This structure is facilitated by a group X which is electron releasing and is hindered by a group which is electron attracting.

Inhibition by amines is more complicated than inhibition by phenols because of the frequent formation of stable nitroxide radicals in the reaction between the amino radical and a peroxy radical.

$ROO\cdot + \diagdown N\cdot \rightarrow$ Nonradical products	[5]
$ROO\cdot + \diagup N\cdot \rightarrow RO\cdot + \diagdown NO\cdot$	[5a]

[1] Presented at the AOCS Meeting, San Francisco, April 1969.
[2] Issued as NRCC No. 11296.

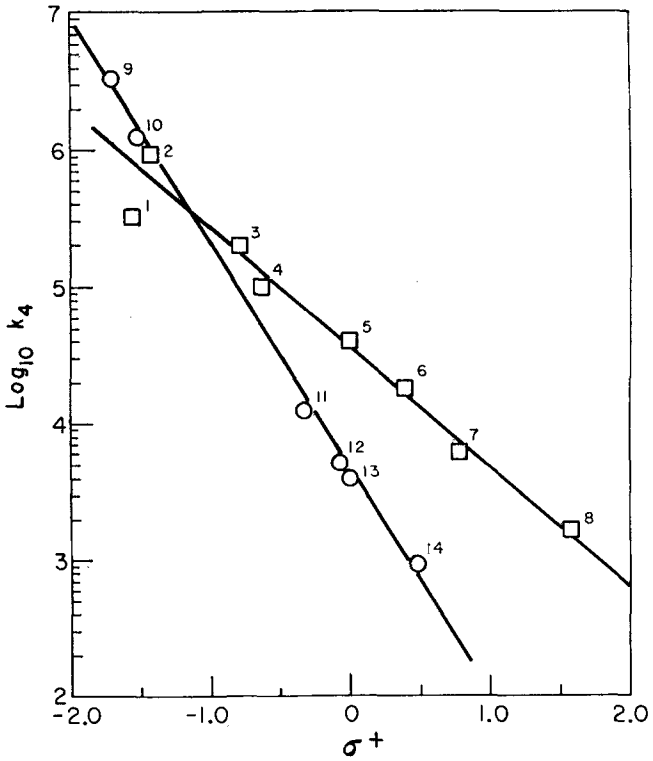
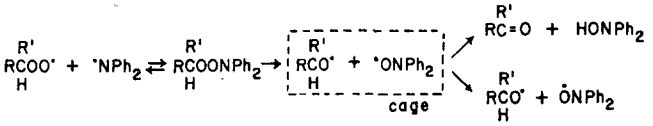


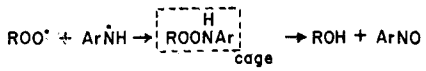
FIG. 1. $\log_{10} k_4$ versus σ^+ for substituted diphenylamines (□) and substituted N-methylanilines (○). The individual points refer to: 1. 4,4′-Dimethoxydiphenylamine; 2. N,N′-Diphenyl-*p*-phenylenediamine; 3. 4-Methoxydiphenylamine; 4. 4,4′-Dimethyldiphenylamine; 5. Diphenylamine; 6. 3-Chlorodiphenylamine; 7. 4-Nitrodiphenylamine; 8. 4,4′-Dinitrodiphenylamine; 9. N,N,N′-Trimethyl-*p*-phenylenediamine; 10. N,N′-Dimethyl-*p*-phenylenediamine; 11. 4-Methyl-N-methylaniline; 12. 3-Methyl-N-methylaniline; 13. N-Methylaniline; 14. 4-Carbomethoxy-N-methylaniline.

We have recently studied Reaction 5a in some detail by electron spin resonance spectroscopy (3,4). To our surprise we found that primary and secondary peroxy radicals were considerably less efficient than tertiary peroxy radicals at converting any particular amine to its nitroxide. We believe that this is due to disproportionation of the caged alkoxy radical and nitroxide radical to give a carbonyl compound and a hydroxylamine.



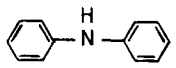
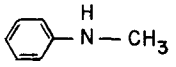
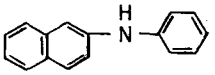
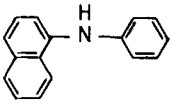
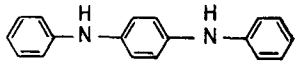
Hydrogen atom transfer of this kind is not possible for a tertiary peroxy radical and tertiary peroxy radicals are therefore more efficient in forming nitroxides than primary or secondary peroxy radicals.

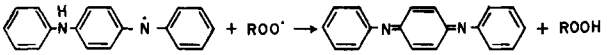
The rates of formation of nitroxides by the oxidation of a number of different amines with *t*-butylperoxy radicals under standard conditions were also measured (4). Several interesting results were obtained. Nitroxides are not formed from primary amines. This is presumably because the amino radical is oxidized to a nitroso compound and the peroxy radical is reduced to an alcohol:



Nitroxides are not formed from tertiary amines either, because these compounds, not having an amino hydrogen, do not give an amino radical on reaction with peroxy radicals. Secondary amines exhibit the most interesting behavior. Some of our results are summarized in Table I. The "efficiency of nitroxide formation" from the amine would be 1.0 if every amine radical was oxidized to nitroxide and every alkoxy radical produced in Reaction 5a regenerated a peroxy radical. Diphenylamines are very efficiently converted to nitroxides. The maximum concentration of nitroxide which builds up during a reaction can become quite large because diphenylnitroxide radicals are relatively unreactive. The efficiencies of conversion of N-methylanilines to nitroxides are also fairly large, but these nitroxide radicals are very reactive and only small concentrations build up in the reactions. In contrast to diphenylamines, only a small proportion of N-phenylnaphylamines are converted to nitroxides. The principal reaction between a peroxy radical and these amino radicals involves the attack of the peroxy radical on the naphthyl ring system (see below). No nitroxide is formed from N,N′-diphenyl-*p*-phenylenediamine, because the second hydrogen atom is lost in Reaction 5 to yield N,N′-diphenyl-*p*-quinonediimine as the major reaction product (5).

TABLE I

Amine	Efficiency of nitroxide formation	Maximum nitroxide conc. (under std. conditions) (4)
	0.56	190×10^{-6}
	≧0.1	3×10^{-6}
	0.015	4×10^{-6}
	0.01	4×10^{-6}
	0	0



The simple kinetics in which the inhibited oxidation rate depends on the first power of the initiation rate and inverse first power of the inhibitor concentration is not always observed. Instead, the oxidation rate is sometimes found to be roughly proportional to the square root of these quantities, i.e.,

$$\frac{-d[O_2]}{dt} \alpha \frac{R_i^{1/2}}{[Inh]^{1/2}} \quad Inh = \begin{matrix} \diagdown \\ NH \text{ and } ArOH \\ \diagup \end{matrix}$$

When these half order kinetics were first observed (5–7) it was suggested that they resulted from the reversible formation of a peroxy radical-inhibitor complex, followed by decomposition of the complex by reaction with a second peroxy radical, i.e.,

$$ROO\cdot + Inh \rightleftharpoons [ROO\cdot\ Inh]$$
$$ROO\cdot + [ROO\cdot\ Inh] \rightarrow \text{Nonradical products}$$

Supporting evidence for this mechanism was the apparent absence of a deuterium isotope effect and the fact that N,N,N′,N′-tetramethyl-para-phenylene-

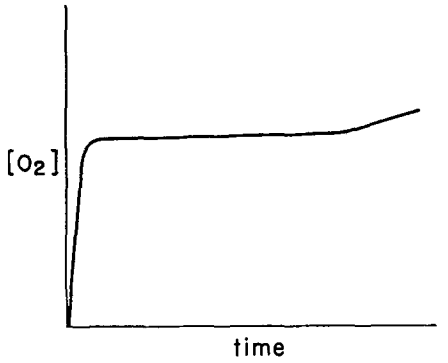
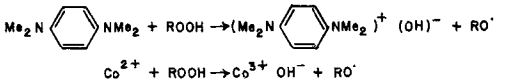


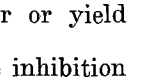
FIG. 2. Typical oxygen absorption curve for a readily oxidizable substrate (e.g., cumene, tetralin, styrene etc.) in the presence of N,N,N′,N′ tetramethyl-*p*-phenylenediamine.

diamine (which has no amino hydrogens) appeared to inhibit oxidation. We now know that these kinetics are actually due to chain transfer reactions involving the inhibitor radical and the substrate or its hydroperoxide (8–10)

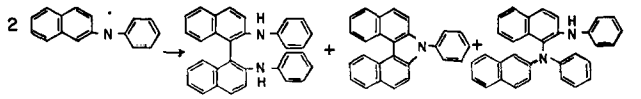
$$In\cdot + RH \rightarrow Inh + R\cdot$$
$$In\cdot + ROOH \rightarrow Inh + ROO\cdot$$

The deuterium isotope effect, k_H/k_D, is actually about 3 for amines (1,2) and 10–15 for phenols (11). The only remaining support for the peroxy radical-inhibitor complex mechanism of inhibition was the reported (6,12) inhibition by N,N,N′,N′-tetramethyl-*p*-phenylenediamine. We have recently found that this compound is in fact actually a pro-oxidant (4). However, its pro-oxidant activity is quickly followed by a period of retarder action so that without careful experimental work it could appear to be an inhibitor (Fig. 2). Its catalytic activity is due to one electron reduction of the hydroperoxide which is formed in the oxidation. That is, it behaves analogously to a reducing transition metal such as divalent cobalt.

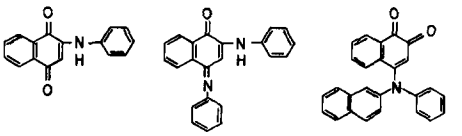


The blue Wurster cation  is readily identified both by its color and e.s.r. spectrum. This radical cation must itself be an inhibitor or yield products which are inhibitors.

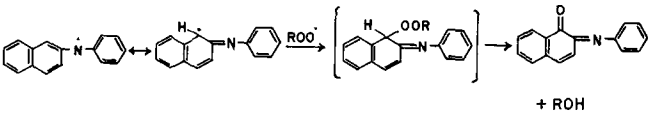
To obtain a full understanding of amine inhibition it is obviously necessary to know what the products of reaction are in a few representative cases. We chose N-phenyl-2-naphthylamine for study because it is a commercially important antioxidant and because it did not yield large amounts of nitroxide. Six products have been identified (13) of which three are formed by coupling of the amino radicals produced in Reaction 4:



The other three products all contain oxygen in the α-position of the naphthyl ring.



These compounds are believed to be formed by attack of some of the nucleophiles present in these reactions (e.g., hydroperoxide, starting amine, etc.) on an *ortho*-quinoneimine which itself is formed by reaction of the amino radical with a peroxy radical.



The postulated *ortho*-quinoneimine could not be isolated, presumably because it was highly reactive.

The nature of the peroxy radical oxidation products formed from most aromatic amines still awaits investigation and is one of the main unsolved problems connected with amine inhibition.

REFERENCES

1. Brownlie, I. T., and K. U. Ingold, Can. J. Chem. *44*, 861 (1966).
2. Brownlie, I. T., and K. U. Ingold, Ibid. *45*, 2419 (1967).
3. Adamic, K., M. Dunn and K. U. Ingold, Ibid. *47*, 287 (1969).
4. Adamic, K., and K. U. Ingold, Ibid. *47*, 295 (1969).
5. Boozer, C. E., G. S. Hammond, C. E. Hamilton and J. N. Sen, J. Am. Chem. Soc. *77*, 3233 (1955).
6. Boozer, C. E., and G. S. Hammond, Ibid. *76*, 3861 (1954).
7. Hammond, G. S., C. E. Boozer, C. E. Hamilton and J. N. Sen, Ibid. *77*, 3238 (1955).
8. Thomas, J. R., Ibid. *85*, 2166 (1963); *86*, 4807 (1964).
9. Mahoney, L. R., and F. C. Ferris, Ibid. *85*, 2345 (1963).
10. Howard, J. A., and K. U. Ingold, Can. J. Chem. *42*, 2324 (1964).
11. Howard, J. A., and K. U. Ingold, Ibid. *40*, 1851 (1962); *41*, 1744, 2800 (1963).
12. Yates, W. R., and J. L. Ihrig, J. Am. Chem. Soc. *87*, 710 (1965).
13. Bowman, D. F., B. S. Middleton and K. U. Ingold, J. Org. Chem. *34*, 3456 (1969).

[Received October 15, 1969]