

Peroxides

XII.[☆] Gas-liquid and high-performance liquid chromatographic analysis of aliphatic hydroperoxides and dialkyl peroxidesThomas A. Foglia*, Leonard S. Silbert^{☆☆} and Peter D. Vail

ABSTRACT

The chromatographic resolution of 1-alkyl hydroperoxides and di-1-alkyl peroxides by either gas-liquid chromatography and/or high-performance liquid chromatography (HPLC) was investigated. The chromatographic methods developed were applied to the compositional analysis of hydroperoxides and dialkyl peroxides in reaction mixtures and to purity determinations. The effect of aliphatic peroxide structure based on the conformations imposed by the dihedral angle of the peroxide bond has strong implications for peroxide resolutions in HPLC compared to their non-peroxy analogues. Comparison of the chromatographic data for peroxide content with that obtained by iodometry show that the methods developed are suitable for peroxide determinations.

INTRODUCTION

Numerous methods of peroxide determination have been devised to cover the range of reactivities shown by diverse peroxide structures. For an aliphatic series of derivatives, the order of increasing O-O bond strength parallels the following decreasing order of reactivity [2,3]: peroxy acid [R-C(O)-O-O-H]; diacyl peroxide [R-C(O)-O-O-C(O)-R]; hydroperoxide (R-O-O-H); perester [R-C(O)-O-O-R]; dialkyl peroxide (R-O-O-R). This peroxide sequence depicts a decreasing reactivity in liberating

iodine from iodide ion [4], and increasing stability based on polarographic half-wave potential ($-E_{1/2}$) and energy of activation (E_a) for decomposition [3]. Because of this wide difference in reactivity, no general analytical method for all peroxide classes has appeared in the literature.

Gas-liquid chromatography (GLC) has been a sensitive method of peroxide determination [5], although the relatively low thermal stability of the peroxygen bond has limited the utility of GLC analysis of peroxides to members of low molecular mass, generally below 10 carbon atoms [5-11] and at column temperatures below 100°C. Hydroperoxides are stable to about 90°C [12] but readily decompose to alkyl alcohols and carbonyl compounds (aldehydes from primary alkyl hydroperoxides and ketones from secondary and tertiary alkyl hydroperoxides). This sensitivity of hydroperoxides to thermal de-

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Methods

Gas-liquid chromatography. The instrument was a Hewlett-Packard (Avondale, PA, USA) Model 5830A gas chromatograph equipped with a capillary inlet system and a flame ionization detector (200°C). The quartz capillary columns were 12 m × 0.2 mm coated with 0.33- μ m methyl silicone fluid (HP-101) and a 4 m × 0.2 mm coated with 0.33- μ m 5% cross-linked phenyl methyl silicone fluid (HP-5). Initial column temperature for the 12-m column was 50°C for hexyl hydroperoxide and 80°C for octyl hydroperoxide, decyl hydroperoxide, and dodecyl hydroperoxide (injector port, 140°C). The carrier gas was helium with a linear velocity of 22.5 cm s⁻¹ at a split ratio of 60:1. Dodecyl hydroperoxide was also analyzed on a 4-m column at 40°C (injector port, 140°C) tetradecyl and hexadecyl hydroperoxides at 110°C (injector port, 160°C) with helium at linear velocity of 12 cm s⁻¹. All components in reaction mixtures were resolved by temperature programming at 2°C min⁻¹ except for hexadecyl hydroperoxide at 5°C min⁻¹ to a final temperature of 150°C, and the important components were identified by comparison with available standards. For differentiation of dialkyl ethers from dialkyl peroxides, the former were prepared by the alcohol alkylation method of Barluenga *et al.* [29].

High-performance liquid chromatography. The HPLC solvent delivery systems used were a Beckman (San Ramo, CA, USA) Model 110A solvent delivery module equipped with an Altex 210 loop injector with either a 20- μ l or 100- μ l sample loop and a Waters differential refractometer detector, Model R401 (Waters Assoc., Milford, MA, USA) and a Hewlett-Packard Model 1090 solvent delivery module equipped with a Rheodyne Model 7125 loop injector with a 20- μ l loop and a Tracor (Austin, TX, USA) Model 945 flame ionization detector operated at 80°C. The HPLC columns used were a 25 cm × 4.6 mm I.D. stainless-steel column prepacked with 5- μ m silica (Zorbax SIL, DuPont, Wilmington, DE, USA) or 5- μ m ODS (Altex Ultra-sphere, Deerfield, IL, USA) for analytical HPLC. Semipreparative isolation of 1-alkyl hydroperoxides was made on a Dynamax (Rainin, Woburn, MA, USA) prepacked 8- μ m silica

column, 25 cm × 10 mm I.D. The integrator/recorder was a Hewlett-Packard Model 3396A. Samples were dissolved in mobile phase at 5 mg ml⁻¹ for analytical HPLC and 100 mg ml⁻¹ for semi-preparative HPLC. Response factors to the refractive index and flame ionization detectors were obtained on the purified peroxides over the range of 0.05–0.5 mg. Hydroperoxides were eluted isocratically from the silica columns with hexane-isopropanol (98:2, v/v) at a flow-rate of 1 ml min⁻¹ (analytical) or 3 ml min⁻¹ (semi-preparative HPLC). Dialkyl peroxides were analyzed isocratically on the ODS column with acetone-acetonitrile (70:30, v/v) at a flow-rate of 0.8 ml min⁻¹.

Iodometry. Iodometric analysis of hydroperoxides by the Wheeler method [4] is the liberation of iodine by iodide reduction of easily reducible peroxides in acetic acid-chloroform solution. The method was recently modified for its application to dialkyl peroxides by incorporating catalysis with perchloric acid or ferric ion in acetic acid at 80–100°C [1].

RESULTS AND DISCUSSION

Hydroperoxides

We have recently developed two new methods of preparing alkyl hydroperoxides, each of which has its advantages [22]. In one method, 1-alkyl hydroperoxides were obtained by perhydrolysis of primary alkyl mercuric tetrafluoroborate which produced primary hydroperoxide with minor amounts of positional hydroperoxide isomers (3%), dialkyl ether and dialkyl peroxide in addition to aldehyde and alkanol. In these studies GLC analysis of the reaction products on a 12-m capillary column was found to be highly efficient for the resolution of hydroperoxides from their reaction co-products. For example, Fig. 1 illustrates the resolution of 1-, 2- and 3-hexyl hydroperoxide isomers and the longer retention time co-products, dihexyl ether and dihexyl peroxide. Alternatively, perhydrolysis of a primary alkyl triflate (trifluoromethanesulfonate) forms the primary hydroperoxide with no formation of positional isomers. Although triflate and hydroperoxide have similar GLC reten-

iodometric data for the series up to decyl (Table I) were in reasonable agreement to within 3% average. For longer chain hydroperoxides, dodecyl and larger, significant thermal decomposition was observed for each GLC value compared to the corresponding iodometric value (Table I).

Since hydroperoxide reaction products beyond decyl could not be quantified by GLC, the longer-chain hydroperoxides were determined by HPLC in two instruments separately equipped with refractive index (RID) or flame ionization (FID) detection systems and interchangeable reversed-phase (RP) or normal-phase (NP) columns. The hydroperoxides also were determined iodometrically for comparison with the HPLC chromatographic quantitations. The selected data presented in Table I are typical for the series of hydroperoxide preparations. RP/FID was effective only for non-volatile compounds which were not thermally evaporated on the heated evaporative belt that functions for solvent removal prior to sample entry into the detector. The RP/FID values were low compared to the iodometric results but the former increased in value with increasing chain length which indicated their relative degree of volatility. The iodometric and reversed-phase HPLC values for hexadecyl hydroperoxide were in good agreement.

The homologous series of alkyl hydroperoxides and their corresponding alcohols were chromatographed isocratically in reversed-phase HPLC. The two series are graphically presented in Fig. 2 where $\log k'$ (capacity factor) vs. carbon number of alkyl residues depict the linearity in their order of elution. In this series, the alcohol has the longer retention time for each hydroperoxide-alcohol analogue pair. The alcohol and hydroperoxide series were obtained under identical conditions for comparison whereas literature data reported for the alcohols [30-32] were unusable for this purpose.

An example of a normal-phase HPLC separation of a hydroperoxide preparation is given in Fig. 3A showing alcohol as more strongly retained than hydroperoxide. Normal-phase hydroperoxide values with either FID or RID were low for all examples examined, although RID

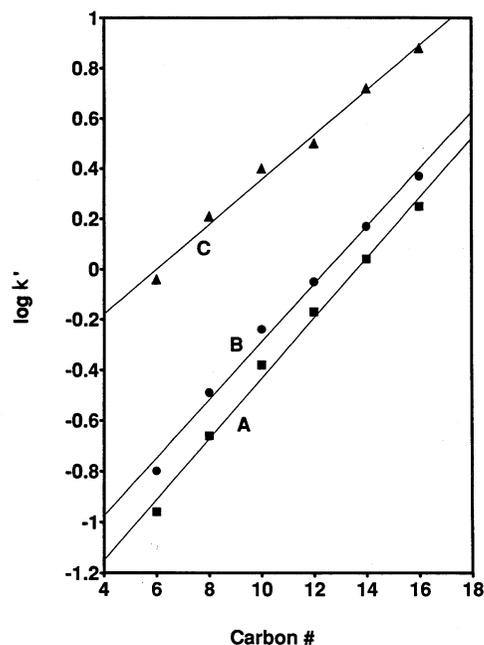


Fig. 2. Plot of $\log k'$ vs. carbon No. (#) of alkyl chain separated by RP-HPLC. A = Alkyl hydroperoxide; B = alkyl alcohols; C = dialkyl peroxides, where carbon No. is half total carbons of dialkyl peroxide.

gave the higher values. The NP/RID method introduced a large negative peak [33,34] with a corresponding uncertainty in the quantitation. This negative peak arises from solvent and pressure effects. Assuming the negative peak contained no overlapping component of identical retention time, the peroxide results could be

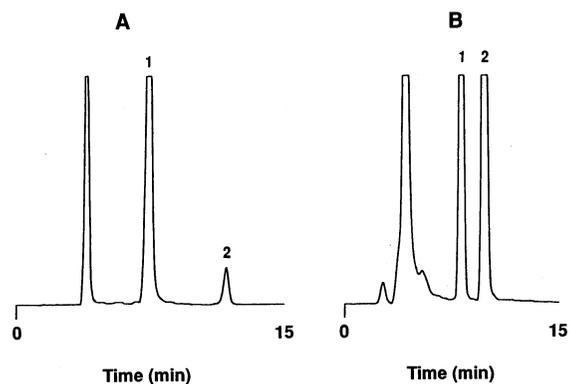
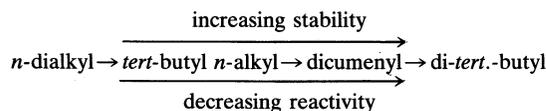


Fig. 3. HPLC-FID: (A) normal-phase (decyl hydroperoxide and decyl alcohol); (B) reversed-phase (didecyl peroxide and didecyl ether). Peaks: (A) 1 = $R_{10}OOH$, 2 = $R_{10}OH$; (B) 1 = $R_{10}OOR_{10}$, 2 = $R_{10}OR_{10}$.

represents the inverse of the hydroperoxide analyses whereby iodometry functioned as the criterion for the chromatographic values.

Table II summarizes these results for which there is good agreement for all the compounds listed except the C₁₂-C₁₆ members. The latter failed to achieve quantitation in the heated acetic acid solution because of poor solubility and decomposition within the melted sample globules. The table includes additional representations of dialkyl peroxide structures analyzed iodometrically. Each class of normal to tertiary alkyl peroxide required specific analytical conditions which permitted the arrangement of an order of increasing stability and decreasing reactivity as follows:

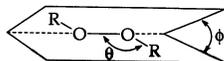


Peroxide structural effects

Peroxides have a dihedral angle as a characteristic structural feature that twists the O-O bond into opposing planes that is aptly described as an open book model (Fig. 5A). The dihedral angle leads to conformations in different peroxide structures in which this angle is enlarged or compressed [35].

Peroxides and their non-peroxy analogues

A



B

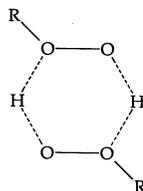


Fig. 5. (A) Structure of peroxides (R=H, alkyl, acyl); ϕ = dihedral angle; θ = R-O-O angle. (B) Cyclic dimer of alkyl hydroperoxide in solution.

were resolved in GLC with the former having the longer retention time in accordance with the peroxide's higher molecular mass. Both the alkyl hydroperoxide and dialkyl peroxide were eluted at longer retention times than their corresponding alcohols and dialkyl ethers, respectively. Resolution of the isomeric di-1-hexyl and 1-butyl 1-octyl peroxides, the latter having the longer retention time, may be explained in terms of the dihedral angle inducing the longer octyl chain into conformations engaging Van der Waals interactions more extensively than the hexyl chain, *i.e.*, the longer the chain, the greater the degree of interaction and the longer the retention time.

By contrast in HPLC, alkyl hydroperoxides elute earlier (less retained) than their corresponding alkyl alcohol analogues in both reversed-phase (Fig. 2) and normal-phase (Fig. 3A) chromatography. Primary hydroperoxides dimerize to an intermolecular hydrogen-bonded cyclic structure (Fig. 5B) in contrast to their alcohol counterpart (dimers and polymers) [36] presumably arising from the greater acidity of the hydroperoxide and the increased stability of the pseudo six-membered ring structure. Accordingly, for normal-phase HPLC, the free terminal hydroxyl group of alcohol hydrogen bonds more strongly to silica leading to increased elution volumes.

In the case of dialkyl peroxides, the dihedral angle about the peroxy bond (Fig. 5A), which exceeds 100°, projects the two alkyl chains at approximately right angles to each other. The alkyl chains are thereby skewed into conformations that diminish their Van der Waals interactions with the octadecyl groups of the bonded stationary phase. The conformations are expressed as a foreshortening of chain length [2] compared to the more linear extension of the non-peroxide analogue. Hence, dialkyl peroxides in HPLC have shorter retention times than their non-peroxide analogues.

The generality of the foregoing relationship may be applied to peroxides of all classes as is further illustrated by the *tert.*-butyl permyristate/*tert.*-butyl myristate pair (Fig. 6) for which the ester was more strongly retained in reversed-phase HPLC. This same relationship would be

- 11 P. Schieberie, W. Maier, J. Firi and W. Grosch, *J. High Resolut. Chromatogr. Chromatogr. Commun.*, 10 (1987) 588.
- 12 C.F. Cullis and E. Fersht, *Combustion Flame*, 7 (1963) 185.
- 13 A.F. Shuskunova, *J. Chromatogr.*, 365 (1986) 417.
- 14 S. Bukata, L. Zabrocki and M. McLaughlin, *Anal. Chem.*, 35 (1963) 885.
- 15 S. Hyden, *Anal. Chem.*, 35 (1963) 113.
- 16 G.A. Blondin, B.D. Kulkarni, J.P. John, R.T. van Allen, P.T. Russell and W.R. Nes, *Anal. Chem.*, 39 (1967) 36.
- 17 W.J.M. van Tilborg, *J. Chromatogr.*, 115 (1975) 616.
- 18 L.A. Cornish, R. Ferris and J.E. Paterson, *J. Chromatogr. Sci.*, 19 (1981) 85.
- 19 P. Jonvel and G. Andermann, *J. Chromatogr.*, 298 (1984) 193.
- 20 M.O. Funk, Jr. and W.J. Baker, *J. Liquid Chromatogr.*, 8 (1985) 663.
- 21 C. P. Patel and S. Lilly, *LC · GC*, 6 (1988) 425.
- 22 T.A. Foglia and L.S. Silbert, *J. Am. Oil Chem. Soc.*, 69 (1992) 151.
- 23 T. Foglia and L.S. Silbert, *Synthesis*, (1992) 545.
- 24 O.L. Magelli and C.S. Sheppard, in D. Swern (Editor), *Organic Peroxides*, Vol. 1, Wiley-Interscience, New York, 1970, Ch. 1, p. 1.
- 25 R. Hiatt, in D. Swern (Editor), *Organic Peroxides*, Vol. 2, Wiley-Interscience, New York, 1971, Ch. 1, p. 1.
- 26 R. Hiatt, in D. Swern (Editor), *Organic Peroxides*, Vol. 3, Wiley-Interscience, New York, 1972, Ch. 3, p. 1.
- 27 R.D. Mair and A.J. Graupner, *Anal. Chem.*, 36 (1964) 194.
- 28 L.S. Silbert and D. Swern, *J. Am. Chem. Soc.*, 81 (1959) 2364.
- 29 J. Barluenga, L. Alonso-Cures and G. Asensia, *Synthesis*, (1979) 962.
- 30 F.E. Lockwood, L.J. Matienzo and B. Sprissler, *J. Chromatogr.*, 262 (1983) 397.
- 31 J.E. Parkin, *J. Chromatogr.*, 287 (1984) 457.
- 32 J.E. Parkin, *J. Chromatogr.*, 314 (1984) 488.
- 33 K. Šlais and M. Krejčí, *J. Chromatogr.*, 91 (1974) 161.
- 34 L.R. Snyder and J.J. Kirkland, *Introduction to Modern Chromatography*, Wiley, New York, 2nd ed., 1979, p. 810.
- 35 L.S. Silbert, in D. Swern (Editor), *Organic Peroxides*, Vol. 2, Wiley-Interscience, New York, 1971, Ch. 7, p. 637.
- 36 L.S. Silbert, in D. Swern (Editor), *Organic Peroxides*, Vol. 2, Wiley-Interscience, New York, 1971, Ch. 7, pp. 742 and 778.
- 37 W.H.T. Davison, *J. Chem. Soc.*, (1951) 2456.
- 38 P.A. Giguire and A.W. Olmos, *Can. J. Chem.*, 30 (1952) 821.