

Antioxidants – A Research Report

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Introduction

Research literature on antioxidants appear in two broad application areas – Industrial and Biomedical. We will concentrate mainly on industrial applications in the following analysis, although some references will be made to studies in the biomechemical/ biomedical field because the fundamental mechanisms of antioxidant activity are the same.

Review

Many industrial polymers (solids as well as adhesives, etc.) are subject to degradation resulting from mechanical, heat, and light (e.g., UV) stresses. A primary cause of the degradation has been recognized to be an autocatalytic (chain reaction) process resulting from the generation of free radicals following the mechanical, temperature, or light stress. The free radical mediated oxidation/degradation process in a polymer system is known to be in terms of the mechanism illustrated in Fig. 1. Unchecked degradation leads to two types of damages – embrittlement due to the formation of cross links by alkoxy radicals coupling with carbon radicals, or disproportionation reactions leading to chain scission and polymer softening. In terms of their mechanism of action antioxidants can be classified as one of three major types – (1) those that trap the carbon radicals (R^*) that are generated by the external stress or the interaction of the alkoxy (RO^*) and hydroxy (HO^*) radicals generated in the degradation cycle, (2) Primary antioxidants that trap the peroxy radicals (ROO^*) generated by the reaction of the carbon radicals with oxygen, and (3) Secondary antioxidants that prevent the formation of alkoxy and hydroxy radicals by the decomposition of the hydroperoxide ($ROOH$) formed when the peroxy radicals abstract a labile hydrogen from the polymer backbone.

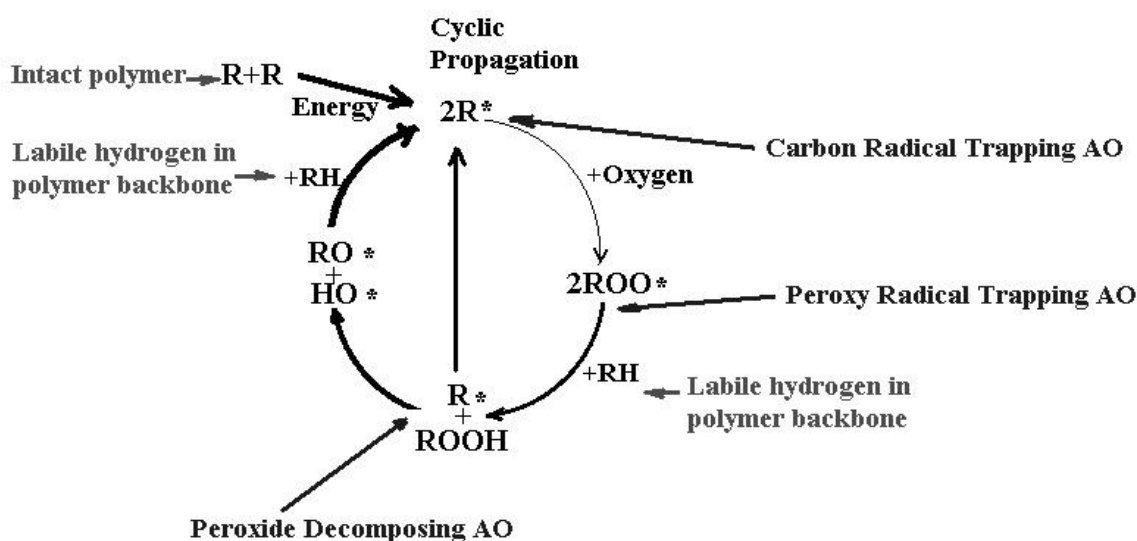


Fig. 1

An example of the carbon radical trapping AO are the benzofuranones recently added to the antioxidant arsenal. They are extremely potent radical scavengers capable of reacting directly with carbon-centered radicals and interrupting the auto-oxidation cycle earlier than primary and secondary antioxidants. Due to their effectiveness at low concentrations, they are typically formulated as a minor component in combination with secondary antioxidants.

The Primary antioxidants consist mainly of hindered phenols and hindered aromatic amines. They scavenge and destroy the chain propagating peroxy and alkoxy radicals before they can react with the polymer.

These materials contain hydrogen atoms that can be easily donated to the chain-propagating peroxy, alkoxy, and hydroxy radicals. The alkoxy and hydroxy radicals are converted to alcohols and water, respectively, which are inert and do not hamper polymer stability. The antioxidant radicals formed are stable and do not abstract more hydrogens from polymer. A typical primary antioxidant of the hindered aromatic amine variety is AO-TMQ (Polymerized 1,2-dihydro-2,2,4-trimethylquinoline), shown in [Fig 2](#). AO-445 (4,4'-bis(dimethylbenzyl)diphenylamine, or, p-dicumyldiphenylamine) shown in [Fig. 3](#), is another commonly used primary antioxidant of the hindered aromatic amine type. AO-1010 (Tetrakis(methylene(3,5-di-t-butyl-4-hydroxy-hydrocinnamate)) methane), a component of the commercial formulation IRGANOX 1010 of CIBA Speciality Chemicals, shown in [Fig. 5](#) exemplifies primary antioxidants of the hindered phenol type.

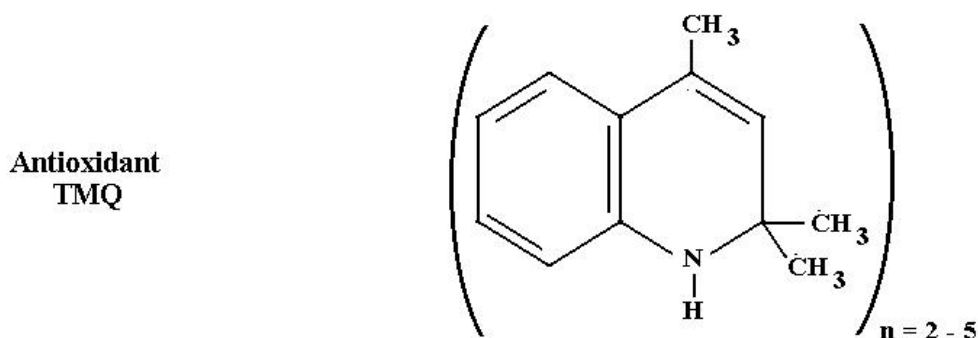


Fig. 2

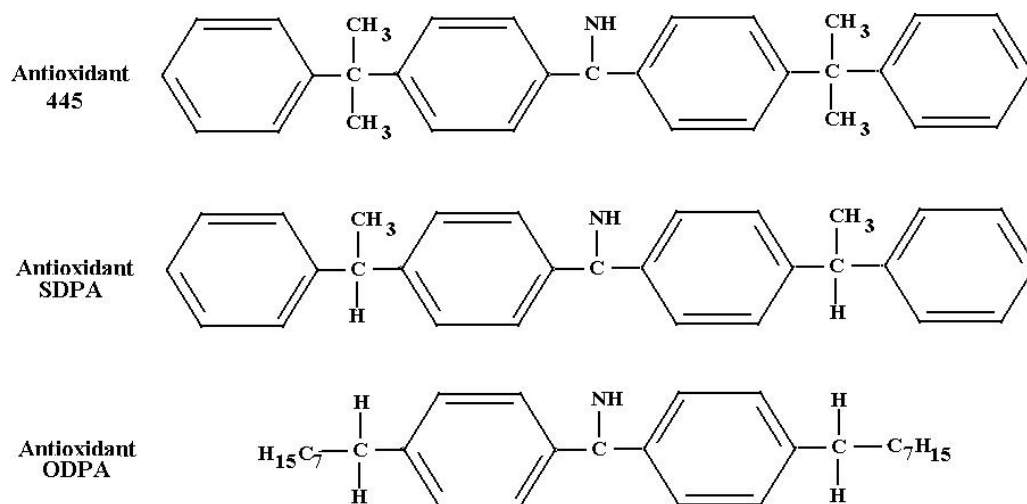


Fig. 3

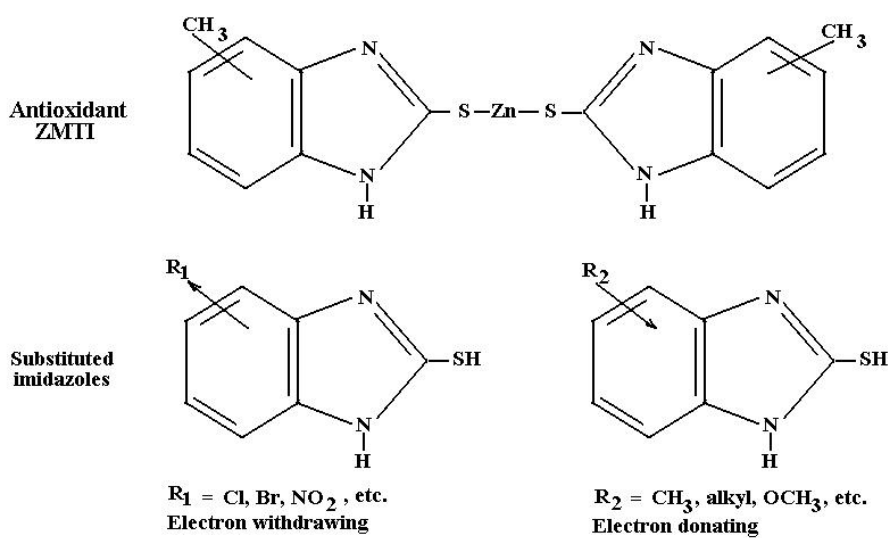


Fig. 4

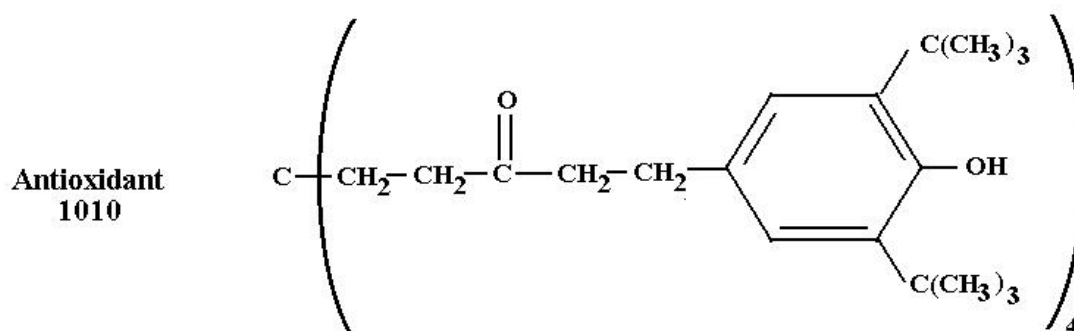


Fig. 5

AO-NDMC (Nickel dimethyldithiocarbamate), shown in Fig. 6, and its Zinc analog are examples of antioxidants of the Secondary type (hydroperoxide decomposer). AO-ZMTI (Zinc 2-mercaptotoluimidazole), shown in Fig. 4 is a commonly used and versatile additive. It probably functions as a radical scavenger, in addition to being a Secondary antioxidant. In many applications it is common to use a combination of Primary and Secondary AO's and ZMTI is often the synergist Secondary AO of choice.

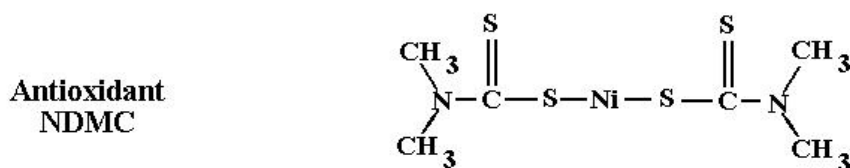


Fig. 6

The amine antioxidants are generally more powerful than the hindered phenols. This is due to a cyclic process which the amine antioxidant undergoes in which a nitroxyl radical is regenerated and consumes more radicals. A drawback of the aminic AO's is that they are oxidized to products which are more discoloring and staining than their hindered phenol counterparts. AO-1010 is exceptional among hindered phenolic AO's. It has one of the highest molecular weights in its class and is non-staining, non-discoloring, and effective in non-black, colorable rubber compounds.

Good reviews of the mechanisms of action of antioxidants are available[1-4]. While antioxidants in general turn out to be stabilizers counteracting the oxidative degerative processes mediated by free radicals as illustrated in Fig. 1, there are special applications requiring refined antioxidant treatment considerations. For example, peroxide curing is a procedure similar to but considered better than vulcanising (that builds sulfur containing cross-links). In peroxide curing, peroxides are used as additives to build cross links between polymer chains, much like the cross links that arise in degradative embrittlement. In these peroxide cured polymers antioxidants still find refined application to moderate and engineer the cross-links. Ferradino has described this application in detail [1]. Similarly, special considerations required in the choice of antioxidants with polyurethanes which are prone to degradation both during processing and end-use, as a result of the combined effects of mechanical shear, thermal-oxidative and UV light exposure have been described in detail by Rota, Schrinner, and Xanthopoulos [2].

Quoting from Petrie[3], Some of the more significant new product development trends in antioxidants include the following:

- (1) A new phosphite secondary antioxidant, based on butyl ethyl propane diol, reputedly yields high activity, solubility, and hydrolytic stability in a range of polymers.
- (2) Lactone stabilizers (derivatives of the benzofuranone family) are claimed to stop the autoxidation process before its starts. They can interrupt the autoxidation cycle earlier than

phenolic and phosphite type stabilizers. These additives are claimed to provide some thermal protection to inert atmospheres, whereas traditional antioxidants are only effective in the presence of oxygen.

(3) Multifunctional antioxidants combine the functionality of both primary and secondary antioxidants in one compound. These materials have only recently become available.

(4) Hydroxylamines act as both primary and secondary antioxidants. They are capable of scavenging carbon-centered radicals.

(5) Antioxidants in the form of liquids and pellets are challenging the powder form. Advantages include low dusting, improved safety, and lower cost.

(6) A new antioxidant based on butyl ethyl propane diol is claimed to have high efficiency and solubility to allow lower concentration levels. It is also claimed to provide improved hydrolytic stability.

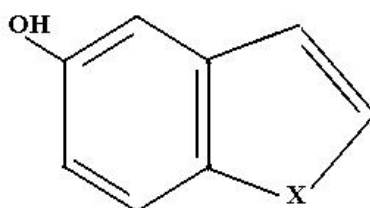
In addition to the reviews mentioned above, some technical details about industrial AO's in use are available from industry websites [5,6].

It is particularly interesting to explore if quantitative structure activity studies can be performed using antioxidant activity (or comparable) data available in the literature and extrapolate from such a study as per established QSAR methods (Hammett equation, etc.) to predict activities of new compounds, not yet used. However, prerequisite data in this regard is not available. A number of studies comparing activities of related structures are available. For instance AO activity (elongation retentions after 70 hrs. at 177 deg. C, in peroxide cured EPDM) comparisons have been made [1] between AO-445, AO-SDPA (styrenated diphenylamine), and AO-ODPA (dioctyl diphenylamine) which have subtle differences in their chemical structures (see [Fig. 3](#)). The elongation retentions were found to be 84, 76, and 65, for AO-445, AO-SDPA, and AO-ODPA, respectively, in contrast to only 10 when no AO is used. Similarly, the Compression Set (70 Hrs. @ 100 deg. C) for these three AO's were measured to be, 14, 15, and 17, respectively, compared to 6 in the absence of any AO. In these above measurements the AO's were used along with AO-ZMTI as synergist. These structural variations, however, do not lend themselves to extrapolation to ring substitutions on AO-445, for instance, except, for the observation that the antioxidant potency depends on 'labile hydrogen availability', estimated by taking into consideration the lability of individual labile hydrogens as well as the total number of available labile hydrogens.

Khanra et al. [7] observed in a study on benzazole derivatives that ring substitution by electron-donating groups (such as methyl, alkyl, methoxy) increase antioxidant activity while electron-withdrawing groups (halogen, nitro) decrease antioxidant activity. Comparing the similarity between AO-ZMTI and imidazole (See [Fig. 4](#)), it is obvious that a similar effect of the substituents can be expected in AO-ZMTI, and in fact, also in the case of AO-445.

Malmstrom [8] has devised methods to synthesise and compare activities of a novel class of antioxidants, 2,3-dihydrobenzo[b]furan-5-ol, and its analogs ([Fig. 7](#)). The table below (reproduced from [8]) summarises the structure activity relation observed by Malmstrom.

**2,3-dihydrobenzo[b]furan-5-ol
& analogs**



X = O
X = S
X = Se
X = Te

Fig. 7

Table: Inhibited rate of peroxidation, R _{inh} , and time of inhibition, T _{inh} , for antioxidants tested in the presence and absence of N-acetylcysteine (NAC)				
Antioxidant	R _{inh} and T _{inh} in the presence of NAC		R _{inh} and T _{inh} in the absence of NAC	
	R _{inh} (M/h) a	T _{inh} (min) b	R _{inh} (M/h) a	T _{inh} (min) b
45a	44	140	46	90
45b	36	180	30	85
45c	36	>300	64	50
45d	17	60	370	0
• -Tocopherol	11	90	10	80
Sulfide	21	70	20	65
Telluride	34	160	370	0

a Rate of peroxidation during the inhibited phase (uninhibited rate ~370 M/h). b Duration of the inhibited phase of peroxidation.

Theoretical studies

In the opinion of the present the best technique available for the current problem, namely to predict AO activity of a particular new (not yet made) analog like any alkylated diphenylamine is through theoretical quantum chemical studies. In these studies the bond dissociation energy (BDE) of the bond connecting the labile hydrogen to the rest of the molecule is evaluated. References [9-14] represent studies of this

type in the literature, but most of the studies till now have been on structures related to biological antioxidants like tocopherol. Articles published by Wright and coworkers [11-14] are particularly interesting. While the molecules of interest are usually too large for treatment by ab-initio quantum chemical methods, Wright has adopted interesting partitioning strategies with highly accurate descriptions of the labile hydrogen region and moderately accurate handling of the rest of the molecule. The present author is equipped to carry out such calculations, if required, on alkylated diphenylamines or other structures of interest.

Data Acquisition

Most of the material used for the present review were obtained through Internet search with judicious search strategies. Several documents are available in the public domain and links have been provided for these in the reference citation. As a rule, only abstracts are accessible freely for the articles published in journals. Full texts are available only to subscribers or for purchase on a 'single article purchase' basis. Full text versions were not obtained for references [15-21], as they appeared not likely to provide the specific details required for a QSAR study in the industrial antioxidant field.

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Edward M. Petrie, Member of SpecialChem Technical Expert Team

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By Joseph J. Fay, Ph. D., Senior Staff Scientist, and Chris Fagouri, Marketing Manager, Ciba Specialty Chemicals, Tarrytown, NY

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