Secondary Organic Aerosol Formation from Isoprene: Selected Research, Historic Account and State of the Art

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Abstract: In this review, we cover selected research on secondary organic aerosol (SOA) formation from isoprene, from the beginning of research, about two decades ago, to today. The review begins with the first observations of isoprene SOA markers, i.e., 2-methyltetrols, in ambient fine aerosol and focuses on studies dealing with molecular characterization, speciation, formation mechanisms, and source apportionment. A historic account is given on how research on isoprene SOA has developed. The isoprene SOA system is rather complex, with different pathways being followed in pristine and polluted conditions. For SOA formation from isoprene, acid-catalyzed hydrolysis is necessary, and sulfuric acid enhances SOA by forming additional nonvolatile products such as organosulfates. Certain results reported in early papers have been re-interpreted in the light of recent results; for example, the formation of C₅-alkene triols. Attention is given to mass spectrometric and separation techniques, which played a crucial role in molecular characterization. The unambiguous structural characterization of isoprene SOA markers has been achieved, owing to the preparation of reference compounds. Efforts have also been made to use air quality data to estimate the influence of biogenic and pollution aerosol sources. This review examines the use of an organic marker-based method and positive matrix factorization to apportion SOA from different sources, including isoprene SOA.

Keywords: particulate matter; secondary organic aerosol; isoprene; 2-methyltetrols; 2-methylglyceric acid; C₅-alkene triols; IEPOX; organosulfates; source apportionment

1. Introduction

In this review, selected research on secondary organic aerosol (SOA) from isoprene (2-methyl-1,3-butadiene, C₅H₈) will be covered from the beginning of research to today. Unlike SOA research from monoterpene such as α-pinene, SOA research from isoprene started much later, with the discovery of marker compounds, the 2-methyltetrols, which have retained the C₅-isoprene skeleton. By now, it is very well established that isoprene is a precursor for SOA, but there has been a time that it was widely accepted that isoprene only resulted in volatile organic compounds (VOCs) upon photo-oxidation in the atmosphere. It was then not surprising that the discovery of SOA from isoprene met with some criticism in the atmospheric research community. The literature on isoprene SOA research is very large, so it is impossible in this review to deal with most papers on this topic. A search on the web-of-science with 'isoprene' and 'secondary organic aerosol' as topics led to a number of over 1000, with the paper on the discovery of the 2-methyltetrols in Amazonian aerosols the second most cited one [1]. This review begins with the first observations of isoprene SOA marker compounds in ambient aerosol and mainly focuses on studies dealing with molecular characterization, speciation, formation mechanisms, and source apportionment. In this review, the term 'marker' is preferred instead of the term 'tracer' because organic compounds in the atmosphere generally do not fulfill the requirement of preservation...
(e.g., due to reactions decreasing their concentrations in the atmosphere). By definition, an atmospheric tracer is “an entity which preserves its identity as it moves with the air from a known source, where the tracer is created or otherwise introduced into the atmosphere, to a known sink where it is destroyed or removed from the atmosphere” [2].

Pathways leading to SOA formation have been intensively explored during the past two decades. The current status is briefly summarized in Figures 1–3. Comprehensive reviews are available where the topics of the formation, mass yield, modelling and measurement of isoprene SOA have been documented [3–5].

![Formation pathways of isoprene SOA at low-NOX. For simplicity, only dominant pathways are presented. Dimers and degradation products of methyltetrol organosulfates (e.g., C5-alkene triols) are not included (adapted from Surratt et al., 2010 [6]). The four stereoisomeric forms of the 2-methyltetrols are shown in the box; the 2-methyltetrols occur in two diastereoisomeric forms, 2-methylthreitol and 2-methylerythritol, and each of them has two enantiomers. Also shown are MW 212 and 214 organosulfates, formed by further processing of 2-methyltetrol-related MW 216 organosulfates.](image-url)

**Figure 1.** Formation pathways of isoprene SOA at low-NOX. For simplicity, only dominant pathways are presented. Dimers and degradation products of methyltetrol organosulfates (e.g., C5-alkene triols) are not included (adapted from Surratt et al., 2010 [6]). The four stereoisomeric forms of the 2-methyltetrols are shown in the box; the 2-methyltetrols occur in two diastereoisomeric forms, 2-methylthreitol and 2-methylerythritol, and each of them has two enantiomers. Also shown are MW 212 and 214 organosulfates, formed by further processing of 2-methyltetrol-related MW 216 organosulfates.
Figure 2. Formation pathway leading to 2-methyltetrols at high-NOx (adapted from Sato, 2008 [7], copyright (2008), with permission from Elsevier).

Figure 3. Formation pathway of isoprene SOA via methacrolein at high-NOx. Abbreviations: MACR: methacrolein; MAE: methacrylic acid epoxide; 2-MG: 2-methylglyceric acid; MPAN: methacryloylperoxynitrate (adapted from Lin et al., 2013 [8]).
2. Early Research (2004–2014): First Observations, Laboratory Studies, Field Monitoring Studies, Quantitation, and Mechanistic Insights

2.1. First Observations

The molecular characterization of isoprene SOA marker compounds, i.e., the 2-methyltetrols, occurred at the start of intensive research on SOA formation from isoprene almost two decades ago [1]. These compounds were discovered in fine particulate matter (PM; PM$_{2.5}$ and PM$_{10}$, PM with an aerodynamic diameter $\leq 2.5$ µm and 10 µm) that was collected in the Amazon region, where isoprene emissions from broadleaf trees are estimated to be very high [9]. Isoprene is quantitatively the most important of the biogenic VOCs, with an estimated global annual emission of about 400–600 TgC. Terrestrial plant foliage is a source of $>$90% of atmospheric isoprene and it is generally assumed that tropical forests provide most of the global isoprene budget. For the chemical characterization of the 2-methyltetrols, use was made of capillary gas chromatography/mass spectrometry (GC/MS), electron ionization (EI), and the derivatization of polar compounds into trimethylsilyl derivatives. Structurally informative EI and methane chemical ionization (CI) spectra were obtained and interpreted in detail, but to support the structural proposal and unambiguous identification of the proposed organic compounds, reference compounds were also synthesized [1,10]. A tentative formation mechanism involving the gas-phase photo-oxidation of isoprene with the OH radical was proposed, but later on, this mechanism had to be revised [6,11]. The 2-methyltetrols occur in two diastereoisomeric forms, 2-methylthreitol and 2-methylerythritol in a ratio of about 1:3, which upon trimethylsilylation are separated by capillary GC, and each of them exists in two enantiomeric forms (Figure 1). It was not realized at that time that the 2-methyltetrols detected in PM were likely, to a major extent, to be in the form of sulfate esters [6,12], because sulfate esters are not stable upon trimethylsilylation (an acid-catalyzed procedure) and are converted into trimethylsilyl esters. Following the detection of 2-methyltetrols in ambient fine aerosol, laboratory photo-oxidation experiments with isoprene were conducted under controlled conditions and molecular evidence was provided for SOA formation, as discussed in Section 2.2. In addition, the SOA mass yield from isoprene was re-evaluated in laboratory photo-oxidation smog chamber experiments under different conditions, e.g., [13,14] (for a review, see [3]). Even with a low SOA mass yield, the total formation of SOA from isoprene in the ambient atmosphere may be very high and contribute substantially to global SOA production, given the high emission rates of isoprene in forested regions. The SOA yield from isoprene is strongly acid-dependent and closely related to the particle-phase acidity, e.g., [15] but decreases upon increasing humidity, e.g., [16].

2.2. Laboratory Studies

The first laboratory photo-oxidation experiments were performed at the National Exposure Laboratory of the United States Environmental Protection Agency in Research Triangle Park (NC, USA) by Edward Edney, Tadeusz Kleindienst and coworkers, and the conditions chosen simulated regional atmospheric conditions (i.e., in the presence of NO$_x$ (NO + NO$_2$) and SO$_2$) [17]. It was suggested that the formation of the 2-methyltetrols was likely acid-catalyzed, although the precise role of sulfuric acid was not clear at that time. It was already evident from this first laboratory study that the formation of 2-methyltetrols was strongly acid-dependent and enhanced in the presence of sulfuric acid. In addition to the 2-methyltetrols, it was also demonstrated that 2-methylglyceric acid, which has partially retained the isoprene skeleton, was formed under the selected conditions. While other polar compounds related to the 2-methyltetrols could also be detected in ambient PM, i.e., C$_3$-alkene triols [18], it was puzzling why these compounds were absent from the isoprene SOA that was generated in the presence of NO$_x$ [17]. Later, it became clear that these compounds are characteristic for low-NO$_x$ conditions [19]. However, it was shown recently that they might be formed in part by the degradation of methyltetrol organosulfates [20]. More comprehensive laboratory experiments were started in 2004 by John Seinfeld and coworkers, at the California Institute of Technology (Pasadena, CA, USA). They were in
a later stage and are still actively pursued in the group of Jason Surratt at the University of North Carolina at Chapel Hill (USA). Photo-oxidation experiments were performed with isoprene with and without the addition of NO to reflect polluted and clean pristine conditions, and markedly different products were formed [19,21]. In the absence of NO, evidence was found for the formation of both the 2-methyltetrols and the C₅-alkene triols, while in the presence of NO, isoprene was mainly transformed to 2-methylglyceric acid and a multitude of derivatives, including oligomers (di- and trimers) and nitrate, formate and acetate esters. Analytical techniques that were currently in use at that time played a crucial role: for the detection of the 2-methyltetrols, the C₅-alkene triols, and 2-methylglyceric acid and its oligomers, gas chromatography (GC/EI-MS) with prior trimethylsilylation, was performed, while for the detection of derivatives of 2-methylglyceric acid, use was made of liquid chromatography (LC) combined with electrospray ionization MS in the negative ion mode (–)ESI-MS or direct injection (–)ESI-MS. It is worth mentioning that at that stage, the detailed mechanisms by which the 2-methyltetrols, the C₅-alkene triols and 2-methylglyceric acid were formed were not known. With regard to the structural characterization, the unambiguous identification of the 2-methyltetrols was achieved by organic synthesis of the proposed compounds. This approach was not followed for the C₅-alkene triols and these compounds were tentatively characterized using detailed interpretation of the EI and methane CI mass spectra of their trimethylsilyl derivatives [18]. The identification of 2-methylglyceric acid was straightforward because this compound was not new and had been characterized before as a human urinary metabolite. Employing GC/EI-MS with prior trimethylsilylation 2-methylglyceric was indicated with high probability using a MS library search, and later confirmed with a synthesized reference compound [22].

2.3. Field Monitoring Studies

Following the laboratory studies mentioned above, numerous field studies have been conducted where isoprene SOA markers were measured in fine ambient aerosol (PM₂.₅ or PM₁₀) and where mainly 2-methyltetrols, C₅-alkene triols and 2-methylglyceric acid were measured using GC/EI-MS with prior trimethylsilylation. As an example, we select a study conducted in the Brazilian Amazon region, where the emission of isoprene is estimated to be very high [23]. Measurements were performed on aerosols that were collected at a pasture site (Rondônia, Brazil) using a high-volume dichotomous sampler (HVDS) within the framework of the 2002 LBA-SMOCC (Large-Scale Biosphere Atmosphere Experiment in Amazonia—Smoke Aerosols, Clouds, Rainfall, and Climate: Aerosols from Biomass Burning Perturb Global and Regional Climate) campaign. The campaign spanned the late dry season (biomass burning), a transition period, and the onset of the wet season (clean conditions). Figure 4 illustrates the power of GC/EI-MS with prior trimethylsilylation for separating isoprene SOA markers with a total ion chromatogram obtained for PM₂.₅ collected during the transition period of the 2002 LBA-SMOCC campaign. The concentrations of the 2-methyltetrols and the C₅-alkene triols were higher in the dry and transition periods than in the wet period; the isoprene SOA marker compounds showed an average concentration of 250 ng m⁻³ during the dry period versus 157 ng m⁻³ during the transition period and 52 ng m⁻³ during the wet period. The percentage of organic carbon (OC) attributable to the isoprene SOA marker compounds was 0.45% in the dry period, 0.83% in the transition period and 1.55% in the wet period. In that study, 2-methylglyceric acid was not measured because its concentrations were very low compared to those of the selected marker compounds (<1 ng m⁻³). The ratio between the threo and erythro diastereoisomers of the 2-methyltetrols was on average 0.30 and a statistically significant correlation was found between them (R = 0.94), consistent with their formation through the same aerosol process, i.e., photo-oxidation of isoprene. Again, the detailed mechanism by which the selected isoprene SOA marker compounds were formed was not known at the time of the cited study.
In the early field monitoring studies, only concentrations of isoprene SOA marker compounds were determined, and such studies were conducted at several sites, including South and North America, Europe, Asia, and the Arctic. These sites included tropical and boreal forests but also rural and urban sites that are impacted by pollution. Measurements also often included monoterpene SOA, biomass burning and fungal spore markers, providing information on other aerosol sources. The references cited here are limited to our own early field monitoring studies [23–27]. The atmospheric concentrations of the 2-methyltetrols were found to be the highest during daytime, consistent with the emission of isoprene which is both light- and temperature-dependent [28], as well as with OH radical formation, which is a complex daytime process (for a review, see [29]). The OH radical is the main oxidant leading to isoprene SOA formation, but ozone has also been reported to be a minor contributor, e.g., [30].

2.4. Quantitation of Isoprene SOA Markers

The quantitation of molecular markers of isoprene SOA has most commonly been performed with GC/EI-MS with prior trimethylsilylation and LC/(–)ESI-MS, with the latter technique applied to organosulfates and nitrooxy organosulfates (see Section 3). Reference standards are needed for accurate quantitation but are unfortunately only available for a few marker compounds. A list of synthesized reference compounds for isoprene SOA (e.g., 2-methyltetrols, 2-methylglyceric acid) and other biogenic SOA molecular markers is provided in the review by Nozière and coworkers [5].

For quantitation, use has often also been made of surrogate standards with structural properties very similar to the targeted analytes when no pure reference compounds were available; for example, for assessing the amounts of the 2-methyltetrols and C₅-alkene triols, the response factor of erythritol and threitol have been applied, e.g., [23,31]. The GC/EI-MS method with prior trimethylsilylation with N,O-bis(trimethylsilyl)trifluoroacetamide (BSTFA) containing an acidic catalyst (1% trimethylchlorosilane (TMSCl)) has generally been performed off-line in early field monitoring studies on PM that was collected on quartz fiber filters and extracted with a polar solvent (e.g., methanol, acetonitrile), e.g., [23–27]. With respect to the choice of an extraction solvent, acetonitrile is to be preferred above others. For acetonitrile, the quantitation of isoprene SOA markers obtained for a fine daytime HVDS filter sample collected during the transition period of the 2002 LBA-SMOCC campaign. The quantitation of molecular markers of isoprene SOA has most commonly been performed with GC/EI-MS with prior trimethylsilylation and LC/(–)ESI-MS, with the latter technique applied to organosulfates and nitrooxy organosulfates (see Section 3). Reference standards are needed for accurate quantitation but are unfortunately only available for a few marker compounds. A list of synthesized reference compounds for isoprene SOA (e.g., 2-methyltetrols, 2-methylglyceric acid) and other biogenic SOA molecular markers is provided in the review by Nozière and coworkers [5].

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methanol, because of the risk of methylation artefacts in acidic medium, e.g., [32]. An online measurement technique, applied successfully in later studies and allowing the assessment of isoprene SOA, e.g., [33], is thermal desorption aerosol gas chromatography (TAG)/MS, where in situ derivatization using N-methyl-N-(trimethylsilyl)trifluoroacetamide (MSTFA) has been implemented [34].

Selected field studies that deal with source apportionment of PM, OC and SOA, comprising isoprene SOA, are covered in this review. These studies involved source apportionment with an organic marker-based method or positive matrix factorization (PMF) and are discussed in Section 5.

2.5. Mechanistic Insights into the Formation of the 2-methyltetrols, 2-methylglyceric acid, and Derivatives

Gas-phase photo-oxidation studies provided important insights into the formation of the 2-methyltetrols and related SOA marker compounds from isoprene. An important breakthrough was the discovery of dihydroxyepoxides, referred to as IEPOX, in the gas phase upon photo-oxidation of isoprene [11]. Under pristine (low-NO\textsubscript{x}) conditions, isoprene is rapidly oxidized by the OH radical to hydroxyhydroperoxides, which are further oxidized with OH, resulting in the formation of dihydroxyepoxides (i.e., $\beta$-IEPOX and $\delta$-IEPOX). These dihydroxyepoxides were identified as crucial intermediates in the formation of isoprene SOA, including 2-methyltetrols, C\textsubscript{5}-alkene triols, and sulfate esters of methyltetrols and dimers thereof [6]. The latter study clearly revealed that the formation of isoprene SOA requires acidic conditions, i.e., the presence of sulfuric acid. Additional insights were obtained in laboratory experiments where synthesized isoprene epoxydiods were studied for their potential to form SOA via reactive uptake in the presence of acidic seed aerosol [35]. This study demonstrated that the reactive uptake of isoprene epoxydiods explains the formation of known isoprene SOA tracers found in ambient aerosols, including 2-methyltetrols, C\textsubscript{5}-alkene triols, dimers, and IEPOX-derived organosulfates. In addition, it provided evidence for an unreported acid-catalyzed intramolecular rearrangement of isoprene epoxydiods to cis- and trans-3-methyl-tetrahydrofuran-3,4-diols in the particle phase. Figure 1 summarizes the formation mechanism of major isoprene SOA marker compounds at low-NO\textsubscript{x}.

Insights were also obtained into the formation of isoprene SOA that is formed under high-NO\textsubscript{x} conditions, simulating a polluted environment. It was demonstrated by Sato [7] that SOA from laboratory experiments of isoprene in the presence of NO contained 2-methyltetrols, methylnitrooxybutanetriols, and methyldinitrooxybutane diols, of which the 2-methyltetrols should be regarded as hydrolysis products formed together with nitric acid (Figure 2). The reaction of isoprene with OH radicals proceeds through addition to one of the double bonds. The adduct radical thus produced has two resonance structures as a result of the addition of an OH radical to a terminal carbon; for simplicity, only the subsequent reactions of the former radical are shown. The adduct radicals react with O\textsubscript{2} under atmospheric conditions to form peroxy radicals (RO\textsubscript{2}), which react with NO to form either alkoxy radicals or organic nitrates in the presence of NO. The organic nitrates produced through the reaction $\text{RO}_2 + \text{NO} \rightarrow \text{RO} + \text{NO}_2$ during the isoprene oxidation are methyl-nitrooxybutenol isomers. The subsequent oxidation of methyl-nitrooxybutenol leads to methyl- and methyldinitrooxybutadiol isomers (A). If reaction $\text{RO}_2 + \text{RCH}_2\text{O}_2 \rightarrow \text{ROH} + \text{O}_2 + \text{RCHO}$ occurs, methyl-nitrooxybutenol isomers (B) are also formed. This $\text{RO}_2 + \text{RCH}_2\text{O}_2$ type reaction may occur at very low NO levels observed upon SOA formation, but the concentration of the 2-methyltetrols and the methyl-nitrooxybutanetriols produced should be lower than that of the nitrooxypolys in the presence of NO\textsubscript{x}. Nitrooxypolys (products A and B) produced by the gas-phase reaction are absorbed on the existing particles following the establishment of a gas–particle equilibrium. Methyl-nitrooxybutanediols (A) hydrolyze to form methyl-nitrooxybutanetriols (B) and nitric acid, and methyl-nitroxybutanetriols undergo further hydrolysis to form 2-methyltetrols (C) and nitric acid.

With regard to the formation of 2-methylglyceric acid at high-NO\textsubscript{x}, 2-methyloxirane-2-carboxylic acid (methacrylic acid epoxide; MAE), arising from the decomposition of the
OH adduct of methacryloylperoxynitrate, was shown to be a precursor [8,36]. The mechanism proposed in Figure 3 shows the route to methacryloylperoxynitrate (MPAN) via H-abstraction of the branching of methacrolein with OH. The OH adduct of MPAN undergoes an intramolecular rearrangement to MAE, which yields high-NO\(_x\) SOA compounds, including 2-methylglyceric acid (2-MG), its organosulfate, 2-MG dimer, and an organic nitrate, 2-hydroxy-2-methyl-3-nitrooxypropionic acid.

3. Isoprene SOA-Related Organosulfates: Detection, Structural Characterization, Formation Mechanisms, Analytical Challenges, and Degradation

A comprehensive review on organosulfates in ambient aerosol covering the state of knowledge and future research directions on formation, abundance, fate and importance has recently been published [37]. In the current review, we focus on organosulfate formation from isoprene.

3.1. Detection and Structural Characterization

The application of LC/(−)ESI-MS led to the detection of organosulfates (OSs) related to isoprene and monoterpene SOA in ambient PM [12,38]. Due to the hydrophilicity of organosulfates related to isoprene, C\(_{18}\)-reversed-phase LC columns showing increased polar retention had to be employed, such as the Atlantis dC\(_{18}\) and tC\(_{18}\) column (Waters). These columns contain di- or trifunctionally bonded C\(_{18}\) alkyl residues preventing stationary phase collapse when an aqueous mobile phase is used. Both regular high (HPLC) and ultra-high-performance LC (UHPLC) have been employed with the latter technique using columns containing smaller stationary phase particles by which larger pressures can be applied and elution times are shorter. The major organosulfates related to isoprene SOA were identified in ambient PM\(_{2.5}\) as organosulfate esters of methyltetrols (MW 216), but in addition, a number of less abundant organosulfates could be identified, including OSs related to volatile oxidation products of isoprene, i.e., methacrolein (MW 200) and methyl vinyl ketone (MW 184), and MW 212 OSs.

The major MW 200 OS related to methacrolein could be identified as a derivative of 2-methylglyceric acid with a terminal sulfate group, i.e., 2-hydroxy-2-methyl-3-sulfoxypropionic acid [39], whereas the MW 184 OS related to methyl vinyl ketone could be elucidated as 4-hydroxy-3-sulfoxybutan-2-one [40]. Using detailed interpretation of LC/(−)ESI-MS data, including tandem MS (MS/MS), a structure was proposed in each case and in a following step, the proposed compound was confirmed using organic synthesis and comparison of its MS and chromatographic characteristics. As an example, we mention a specific feature of the MW 200 OS, 2-hydroxy-2-methyl-3-sulfoxypropionic acid, i.e., its terminal sulfate group. This position was indicated by the lack of a [M − H − CH\(_2\)O\(^-\)]\(^-\) ion in the MS/MS spectrum of the deprotonated molecule [M − H\(^-\)] at m/z 199, which is characteristic for a terminal CH\(_2\)OH group. In contrast, in the case of the MW 184 OS related to methyl vinyl ketone, 4-hydroxy-3-sulfoxybutan-2-one, a [M − H − CH\(_2\)O\(^-\)]\(^-\) ion (m/z 153) in the MS/MS spectrum of the deprotonated molecule [M − H\(^-\)] at m/z 183 provided evidence for a terminal CH\(_2\)OH group.

The identification of the MW 212 OSs represented a very complex structural puzzle that took a long time to resolve. These OSs were already detected in early studies [38,39]; their cyclic lactone structures were proposed [41] but were only recently structurally confirmed [42]. In an effort to produce the targeted MW 212 OSs and to support their structures, sulfate esters of 3,4-dihydroxy-3-methyl-tetrahydro-2-furanone and 3,4-dihydroxy-4-methyl-tetrahydro-2-furanone were prepared by the aqueous-phase reaction of authentic 3-methyl-2-furanone or 4-methyl-2-furanone with the sulfate radical anion [43]. A mixture of six m/z 211 compounds was obtained, which showed the same retention times and MS properties as those observed for ambient PM\(_{2.5}\) and smog chamber laboratory samples. A detailed MS characterization could be achieved for four of the six isomers. Taking into account that the MW 216 methytetrol-related OSs are formed from isoprene and are abundantly present in ambient PM\(_{2.5}\), it was logical to propose that they could serve as precursors for the MW 212 OSs. They can be explained by OH oxidation of a terminal hydroxyl group to a carboxylic
acid group, followed by lactonization [43] or, alternatively, by further reaction of the MW 214 OSs, formed by OH oxidation of a terminal hydroxyl group to an aldehyde group, followed by cyclic hemiacetal formation. The MW 212 OSs can be regarded as processed or aged isoprene SOA marker compounds. During a field monitoring study conducted during a 2007 summer episode in Brasschaat, Belgium [44], it was noted that the MW 212 OSs correlated very well (R = 0.93) with 3-methylbutanetricarboxylic acid (MBTCA), a known marker compound for aged α-pinene SOA [45]. MW 214 methyltetrol-related OSs have also been reported, of which four of the five isomers were identified as cyclic hemiacetals and can be regarded as intermediates in the formation of the MW 212 OSs [41,46]. A recent study provided evidence that 2-methyltetrol OSs undergo oxidative aging to OSs with MWS 156, 168, 200, 212, 214, 230 and 232, with some of them also being detected in ambient PM2.5 [47]. It is noted that MW 156, 168 and 200 OSs present in aged summer PM2.5 from K-puszta, Hungary, already received ample attention in early reports focusing on structural characterization by MS/MS [39,40]. For example, the MW 156 and 168 OSs were identified as glycolic and lactic acid OSs, while minor MW 200 OSs were tentatively assigned to diastereoisomers of 2,3-dihydroxybutanoic acid with the sulfate group located at the 2-position (3-hydroxy-2-sulfoxybutanoic acid). It is also worth mentioning that glycolic and lactic acid OSs have been quantified in ambient PM and that it has been proposed that glycolic acid sulfate represents an important marker for atmospheric processes that form organosulfates in ambient particulate matter, at a time that its origin was still elusive [48].

In addition to isoprene SOA-related OSs, isoprene SOA-related nitroxy organosulfates (NOSs) have been reported in smog chamber experiments performed in the presence of NOx and in ambient PM [38,39,49]. Several derivatives of 2-methyltetrols containing nitrate and sulfate groups have been detected and tentatively structurally characterized (MWS 261, 306, 245, 334 and 332). These markers exist as a mixture of multiple isomers and are partially resolved by C18-reversed-phase LC. It was suggested that the formation of these nitroxy organosulfates involves the nitration of isoprene in the gas phase, followed by sulfation in the particle phase [38]. In this respect, it was shown that the irradiation of isoprene in the presence of NOx results in SOA containing methylnitrooxybutanetriols and methylindinitrooxybutane diols, e.g., [7,50]. Taking into account the instability of both the nitrate and sulfate group, NOSs are converted to the trimethylsilylated derivatives of their free hydroxyl forms upon GC/EI-MS analysis with prior trimethylsilylation. Using this analysis method, unknown N-containing SOA markers have been reported in smog chamber experiments where isoprene was irradiated in the presence of NOx and ammonium sulfate/sulfuric acid inorganic seed aerosol, which were also observed in ambient PM2.5 [51]. For a comprehensive list of OSs and NOSs characterized in isoprene SOA and ambient PM, see [49].

3.2. Formation Mechanisms

With regard to the formation mechanism of isoprene-related OSs, several mechanisms have been proposed (for a review, see [37]). In addition to the heterogeneous reaction of epoxides with the sulfate anion, as in the case of the OSs related to methyltetrols [6] and 2-methylglyceric acid [8], evidence has been provided for an alternative formation mechanism, i.e., the reaction of alkenes with the sulfate radical anion in aqueous solution [43]. It was shown that the aqueous phase reaction of isoprene, methacrolein and methyl vinyl ketone with the sulfate radical anion results in OSs from methacrolein and aqueous solution [43]. The reaction with the sulfate radical anion has also been exploited in the synthesis of reference compounds, including the MW 212 isoprene-derived OSs [42], and OSs related to green leaf volatiles [56,57].

3.3. Analytical Challenges and Quantitation

The chromatographic analysis of OSs in a complex matrix such as PM extracts is challenging, because of their isomeric complexity, various precursor origins, and their hydrophilicity. Hydrophilic OSs are not only formed from isoprene and their gas-phase
For quantitation, reference standards recently became available for isoprene SOA-related organosulfates. Methyltetrol sulfates (MW 216) have been synthesized following different sulfation strategies starting from δ-IEPOX or 2-methyltetrol [20,62]. They were
employed in the study by Glasius and coworkers [63] to determine concentrations of methyltetrol OSs as well as other related OSs (MWs 156, 170, 184, 200, 212 and 214) in Amazonian PM$_1$. In addition, MW 212 OSs have been synthesized starting from 3-methyl-2-furanone or 4-methyl-2-furanone with sulfate radical anions [42]. Procedures for the synthesis of low MW OSs associated with the aging of methyltetrol OSs, i.e., glycolic acid and lactic acid sulfate (MW 156 and 168), have also been reported [47,48]. Quantitative determinations have been performed in several studies but in most cases should be regarded as semi-quantitative because of several uncertainties, including the lack of reference compounds, e.g., [32,63–65]. In the study by Gómez-González and coworkers [44], where isoprene SOA-related OSs (MWs of 216 and 212) and NO$_x$OSs (MWs 261 and 306) were measured, ethanesulfonic acid was used as a surrogate standard, because of its close LC retention time and acidic character, while sebacic acid was chosen as an internal recovery standard to compensate for losses during the sample work-up procedure. In the study by Kristensen and Glasius [32], camphorsulfonic acid was used as a surrogate standard to determine concentrations of MW 216 methyltetrol OSs. Using this method, it could be shown that the absolute concentrations of MW 216 OSs were underestimated 5–10 times compared to determinations where OSs derived from the dihydroxy epoxide of butadiene, structurally related to the MW 216 OSs, were employed [65]. Nevertheless, semi-quantitative methods for the determination of organosulfates can provide important information on variation in levels and time trends and remain useful for marker-based source apportionment.

Direct MS analysis (without chromatography), i.e., nanoelectrospray (nanoESI) ultra-high-resolution mass spectrometry (UHRMS), has potential to obtain valuable insights into the enormous complexity of biogenic and anthropogenic aerosol, e.g., [66,67]. For example, in the last cited study, this approach was applied to the molecular characterization of ambient PM$_{2.5}$ collected during dry and wet seasons at a site in central Amazonia. Comprehensive mass spectral data evaluation methods (i.e., Kendrick mass defect, Van Krevelen diagrams, carbon oxidation state and aromaticity equivalent) were used to identify compound classes and mass distributions of the detected species. Isoprene-derived organosulfate (IEPOX OS) was found to correspond to the most abundant ion in most of the analyzed samples and strongly followed the concentration trends of the gas-phase anthropogenic tracers, confirming its mixed anthropogenic–biogenic origin.

3.4. Degradation of Organosulfates

With regard to the possible degradation of organosulfates, it has been reported that trimethylsilylated sulfuric acid is formed upon the trimethylsilylation of isoprene SOA generated in the presence of SO$_2$ and analyzed by GC/MS [51]. Trimethylsilylation is commonly performed with a trimethylsilylation reagent (i.e., BSTFA or MSTFA) in the presence of an acidic catalyst (i.e., trimethylsilylchlorosilane). The formation of the 2-methyltetrols and related isoprene SOA markers (i.e., C$_5$-alkene triols, 2-methylglyceric acid) is thus expected when PM extracts containing organosulfates of the 2-methyltetros, 2-methylglyceric acid, and corresponding oligomers or derivatives, are trimethylsilylated. Moreover, the acid-catalyzed degradation can be enhanced by the release of sulfuric acid (and/or nitric acid). Nevertheless, the 2-methyltetros and C$_5$-alkene triols formed by the degradation of OSs upon acid-catalyzed trimethylsilylation can serve as a proxy for isoprene SOA and remain useful in marker-based source apportionment.

4. Markers for Isoprene SOA Aging

In recent studies, attention has been given to the structural characterization of aged or processed highly oxygenated isoprene SOA markers. In Section 3.1, we already discussed MW 212 organosulfates, which can be considered as markers for aged isoprene SOA. In addition, seven hydroxy acids were identified using GC/MS with prior derivatization as highly oxygenated markers for aged isoprene SOA, including 2-methyltartronic acid, 2-methylerythronic acid, 3-methylerythronic acid, 2-methylthreonic acid, 3-methylthreonic acid, 2-methylthreonic acid, and 3-methylthreonic acid.
acid, *erythro*-methyltartaric acid, and *threo*-methyltartaric acid [68]. Reference compounds were synthesized to support the proposed structures. Of the identified markers, methyltartaric acids and 2- and 3-methylthreonic acids were found to be representative of aged isoprene aerosol because they occur both in laboratory chamber aerosol and ambient PM$_{2.5}$ from different locations in the USA and Poland. It is worth noting that diastereoisomeric C$_5$-dihydroxypentanedioic acids (MW 164) were already reported in Amazonian aerosol and mentioned in the supplement of the early paper by Claeys and coworkers [1] on the discovery of the 2-methyltetrols. The MW 164 compounds were tentatively assigned in that paper to linear C$_5$-dihydroxypentanedioic acids but taking into account the EI-MS data and the recent paper by Jaoui and coworkers [68], their structures should be revisited as *threo*- and *erythro*-methyltartaric acids (2,3-dihydroxy-2-methylbutanedioic acids). Once again, it turned out that structures of unknown compounds can only be identified unambiguously with synthesized reference compounds. Interestingly, organosulfates related to 2-methyltartaric acid (MW 244) and 2-methylthreonic acid (MW 230) have also been identified in smog chamber aerosol, generated in the presence of NO$_x$ and ammonium sulfate/sulfuric acid inorganic seed aerosol, and in ambient PM, using the detailed interpretation of ESI mass spectral data [49]. As discussed above, they likely undergo acid-catalyzed degradation in the GC/EI-MS analysis with prior trimethylsilylation, resulting in the TMS-derivatives of the free hydroxyl forms.

5. Source Apportionment

Two approaches for source apportionment are covered in this section, i.e., an organic marker-based method and positive matrix factorization, where organic markers for isoprene SOA were measured in PM$_1$, PM$_{2.5}$, or PM$_{10}$, thereby mainly using capillary GC/EI-MS with prior trimethylsilylation and in one case HILIC/ESI-MS for the determination of isoprene SOA-related organosulfates.

5.1. The Organic Marker-Based Approach

An organic marker-based method containing laboratory and field study components was developed by Kleindienst and coworkers [69]. In it, the mass concentrations of organic markers are multiplied by experimentally determined conversion factors to obtain the organic mass that is attributed to the sources and thus to estimate the SOA contributions of biogenic and anthropogenic hydrocarbons to ambient OC concentrations in PM$_{2.5}$, or thus the secondary OC (SOC). An advantage of this approach is that it can be applied separately on each individual sample and thus also on a single sample. Kleindienst and coworkers [69] performed smog chamber experiments in the laboratory whereby isoprene, α-pinene, β-caryophyllene, and toluene were individually irradiated in the presence of NO$_x$. The method was first applied to 33 PM$_{2.5}$ samples collected at Research Triangle Park (NC, USA), located in southeastern USA and impacted by urban pollution. The samples were analyzed for (1) molecular markers observed in the laboratory irradiations, (2) levoglucosan, a biomass burning marker, and (3) total OC. For each of the four hydrocarbons, the SOA contributions to ambient OC concentrations were estimated using the organic marker concentrations and the laboratory-derived mass fractions. The estimates show SOA formation from isoprene, α-pinene, β-caryophyllene, and toluene contributed significantly to the ambient OC concentrations. The relative contributions were highly seasonal, with biomass burning in the winter accounting for more than 50% of the OC concentrations, while SOA contributions remained low. However, during the 6-month period between May and October, SOA from the precursor hydrocarbons contributed more than 40% of the measured OC concentration. It was pointed out that the organic marker-based method is subject to considerable uncertainty due to the simplification of replacing the complex set of chemical reactions responsible for SOA with a laboratory-derived single-valued mass fraction. The results suggest that this approach is useful to identify major sources of SOA. Following the development of this method, it has been applied in several field campaign studies that were conducted at locations where biogenic and anthropogenic SOA
formation is believed to play a role. In order to obtain a more complete source apportionment, including primary organic aerosol (POA), measurements often also included key molecular markers for anthropogenic and biogenic POA, allowing for the estimation of the contribution of biomass burning, fungal spores, plant pollen, plant detritus, coal burning, meat cooking, waste burning, vehicle exhaust, et cetera, e.g., [69–80].

5.2. Positive Matrix Factorization

An approach that has been applied more recently in field campaign studies for source apportionment of PM, OC and SOA, and where key molecular marker compounds for different SOA and POA sources can be included, is positive matrix factorization, a mathematical receptor model that provides scientific support for the development and review of air quality standards (for a review, see [81]). The fundamental principle of source/receptor relationships is that mass conservation can be assumed, and a mass balance analysis can be used to identify and apportion sources of airborne PM in the atmosphere. The approach to obtaining a data set for receptor modeling is to determine a large number of chemical constituents such as molecular markers for SOA and POA, trace elements, inorganic ions, and light absorption data. A large sample set is needed in PMF, preferably consisting of at least 100 samples. It could be demonstrated in several studies that PMF including molecular markers for biogenic and anthropogenic SOA has a distinct advantage in resolving isoprene SOA and other SOA, and in capturing aged SOA, e.g., [82–86]. Generally, a good agreement was found between the PMF-derived results with estimated SOA concentrations based on SOA marker yield estimates obtained from smog chamber experiments, e.g., [81,85], except in cases where there was evidence for aging, e.g., [84]. In a recent study, organosulfates have been included in the PMF data base, allowing additional insights into sources of biogenic SOC, such as isoprene SOC formed under low-NOx conditions, isoprene SOC formed under high-NOx conditions, SOC formed by photochemical reactions, oxidatively aged biogenic SOC and sulfuric acid-influenced SOC [87]. It should be noted that the organic marker-based approach and PMF can be used on the same data set and that the results of both can be compared to estimate the uncertainties that are associated with each of the two approaches, as was performed in [85].

With regard to source apportionment of OC and PM where isoprene SOA is resolved, it is noted that the PMF method has also been applied successfully on data bases containing data other than GC/EI-MS and/or LC/MS measurements of isoprene SOA markers compounds. This approach involves low- and high-resolution Aerodyne Mass Spectrometer (AMS) measurements, where a highly characteristic IEPOX SOA-related ion signal is generated at m/z 82 (C_5H_6O^+), e.g., [88–90]. Using PMF, an IEPOX-SOA factor could be extracted, which strongly correlated with 2-methyltetrols, C_5-alkene triols, IEPOX-derived organosulfates, and dimers of organosulfates, confirming the role of IEPOX chemistry as the source [91].

6. Overview of Molecular Markers

Table 1 summarizes the molecular markers for isoprene SOA that were discussed in this review and are useful for source apportionment. Molecular structures are presented, and information is given about the chemical name, MW, formation mechanism (figure), analysis method, and selected references.
Table 1. Overview of molecular markers for isoprene SOA. Abbreviations: 2-MG, 2-methylglyceric acid; NOS, nitrooxy organosulfate; OS, organosulfate. The compounds are listed according to increasing MW.

| Molecular Structure + Chemical Name (Trivial Name) | Chemical Formula MW | Figure | Analysis Method | Selected References |
|---------------------------------------------------|---------------------|--------|-----------------|---------------------|
| 3-methyl-3-butenetriol + tautomer (C₅-alkene triol) | C₅H₁₀O₃ 118 | – | GC/MS | [6,18,20] |
| 3-methyl-2-butene-1,2,4-triol (C₅-alkene triol) | | | |
| 2,3-dihydroxy-2-methylpropanoic acid (2-MG) | C₄H₈O₄ 120 | 3 | GC/MS | [8,17,21,22] |
| 2-methylbutane-1,2,3,4-tetrol (2-methyltetrol) | C₅H₁₀O₃ 136 | 1 | GC/MS | [1,6,10,17,19] |
| sulfoxyethanoic acid (glycolic acid OS) | C₂H₄O₆S 156 | – | LC/MS | [39,40,47,48] |
| 2,3-dihydroxy-2-methylbutanedioic acid (2-methyltartaric acid) | C₅H₈O₆ 164 | – | GC/MS | [1,68] |
Table 1. Cont.

| Molecular Structure + Chemical Name (Trivial Name) | Chemical Formula MW | Figure | Analysis Method | Selected References |
|--------------------------------------------------|---------------------|--------|-----------------|-------------------|
| [Chemical Structure Image] | C$_3$H$_6$O$_6$S | 170 | – | LC/MS | [39,40,47] |
| 2-sulfoxypropionic acid (lactic acid OS) |

| [Chemical Structure Image] | C$_4$H$_8$O$_7$S | 200 | 3 | LC/MS | [8,38–40] |
| 2-hydroxy-2-methyl-3-sulfoxypropanoic acid (2-MG OS) |

| [Chemical Structure Image] | C$_5$H$_8$O$_7$S | 212 | 1 | LC/MS | [41,42,46,47] |
| + isomers |
| 3-hydroxy-4-methyl-4-sulfoxy-2(3H)-dihydrofuranone |

| [Chemical Structure Image] | C$_5$H$_8$O$_7$S | 214 | 1 | LC/MS | [41,46,47] |
| + isomers |
| 2,3-dihydroxy-4-methyl-4-sulfoxytetrahydrofuranone |
2-hydroxy-2-methyl-3-sulfoxybutanedioic acid

C$_5$H$_{10}$O$_8$S

230 – LC/MS [49]

Several isomers

(2-MG dimer)

2,3-dihydroxy-3-methyl-4-sulfoxybutanoic acid

C$_6$H$_{14}$O$_7$

222 3 GC/MS [21]

3-methyl-4-nitrooxy-3-sulfoxybutane-1,2-diol

C$_5$H$_{11}$O$_9$NS

261 – LC/MS [38,39]

3-sulfoxybutane-1,2-diol

Several isomers

(2-methyltetrol NOS)

3-sulfoxybutanoic acid

C$_5$H$_{10}$O$_7$S

214 1 LC/MS [41,46,47]

3-methyl-2-sulfoxy-3-sulfoxybutanedioic acid

C$_8$H$_{14}$O$_7$

306 – LC/MS [38]

3-sulfoxybutane-2-ol

C$_5$H$_9$O$_9$S

216 1 LC/MS [12,38,39]

3-methyl-4-nitrooxy-2-hydroxy-2-methyl-3-sulfoxybutane-1,2-diol

C$_5$H$_{12}$O$_7$S

244 – LC/MS [49]

3-methyl-2-sulfoxy-3-methyl-4-nitrooxy-2-hydroxy-2-methyl-3-sulfoxybutane-1,2-diols

C$_7$H$_{16}$O$_8$S

244 – LC/MS [49]

3-sulfoxybutane-1,2-diol

C$_5$H$_{10}$O$_7$S

214 1 LC/MS [41,46,47]

3-methyl-4-nitrooxy-3-sulfoxybutane-1,2-diol

C$_5$H$_{11}$O$_9$NS

261 – LC/MS [38,39]

2,3-dihydroxy-3-methyl-4-sulfoxybutanoic acid

C$_6$H$_{14}$O$_7$

222 3 GC/MS [21]

3-sulfoxybutane-1,2-diol

C$_5$H$_{10}$O$_8$S

230 – LC/MS [49]

Several isomers

(2-MG dimer)

2,3-dihydroxy-3-methyl-4-sulfoxybutanoic acid

C$_6$H$_{14}$O$_7$

222 3 GC/MS [21]

3-sulfoxybutane-1,2-diol

C$_5$H$_{10}$O$_8$S

230 – LC/MS [49]
### 7. Concluding Remarks

Understanding the formation of isoprene SOA and assessing its relevance for air quality has been a process of advancing insights, where analytical developments also played an important role. In this review, we have presented a historical account of isoprene SOA research which started with the field detection of the 2-methyltetrols in Amazonian aerosols. For SOA formation from isoprene, acid-catalyzed hydrolysis is necessary, and sulfuric acid enhances SOA by forming additional nonvolatile products such as organosulfates. The isoprene SOA system is very complex since it involves the reaction of gas-phase oxidation products, photo-oxidation at low- and high-NOx, nitration reactions in the gas phase, sulfation reactions in the particle phase, and aging. In early field monitoring campaigns, marker compounds for isoprene SOA were measured using capillary GC/EI-MS with prior trimethylsilylation, which enabled the detection of the 2-methyltetrols as major products and the separation of their diastereoisomeric forms, 2-methylthreitol and 2-methylerythritol, as well of 2-methylglyceric acid. Advanced analytical techniques based on LC/MS have become available, with HILIC being a useful method for separating polar isoprene SOA-related organosulfates that exist in different positional isomeric and diastereoisomeric forms. The structural characterization of isoprene SOA markers has been a tremendous challenge, and it has become evident that synthesized reference compounds are needed for their unambiguous characterization. Multifunctional isoprene SOA markers containing nitroxy, sulfoxyl and hydroxyl groups exist as complex isomeric mixtures and warrant further characterization. There is also still limited insight into the formation of aged isoprene SOA marker compounds, such as the MW 212 and 214 organosulfates. Evidence has been obtained that methyltetrol organosulfates undergo degradation upon GC/EI-MS analysis with prior trimethylsilylation to 2-methyltetrols and C₅-alkene triols. Source apportionment of SOA, OC and PM, incorporating isoprene SOA employing a marker-based approach or PMF has been developed. It has been shown that for the latter approach, molecular markers are needed to resolve isoprene SOA. In most cases, isoprene SOA markers have been determined with GC/EI-MS with prior trimethylsilylation and only in a selected case markers of the OS type, determined with HILIC/(−)ESI-MS, have been included in PMF. More refined source apportionment allowing for the assessment of aged isoprene SOA is to be expected in the future when suitable markers are included in the analysis.

During the past two decades, detailed insights have been obtained into the fate of isoprene in the atmosphere, and over the years, we have seen that isoprene science is continuously progressing and has not revealed its secrets all at once.

### Table 1. Cont.

| Molecular Structure + Chemical Name (Trivial Name) | Chemical Formula MW | Figure | Analysis Method | Selected References |
|---------------------------------------------------|---------------------|--------|-----------------|---------------------|
| ![Image](image.png) 1,4-dinitrooxy-3-methyl-3-sulfoxybutane-2-ol | C₈H₁₄O₁₀S₃₀₂ | – | LC/MS | [8,38] |
| ![Image](image.png) 1,4-dinitrooxy-3-methyl-3-sulfoxybutane-2-ol –several isomers | C₃H₁₀O₁₁N₂S₃₀₆ | – | LC/MS | [38] |

**References**

[8, 38]
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