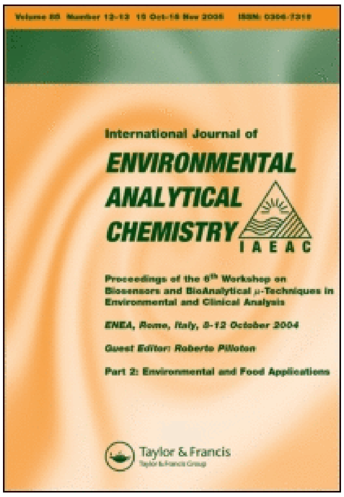

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B. L. Van Duuren[a]
[a] Laboratory of Organic Chemistry and Carcinogenesis Institute of Environmental Medicine New York University Medical Center, New York, N.Y., U.S.A.

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Epoxides, Hydroperoxides and Peroxides in Air Pollution†

B. L. VAN DUUREN

Laboratory of Organic Chemistry and Carcinogenesis
Institute of Environmental Medicine
New York University Medical Center, New York, N.Y. 10016, U.S.A.

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A major source of air pollutants in urban areas is automobile exhaust. Olefins constitute a substantial proportion of the chemicals emitted by this source. Olefins undergo autoxidation and photochemical oxidation in air to hydroperoxides, peroxides, epoxides and other oxygenated aliphatics, frequently of low molecular weight. Long-term carcinogenicity assays of these compounds in mice and rats by various routes of administration have shown that some of these compounds are carcinogenic. Hence, their detection and elimination as air pollutants should be vigorously pursued. This report describes the current status of air pollution research on these compounds, their carcinogenicity, structure-activity relationships and areas which deserve attention in future research. Oxidation products of aromatic hydrocarbon pollutants are also important and will be described.

Aliphatic Hydroperoxides, Peroxides and Epoxides

In 1962, a conference was held in Cincinnati on the analysis of carcinogenic air pollutants. During that symposium, which was published as a monograph,[1] a variety of analytical techniques were described for the isolation and characterization of a long list of aromatic hydrocarbons from polluted air. Also, during the symposium, it was pointed out that oxygenated aliphatic compounds may make a contribution to the carcinogenicity of air pollutant concentrates.[2] At that time we had just started a systematic survey of the carcinogenicity of epoxides, β- and γ-lactones, hydroperoxides and peroxides.

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To date we have tested about fifty compounds of these structural types.[3,4] Although considerable progress was made on structure-carcinogenicity relationships in this series of compounds, almost no progress has been made on their characterization from air pollution sources. This is an unfortunate state of affairs but it is readily explained. In the comprehensive network of air-sampling stations in the United States only particulate matter is collected. Since most of the compounds under discussion here are low molecular weight volatiles, it is unlikely that they will be collected with the particulate matter. Also, there are at present no systematic analytical procedures for their detection and quantitation. Although problems are to be expected in the collection of volatile aliphatic compounds from city air, these problems are largely of an engineering nature and such studies should be undertaken. The present discussion is concerned with the origin of these compounds in air, their mode of formation, and their carcinogenicity or tumor-promoting activity.

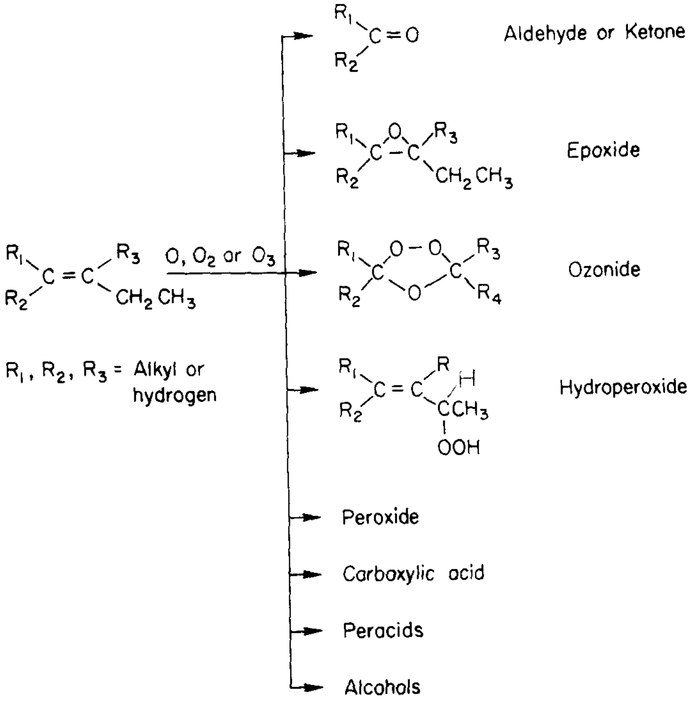


CHART 1 Olefin oxidation products.

Engine exhaust from automobiles, trucks and buses is undoubtedly the major source of olefinic hydrocarbons in air. Although the olefins are probably harmless and non-carcinogenic, their photochemical oxidation products may be more important as airborne carcinogens than are aromatic hydrocarbons. Several schemes have been suggested whereby compounds of these types may be formed in air. Some of the possible products are shown in Chart 1. Olefins which are components of engine exhaust, can readily undergo photochemical oxidation in air via ozonides which can in turn break down to give aldehydes, ketones and alcohols. Epoxides, hydroperoxides, peracids, and peroxides can similarly be formed by reactions involving molecular

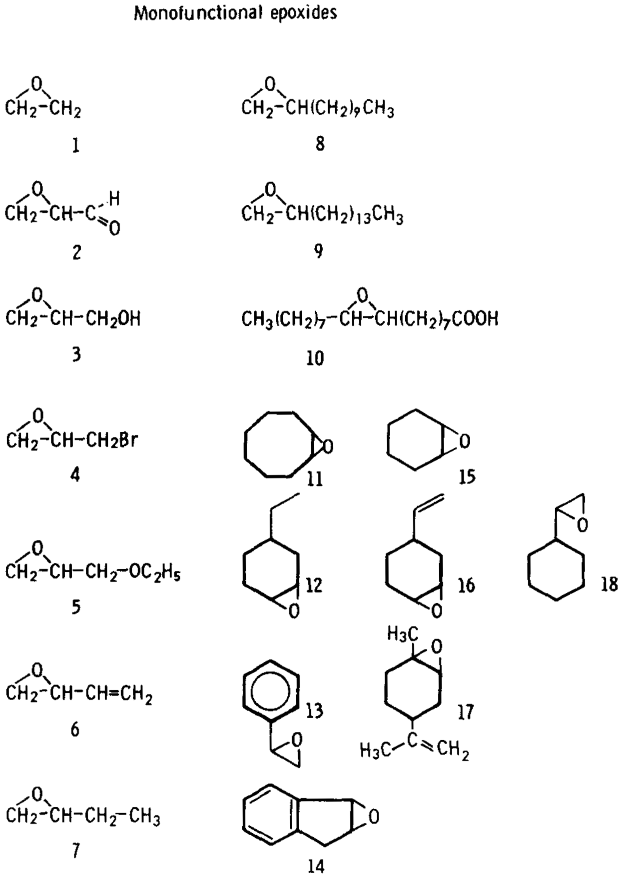


CHART 2 Monofunctional epoxides.

oxygen or activated oxygen species. In addition to these products, oxygenated free radicals are in all probability also produced and these will give rise to a variety of additional products. Some of these compounds are highly reactive and will not remain in the air for any length of time; others will remain for a sufficient length of time to be detected, and to be deleterious to human health. Laboratory studies on olefin oxidation and ozonization have led to the isolation of epoxides, peroxides, aldehydes and ketones.[5]

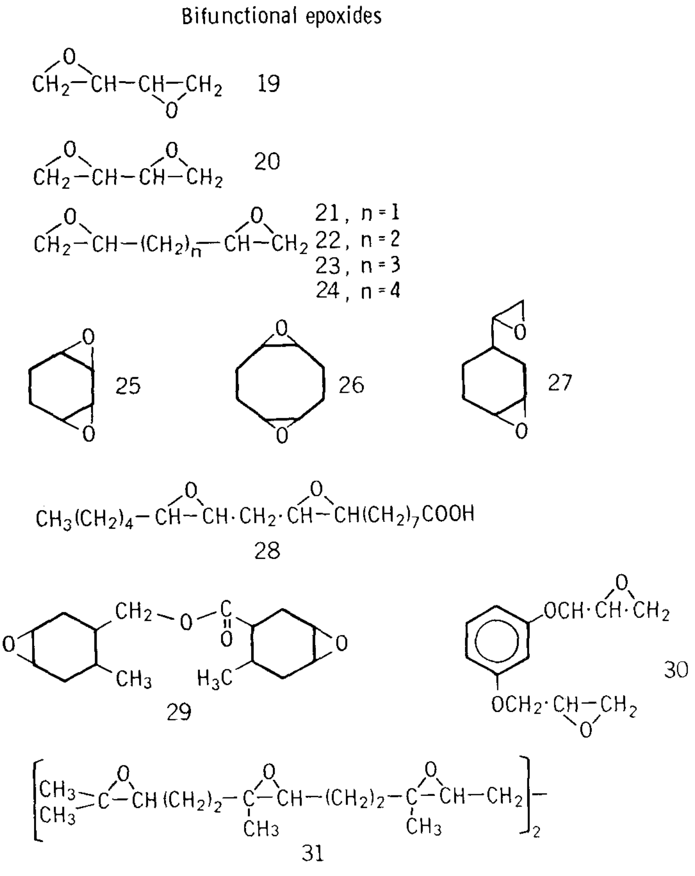


CHART 3 Bifunctional epoxides.

A series of compounds in these categories was tested for carcinogenic activity in mice and rats by various routes of administration.[3,4] The monoepoxides tested are listed in Chart 2 and the diepoxides are shown in Chart 3.

Several features of structure-carcinogenic activity were uncovered.[3,4] Thus, the bifunctional epoxides were frequently carcinogenic, whereas most of their monofunctional analogs were inactive. Some monofunctional agents were active but only when the compound had an adjacent center of unsaturation, *e.g.*, 1,2-epoxybutene-3 (structure 6). It is possible that these compounds become activated *in vivo* to bifunctional agents. Another feature of the active carcinogens is molecular flexibility as shown in Chart 3. The open-chain compounds 19–24 are all carcinogenic, but their more rigid cyclic analogs such as 1,2,3,4-diepoxycyclohexane (structure 25) and 1,2,5,6-diepoxycyclooctane (structure 26) are not. Details on the carcinogenicity testing of these compounds have been reported in earlier publications.[3,4]

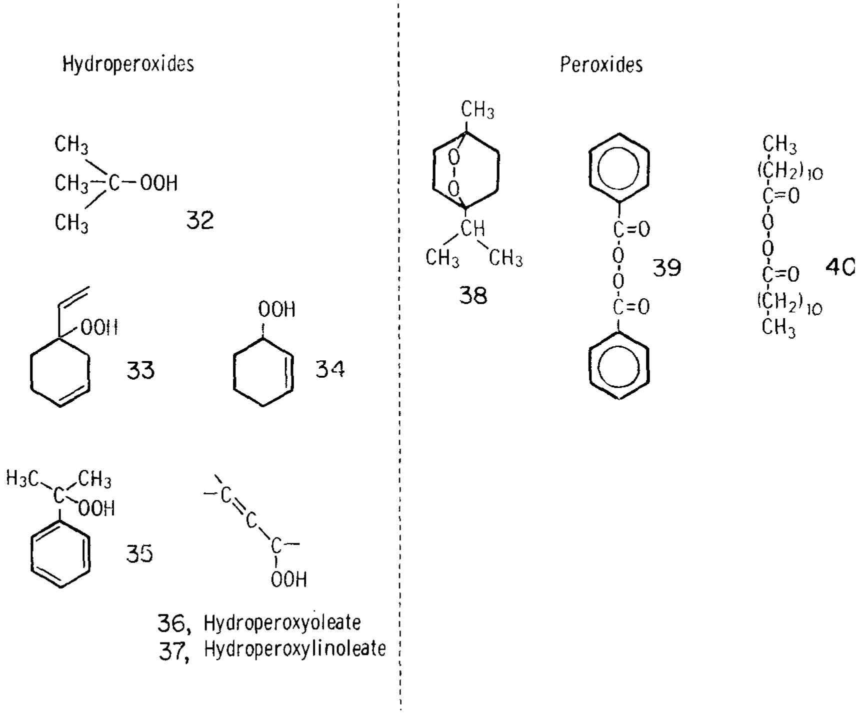


CHART 4 Hydroperoxides and peroxides.

Several hydroperoxide and peroxy compounds have also been tested and found to be carcinogenic. The compounds tested[4] are shown in Chart 4. The carcinogens include cyclohexene hydroperoxide (structure 34), 1-hydroperoxyvinylcyclohex-3-ene (structure 33) and lauroyl peroxide (structure 40).

In view of the obvious importance of these aliphatic compounds, it is imperative that studies be undertaken on the analysis of volatile organic air pollutants.

Photo-oxidation Products of Aromatic Hydrocarbons

A study of the photo-oxidation products of aromatic hydrocarbons is relevant to air pollution for two reasons: firstly, it is important to examine the rate of disappearance of carcinogenic aromatic hydrocarbons from air and, secondly, the photo-oxidation products themselves may have deleterious biological properties, including carcinogenicity.

These products will probably be collected in the particulate matter filters if they are stable enough, and they are therefore more amenable to analytical studies than the aliphatic compounds discussed above. The problem is, however, complicated by the fact that in air pollution the compounds are adsorbed on soot and other airborne particles, and laboratory studies on solutions do not necessarily reflect the situation on adsorbed particles. Only a few studies have been made on oxidation reactions of aromatic hydrocarbons adsorbed on particles.[6,7]

The rate of photo-oxidation of aromatic hydrocarbons adsorbed on airborne particles will show large variations depending on the nature of the particle and conditions of climate. There is also a wide variation in the stability of individual hydrocarbons to photo-oxidation. Benzo(a)pyrene, for example, is very rapidly photo-oxidized, whereas other hydrocarbons, such as chrysene and triphenylene, are more stable. A brief discussion of some of the products that are formed follows.

Anthracene, 41, when adsorbed on silica, is rapidly oxidized to anthraquinone, 42, which upon further oxidation gives 1,4-dihydroxy-9,10-anthraquinone,[6] 43, as shown in Chart 5. Pyrene, 44, is oxidized under the same conditions to the 1,6-(structure 45) and 1,8-dione (structure 46), as shown in Chart 5.

It is also important to consider the action of ozone on these compounds. Various types of products can be obtained from the ozonolysis of aromatic hydrocarbons; an example is benz(a)anthracene, 47, which gives the 5,6-ozonide, 48, and the 7,14-endoozonide structure, 49, which in turn degrades to the 7,14-quinone, 51, and phthalic acid, 52,[8] as shown in Chart 6. Benzo(a)pyrene in the same reaction yields a mixture of the 3,6-, 1,6- and 4,8-diones.

One-electron oxidation of aromatic hydrocarbons also occurs readily. The initial products are unstable radical cations which react rapidly with nucleophiles or with oxygen. Other autoxidation products which readily formed from aromatic hydrocarbons include the endoperoxides, for example, the

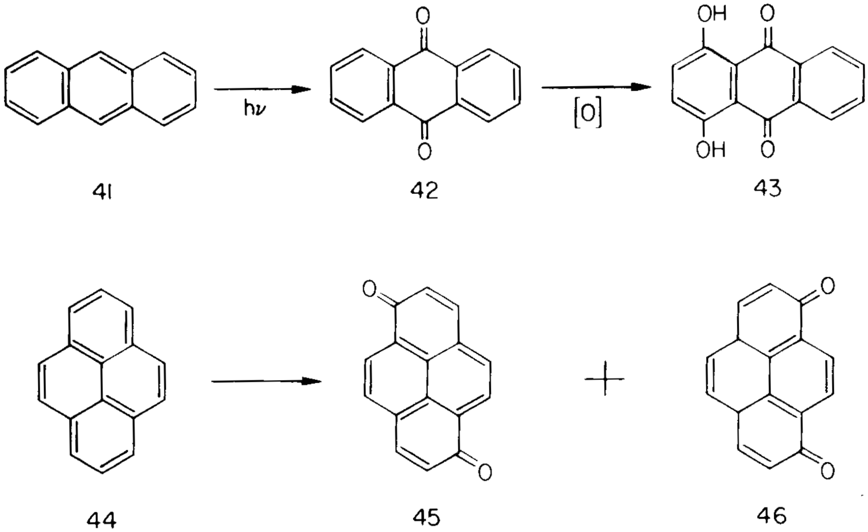


CHART 5 Oxidation products of anthracene and pyrene.

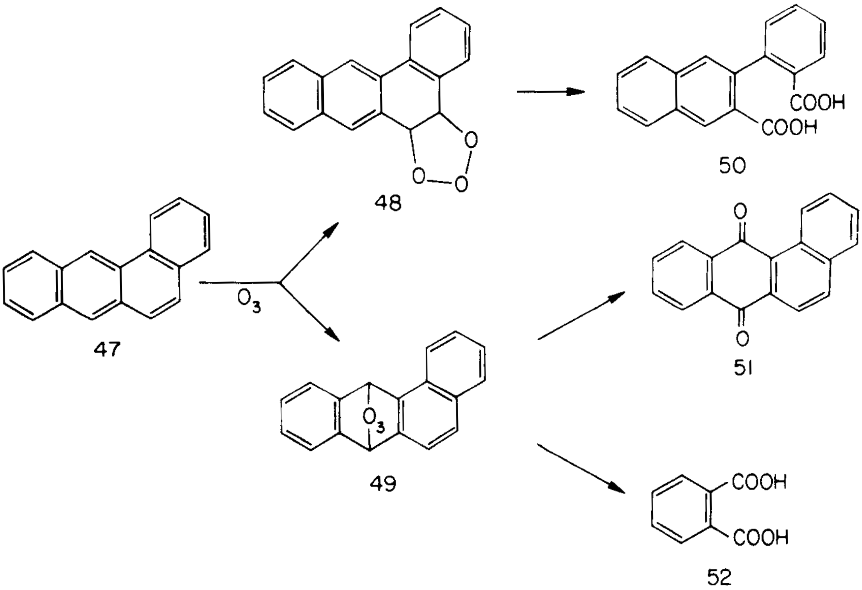
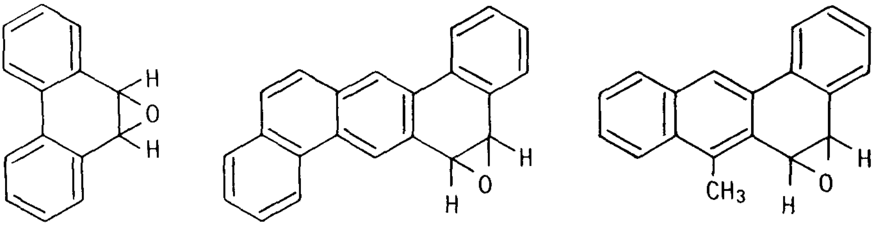


CHART 6 Ozonization products of benz(a)anthracene.

endoperoxide of naphthacene. Hydroperoxides of aromatic hydrocarbons have not been synthesized to date. Epoxides of several aromatic hydrocarbons have been synthesized in the laboratory[9,10] as shown in Chart 7 and two of these have been shown to have weak carcinogenic activity.[3] It is not known whether they occur as air pollutant oxidation products of the hydrocarbons.

From the point of view of biological activity, it is not expected that quinones are carcinogenic and they probably represent true photochemical detoxification products. Nothing is known of the carcinogenicity of ozonides and endoperoxides. However, some phenols and polyphenols derived from aromatic hydrocarbons may be weakly carcinogenic. The compound 1,8-dihydroxy-9-anthrone, for example, has been shown to be a potent tumor-promoting agent.[11]



53 54 55

CHART 7 Synthetic aromatic hydrocarbon epoxides.

Thus, it is clear that some oxidation products may be more active biologically than the parent hydrocarbon, and further research is needed on this important aspect.

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