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# Ambient Levels of Carbonyl Compounds and Ozone in a Golf Course in Ciudad Real, Spain: A ProtoPRED QSAR (Eco) Toxicity Evaluation

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**Abstract:** It is well known that carbonyl compounds play an important role in air pollution and the formation of secondary pollutants, such as peroxyacetyl nitrates (PAN). Additionally, airborne carbonyls have been described as cytotoxic, mutagenic and carcinogenic. In this research, several carbonyl compounds, including aldehydes and ketones, as well as ozone, were monitored during a campaign conducted in July and September-October 2023 at Golf Ciudad Real, a golf course located in a non-industrial area of a south-central province in Spain. Extraction and analysis were carried out following procedures outlined by Radiello®. Analyses were performed using HPLC-DAD and UV-Visible spectrophotometry. Ozone shows seasonal variation (temperature-dependent) concentrations displaying lower values in September/October. Among all the identified carbonyls, butanal was the most abundant, accounting for 40% of the total concentration. The $C_1/C_2$ and $C_2/C_3$ ratios were also calculated to provide information about the main emissions sources of the analyzed carbonyl compounds, indicating that mainly anthropogenic sources contribute to air quality in the area. The data were further supported by Quantitative Structure-Activity Relationship (QSAR) models using the ProtoPRED online server, which employs in silico methods based on European Chemicals Agency (ECHA) regulations to assess the (eco)toxicity of the measured carbonyl compounds.

**Keywords:** outdoor air quality; carbonyls; ozone; golf course; passive samplers; QSAR; human health

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## 1. Introduction

### 1.1. VOCs Impact on Environment and Health

All organic compounds with the potential to evaporate under atmospheric conditions are considered volatile organic compounds (VOCs) and should be accounted for in any assessment of indoor and outdoor air quality impacts. Among carbonyl species, VOCs have been characterized as potential pollutants that significantly affect air quality in both metropolitan and rural areas [1,2]. According to the World Health Organization

(WHO), air pollution is one of the greatest environmental risks to the climate [3] and a major contribution to the human health burden [4]. Particulate matter, carbon monoxide, ozone ($O_3$), nitrogen dioxide, and sulfur dioxide are key indicators of air pollution. It is widely acknowledged that VOCs are released into the atmosphere by both biological and anthropogenic sources in indoor and outdoor environments and are, therefore, commonly detected in the atmosphere [5]. Given that on a daily basis, we are exposed to VOCs, as they comprise a wide group of molecules [6] that might appear in any environment, the impact of exposure to these compounds on health requires thorough study. Most of them pose a significant health risk due to long-term exposure [7] and could lead to chronic diseases such as asthma or bronchitis. VOCs have been found to show carcinogenic, mutagenic, teratogenic, toxicity, and genotoxicity effects in humans [8,9]. Furthermore, benzene, toluene and ethyl benzene, among others, have been identified in blood [10]. As VOCs concentrations are often higher in indoor air than in outdoor air, recent studies have highlighted their impact on kindergartens and primary and high school students [10–15]. Nevertheless, VOCs outdoor levels also have an influence on human health risks, mainly from traffic exhaust pollution exposure in urban areas [16].

Airborne carbonyl compounds, including ketones and aldehydes, play an important role as organic volatile organic compounds (OVOCs) in the troposphere. These compounds are considered one of the main air pollutants, as they serve as reservoirs of peroxy and hydroxy radicals, which are precursors of ozone, particulate matter PM2.5 [17] secondary organic aerosol (SOA) generation [18] and peroxyacetyl nitrate (PAN). They also modify NOx levels, subsequently affecting the oxidative capacity in the area [19], leading to severe atmospheric pollution episodes. Formaldehyde, acrolein and acetaldehyde could be detected as environmental aldehyde sources. All of them are considered carcinogenic and cytotoxic, and formaldehyde and acetaldehyde are also classified by the International Agency for Research on Cancer (IARC) as Group 1 carcinogens [20–22]. Aldehydes are highly reactive electrophiles due to their high electronegativity of the oxygen atom in the molecule, which allows for several possible chemical reactions to occur. The toxicity of these compounds could modify DNA, proteins, and amino acids like histidine, cysteine, or lysine [23,24], ultimately leading to significant risks to human health.

Therefore, measurement and quantification of VOCs, carbonyl compounds and ozone in peripheral regions of metropolitan areas are crucial for understanding their behavior in the atmosphere and assessing their impact on both human health and the environment. Although several studies have been conducted to evaluate pollutants beyond industrial, urban, or metropolitan areas [25–29], only a previous work has addressed the analysis of Biogenic Volatile Organic Compounds (BVOCs) emissions in a golf course [30]. This study additionally evaluated other locations, including a desert shrubland, the campus of the Research Institute and a city public park in Las Vegas (United States). Hence, our work constitutes a pilot study on air pollutants in a golf course in Spain. Golf Ciudad Real is surrounded by small towns (Almagro, Miguelturra, Carrión de Calatrava and Torralba de Calatrava), industrial areas (Malagón, Daimiel and Manzanares) and metropolitan areas (Ciudad Real). This study addresses the influence of air pollution in urban, rural and industrial areas on the air quality of the golf course. Levels of analyzed pollutants were used to determine whether their source was mainly anthropogenic or biogenic. The influence of the analyzed carbonyl compounds on the (eco)toxicity was additionally examined using the ProtoPRED online server (https://protoqsar.com/en/, accessed on 10 September 2024).

### 1.2. ProtoPRED QSAR Model

Computational modeling has become a powerful tool to complement experimental research, offering significant advantages in terms of time, expense reduction and ethical considerations in diverse fields [31–33]. In particular, Quantitative Structure-Activity Relationship (QSAR) models have emerged as a valuable approach for predicting various properties of chemical compounds. These models, based on the correlation between molecular structure and biological activity, enable researchers to anticipate the behavior of new compounds without the need for extensive experimental testing.

Regulatory frameworks, such as the European Union's REACH (Registration, Evaluation, Authorization, and Restriction of Chemicals) initiative, have increasingly recognized the value of such computational approaches. REACH encourages the use of alternative methods, including QSAR, to reduce animal testing while ensuring the safety of chemicals. By adhering to such regulations, QSAR methodologies not only meet the scientific demands for accuracy and reliability but also align with legal and ethical standards, allowing a significant reduction in the number of experimental animals required. Furthermore, QSAR models help to minimize resource consumption and accelerate the research process, making them a highly effective complement to traditional fieldwork in modern scientific investigations.

This study aims to explore the integration of experimental data acquisition and computational predictions through ProtoPRED, a state-of-the-art QSAR modeling platform, to perform the risk assessment of air pollutants identified in a golf course area by analyzing various endpoints related to human and ecological toxicity.

## 2. Materials and Methods

### 2.1. Sampling Site

Golf Ciudad Real is integrated into the El Reino de Don Quijote complex and consists of a 2 km$^2$ area. Golf Ciudad Real stands as the main golf course in Ciudad Real, along Toledo National Road, situated at Carretera de Toledo km 182 in Castilla-La Mancha County (Figure 1).

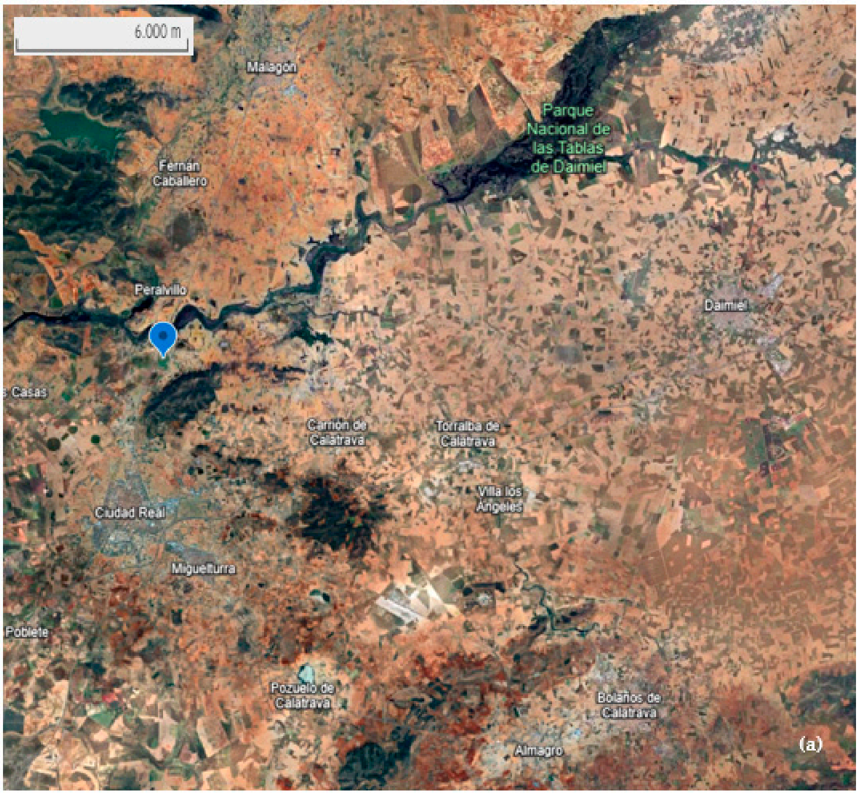

**Figure 1.** *Cont.*

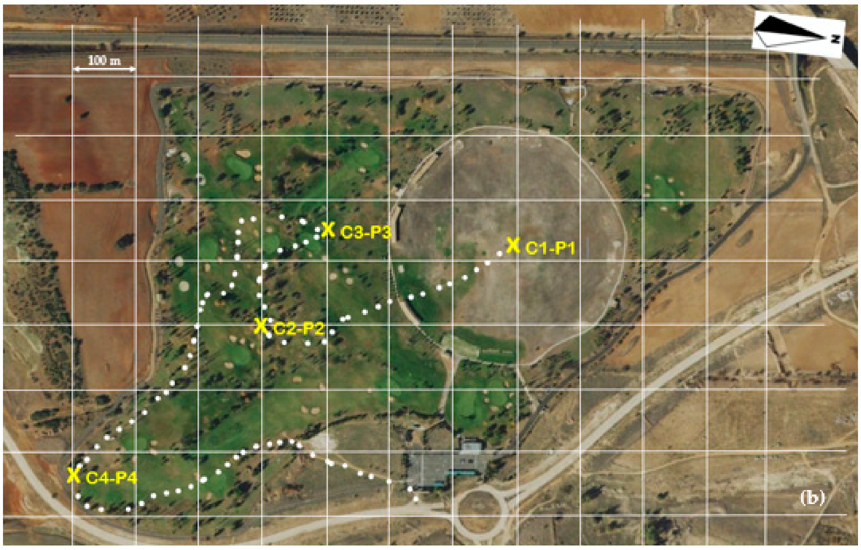

**Figure 1.** (**a**) Golf Ciudad Real whereabouts and geographical context (Google Earth). (**b**) Golf Ciudad Real course sampling locations.

Due to the low industrial activity in Ciudad Real, the most important industrial sites (Repsol and Fertiberia) are located in Puertollano, a town situated 35 km to the southwest of Ciudad Real, traffic and the water treatment industrial sites (Aquona) in the vicinity are likely to be the main air pollution source of the golf course.

The campaign was carried out during July and September-October in the summer and autumn of 2023. During these seasons, Ciudad Real province is meteorologically characterized by high temperature and low humidity, with strong winds that may not disperse the pollutants out of the area, therefore reducing concentrations on a low scale, lingering the air pollutants over this region. Hence, these conditions could play an important role in the evolution of the measured pollutants.

### 2.2. Sampling Methods

The outdoor sampling cartridges were placed within rain-protective devices at 2–2.5 m height and tied to trees by flanges. Passive cartridges were exposed to outdoor air in four different locations on the golf course (Figure 1). None of the sampling sites were placed in indoor air or near them. As described in detail elsewhere [34], Radiello® passive samplers (Fondazione Salvatore Maugeri, Padova, Italy) were used to sample the analytes ozone (code RAD172) and carbonyl compounds (code RAD165) monitored in this study. These passive samplers are long-established radial diffusive sampling devices and are certified by EN 13528:2002 and EN 14662-4.5:2005. It consists of a radial diffusive body made of porous polypropylene where a cartridge with adsorbent is inserted. Due to the nature of the diffusive path inside the micro-porous diffusive membrane, the uptake rate is not affected by wind or air currents.

Depending on the sampling pollutant, the selection of the correct adsorbing or chemi-adsorbing cartridges and the corresponding diffusive body is needed. In this sense, the diffusive body for VOCs sampling was code 120 (white), and for carbonyl compounds and ozone, code 120-1 (blue). The difference between both is that code 120-1 is opaque to light and suitable for light-sensitive compound sampling.

Passive samplers were exposed outdoors by placing them into a mountable shelter (code 196). Samplers for carbonyl compounds and ozone were exposed over a week. During the campaign, from July until October 2023, carbonyl compounds were monitored by the end (September to October), while ozone was sampled in July and the last week of September until early October. A total of 11 sampling cartridges were analyzed, plus two field blanks beyond the passive samplers and one laboratory blank for each target analyte, to establish the blank value.

## *2.3. Chemicals*

Carbonyl content analysis was performed using the following reagents: acetonitrile (ACN) (≥99.9%) HPLC gradient grade was obtained from VWR Chemicals (Radnor, PA, USA). A certified reference material TO-11/IP-6A Aldehyde/Ketone-DNPH Mix multi-component solution containing 15 carbonyl-DNPH derivatives standards (formaldehyde, acetaldehyde, acrolein, acetone, propionaldehyde, crotonaldehyde, butanal, benzaldehyde, valeraldehyde, isovaleraldehyde, o-tolualdehyde, m-tolualdehyde, p-tolualdehyde, hexanal and 2,5-dimethylbenzaldehyde) in acetonitrile (Supelco, Bellefonte, PA, USA) to perform quantitative carbonyl analysis.

Ozone level analysis was carried out by the usage of the following reagents: 4-pyridinecarboxyaldehyde (also known as 4-pyridylaldehyde), 3-methyl-2-benzothiazolinone (MBTH) supplied from ThermoFisher Scientific (Waltham, MA, USA) and sulfuric acid from Honeywell, all were of analytical grade. For ozone and carbonyl analysis, Milli-Q water type I was treated in a Milli-Q water purification system (Milli-Q® Advantage A10 Water Purification System, Merck Millipore, Billerica, MA, USA).

## *2.4. Analytical Methods*

### 2.4.1. Sample Preparation RAD165 and HPLC Analysis

The extraction method was carried out by introducing 2 mL of ACN directly into the cartridge, recap and stirring for 30 min occasionally. The resulting solution was filtered with a 0.22 µm pore size hydrophilic polytetrafluoroethylene (PTFE) filter. This procedure was followed to prepare two field blanks from the same lot number.

TO-11/IP-6A Aldehyde/Ketone-DNPH Mix in acetonitrile analytical standard (lot number: LRAD2025) was used to perform a seven-concentration calibration curve for each compound in the range of 0.075–15 ppm by plotting the peak areas versus the concentration, obtaining responses for all carbonyls measured $R^2 > 0.99$, as shown in Figure 2.

Carbonyl analytes were analyzed on an HPLC-DAD 1260 series Infinity II (Agilent Technologies, Santa Clara, CA, USA), where chromatographic separation was achieved with an Ascentis® RP-Amide 150 × 4.6 mm, 3 µm particle size (Ex. Supelco, # catalog no. 565322-U) using the method parameters described in Table 1.

**Table 1.** HPLC method analysis parameters.

| | |
|---|---|
| Mobile phase A | H2O MilliQ:ACN (60:40) |
| Mobile phase B | H2O MilliQ:ACN (25:75) |
| Injection volume | 10 µL |
| Flow rate | 1 mL $\text{min}^{-1}$ |
| Column temperature | 30 °C |
| Detector wavelength | 360 nm (bandwidth 4 nm) |
| Postrun time | 5 min |

| Gradient | | |
|---|---|---|
| Time (min) | %A | %B |
| 0 | 100 | 0 |
| 5 | 100 | 0 |
| 25 | 40 | 60 |
| 40 | 0 | 100 |
| 45 | 100 | 0 |

One standard solution was injected in the sequence to ensure system precision was in good agreement with ICH guidelines (RSD < 2%). Carbonyl concentration found in field blanks was deducted from RAD165 samplers used in this campaign.

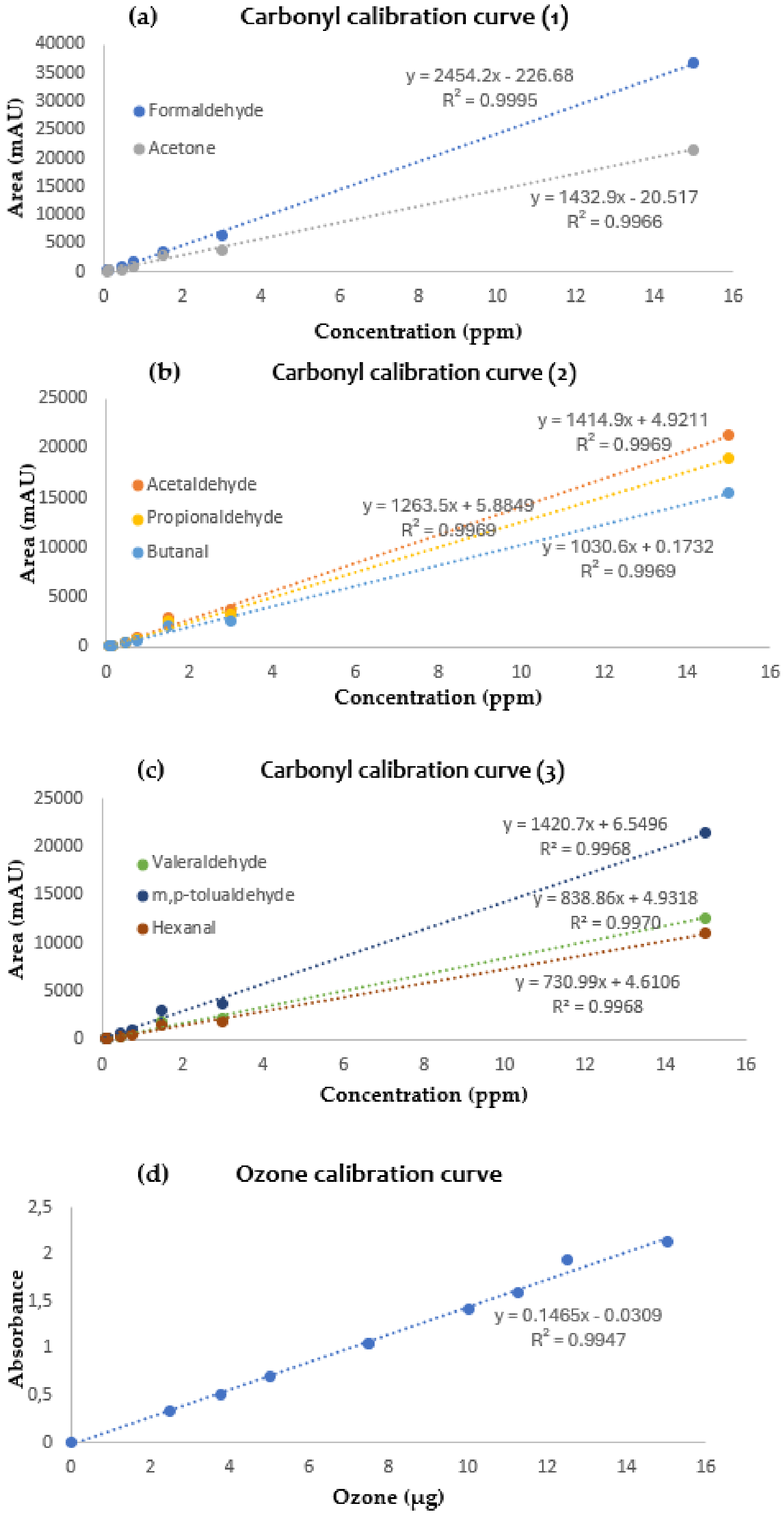

**Figure 2.** Calibration curves for formaldehyde and acetone (**a**), acetaldehyde, propionaldehyde and butanal (**b**), hexanal, valeraldehyde and isomers m,p-tolualdehyde (**c**), and ozone (**d**). Linear equations and regressions are shown in the graphs.

To calculate the final concentration of each carbonyl measured in air, a sampling rate at sampling temperature ($Q_k$) is needed. According to this approximation, the average temperature measurement was used. Radiello® provides several (at conditions 25 °C and 1 atm) of them, but acetone, crotonaldehyde, o-, m-, and p-tolualdehyde and 2,5-dimethylbenzaldehyde were calculated using Graham's law of diffusion and following data given by Uchiyama et al., 2004 [35]. Theoretical sampling rates calculated for acetone, crotonaldehyde, the corresponding tolualdehydes (o-, m- and p-) and 2,5-dimethylbenzaldehyde were 77, 65, 49 and 47 mL $min^{-1}$, respectively.

#### 2.4.2. Sample Preparation RAD172 and UV-Vis Analysis

A nine-point calibration curve was performed (Figure 2d) to cover the range of ozone mass concentration up to 15.03 µg, knowing that 1 µg of 4-pyridylaldehyde is equivalent to 0.224 µg of ozone. To develop the calibration, 4-pyridylaldehyde was diluted in Milli-Q water, and from the mother solution, the rest of the calibration solutions were prepared via dilution. MBTH solution was freshly prepared at 5 g $L^{-1}$ concentration in Milli-Q water and 5 mL per liter of sulfuric acid. Then, 0.5 mL of each calibration solution was treated with 4.5 mL of MBTH solution and allowed to stand in the absence of light for 1 h, turning color solutions into yellow. Solution absorbances were measured at 430 nm afterward, using MBTH solutions to zero the UV-Vis spectrophotometer.

Two field unexposed cartridges were used as blanks. After pouring the silica gel content into the tube, blank and sample extractions were performed by the addition of 0.5 mL of Milli-Q water and 4.5 mL of MBTH solution. After vortexing it for approximately 30 s, the tubes were left standing in the absence of light for one hour, while the solution color turned yellow, meaning a reaction between 4-pyridylaldehyde and MBTH took place. Blank and sample solutions were filtered with a 0.45 µm pore size hydrophilic polytetrafluoroethylene (PTFE) filter before absorbance measurement by a Varian Cary 50 Conc UV-Visible spectrophotometer was carried out.

The sampling rate ($Q_k$, mL $min^{-1}$) at the average measurement temperature was needed to calculate ozone concentrations in air (µg $m^{-3}$). This value is not influenced either by wind speed or by humidity.

### *2.5. ProtoPRED Computational Methodology*

ProtoPRED QSAR computational tool [36] predicts physicochemical, toxicological and ecotoxicological properties of chemical compounds by QSAR models. For this work, this application was used to get an idea of the (eco)toxicological impact the analyzed compounds could have. As molecular descriptors used in QSAR predictions in the ProtoPRED server could not be applied for ozone, its impact on (eco)toxicology was not evaluated by this application tool. ProtoPRED uses the following public Python/Java packages, among others: Rdkit v.2021.03.2; Mordred v.1.2.0.; Sklearn v.1.0.2 and JSME Molecule Editor. All models follow the OECD guidelines; therefore, the results given by QSAR models are accepted for the registration in REACH of new substances according to the ECHA and other regulatory bodies.

## 3. Results and Discussion

Since Golf Ciudad Real course is surrounded by urban, rural and industrial areas (Figure 1a) and air masses loaded with air pollutants from the Ciudad Real metropolitan area and other towns, its air quality might be affected, thus leading to an increase in pollution levels. Hence, this study was addressed to analyze volatile organic compounds in specific locations distributed throughout the golf course.

### *3.1. Carbonyl Concentrations*

Carbonyl compounds were sampled by placing RAD165 cartridges in four sampling areas exposed to outdoor air from the last week of September to the first week of October (Figure 1b).

Figure 3a shows a typical TO-11/IP-6A aldehyde/Ketone-DNPH Mix standard solution chromatographic profile using the HPLC-DAD method described in Table 1. Specificity overlay chromatograms of a blank and a sample eluted (Figure 3b) and overlay of a sample and standard chromatography runs (Figure 3c) are also displayed. Using the previously described method (Table 1), acrolein, crotonaldehyde, benzaldehyde, isovaleraldehyde, o-tolualdehyde and 2,5-dimethylbenzaldehyde were not detected in any of the analyses with RAD165 passive samplers, so they might fall below the HPLC-DAD detection limit, suggesting that a different analytical technique and/or sampling method and cartridge should be used. In contrast, isomers m- and p-tolualdehyde overlapped; hence, they were considered coeluents.

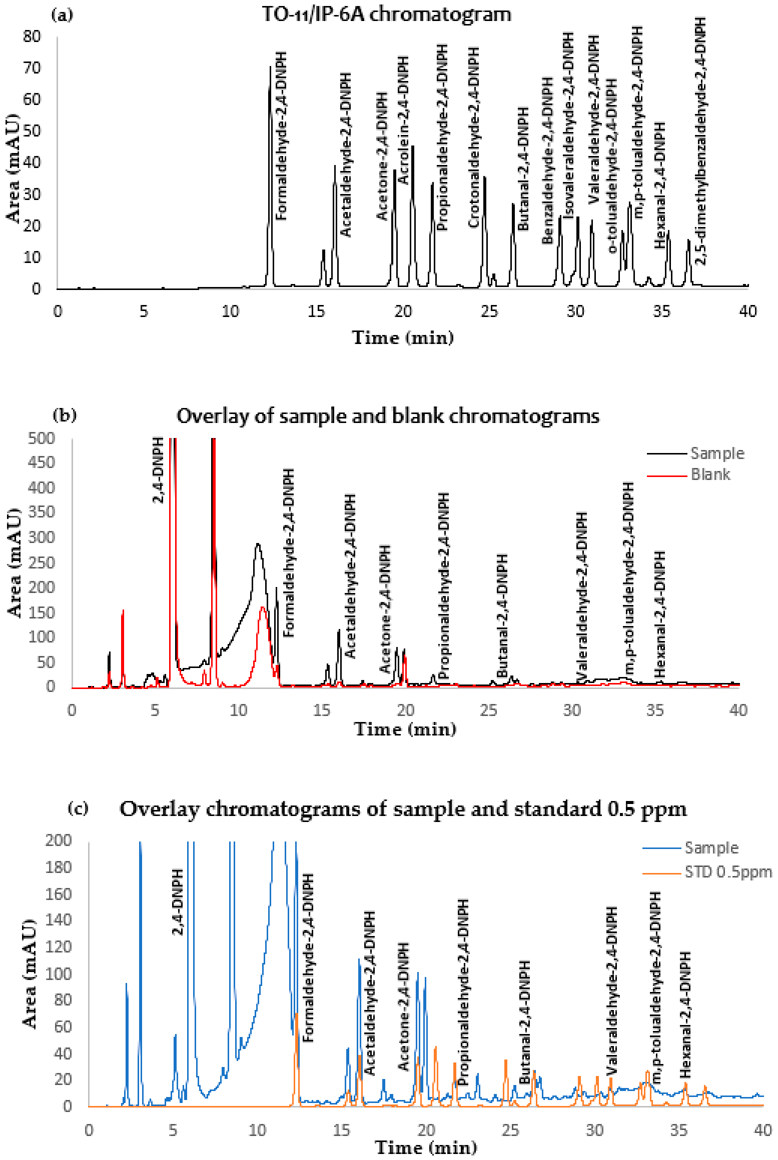

**Figure 3.** (**a**) Chromatogram and elution order obtained in HPLC-DAD system using the analytical method for a TO-11/IP-6A Aldehyde/Ketone-DNPH Mix multicomponent solution (Lot: LRAD2025). (**b**) Overlay chromatograms of RAD165 blank field and eluted sample. (**c**) Overlay of typical sample chromatogram and the standard. Chromatography runs (**b**,**c**) were used for qualitative and quantitative analysis of the identified airborne carbonyls.

All outdoor air samples identified the same nine carbonyl compounds, and their quantification showed consistent results across all measurements. Table 2 shows the obtained airborne carbonyl concentrations measured in this study.

**Table 2.** Carbonyls average concentration values in solution (ppm) and air ($\mu$g m$^{-3}$) given by sampling rate ($Q_k$) at measured temperature.

| **Carbonyl Compound** | **RT (min)** | **Concentration (ppm) *** | **$Q_k$ (mL min$^{-1}$)** | **Concentration ($\mu$g m$^{-3}$) *** |
|---|---|---|---|---|
| Formaldehyde | 12.30 | 1.18 ± 0.13 | 99 | 2.37 ± 0.25 |
| Acetaldehyde | 16.05 | 1.31 ± 0.06 | 84 | 3.11 ± 0.15 |
| Acetone | 19.49 | 1.06 ± 0.14 | 77 | 2.73 ± 0.36 |
| Acrolein | <LOD | <LOD | 33 | <LOD |
| Propionaldehyde | 21.68 | 0.27 ± 0.004 | 39 | 1.36 ± 0.02 |
| Crotonaldehyde | <LOD | <LOD | 65 | <LOD |
| Butanal [a] | 26.40 | 0.43 ± 0.05 | 11 | 7.84 ± 0.90 |
| Benzaldehyde | <LOD | <LOD | 92 | <LOD |
| Isovaleraldehyde | <LOD | <LOD | 61 | <LOD |
| Valeraldehyde | 30.93 | 0.11 ± 0.006 | 27 | 0.78 ± 0.05 |
| o-tolualdehyde | <LOD | <LOD | 49 | <LOD |
| m,p-tolualdehyde [b] | 33.11 | 0.06 ± 0.04 | 49 | 0.23 ± 0.17 |
| Hexanal | 35.36 | 0.11 ± 0.02 | 18 | 1.16 ± 0.22 |
| 2,5-dimethylbenzaldehyde | <LOD | <LOD | 47 | <LOD |

* Average value ± standard deviation. <LOD: below Limit Of Detection. [a] Butanal and 2-butanone coelute in the HPLC-DAD method used; therefore, butanal concentration is overestimated. [b] Isomers m- and p-tolualdehyde coelute using the chromatographic method parameters displayed in Table 1.

Among all, the most prevalent carbonyl compound characterized in ambient air was butanal, displaying an average concentration of 7.84 $\mu$g m$^{-3}$. As shown in Figure 4, the DAD detector demonstrates that butanal coelute with another analyte, not characterized by the TO-11/IP-6A analytical standard used. Resolution (Rs) between both peaks was $<1.5$, which could lead to an inaccurate evaluation of butanal concentration levels. This coelution has been found in previous studies [26], which have identified the overlapped peak as 2-butanone (MEK), one of the most abundant ketones in the atmosphere that could be oxidized into a neurotoxic metabolite [37]. Butanal and 2-butanone (MEK) values obtained in Cabañeros National Park by Villanueva et al., 2014 [26] oscillated between 1.66 and 9.40 $\mu$g m$^{-3}$, with the greatest value observed in July. A variation in butanal levels during different seasonal periods suggests that temperature might influence butanal concentrations in rural and dense vegetation environments. Thus, a good correlation with the average concentration value obtained in our study was observed.

Butanal could be generated via secondary organic aerosol (SOA), a reaction primarily dominated by OH radical during daylight time [38] and mainly by $NO_3$ radical at nighttime, generated through the reaction between $O_3$ and $NO_2$ [39]. Butanal is also naturally formed in some plant oils and constitutes a volatile chemical released by some plants [40]. Indeed, vegetation area emissions could provide a plausible explanation for the butanal levels observed in the golf course, as butanal and hexanal can be emitted from grassland [41]. The distributions obtained in our study are in concordance with the ones found by Notario et al., 2013 [42], wherein carbonyl compounds were analyzed by RAD165 in Cabañeros National Park, and butanal was found to be the most abundant in average concentration. Nonetheless, its levels were found to be beneath the levels observed in the present study.

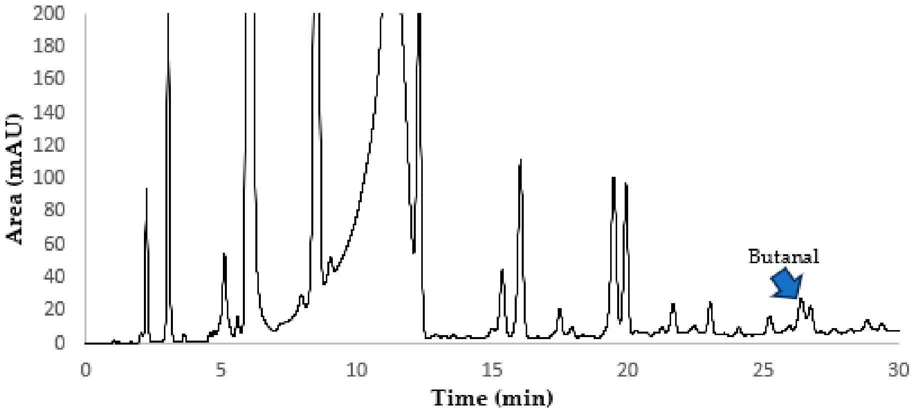

**Figure 4.** Typical sample chromatogram of carbonyl compounds using RAD165 samplers.

The concentration values of the studied carbonyl compounds obtained by Notario et al., 2013 [42] were lower than those observed in the current study. Specifically, the butanal average concentration was found to be 3.9 µg $m^{-3}$ during the observation period in August and September. However, only one sampling location was monitored. Hence, additional sampling locations to measure carbonyl levels could reveal different butanal values in Cabañeros National Park, similar to those obtained in [26].

As described by Huang et al., 2008 [43], the average butanal levels in ambient air in Shanghai during October was 1.90 µg $m^{-3}$. Only values observed in summer were comparable to those measured in Golf Ciudad Real. This could be explained by the increase in the temperature levels over the last few years (Global Warming) in the world due to Climate Change, which could have an impact on VOCs released into the studied area. Additionally, the lack of previous studies conducted on this golf course impedes us from establishing whether any abnormal circumstance could influence the measured values.

Similar butanal levels were found by Custódio et al., 2010 [44] in Tijuca Forest, one of the largest urban forests in the world. Except for acetone, which was detected in similar values, the studied carbonyl compounds were found at considerably different concentrations, although valeraldehyde was not measured. As Tijuca Forest is surrounded by Rio de Janeiro, a similar behavior for carbonyl compounds is expected compared to Shanghai. In both areas, butanal levels were monitored in July, and the values obtained were comparable to the ones found in Golf Ciudad Real.

Results from urban areas, such as Shanghai [43], and rural areas near major cities, like Rome [45], show similar aldehyde concentrations to those found in the present study. However, there is a significant deviation in the levels of formaldehyde, acetaldehyde and acetone levels during the same sampling period, with concentrations being notably higher, except for acetaldehyde levels in Montelibretti (Rome). Nevertheless, similar aldehyde values were observed in studies conducted in locations far from urban areas, such as the one developed by Villanueva et al. [26] in Natural Parks. However, formaldehyde, acetaldehyde and acetone concentrations were lower than values obtained in this study during the same sampling period.

To compare the airborne carbonyl levels observed at the golf course with those monitored in different natural and rural areas, aiming to identify the main anthropogenic or biogenic sources, the values measured by Possanzini et al., 2007 [45] in September at Montelibretti (Rome) showed higher acetone and formaldehyde concentrations, as expected, due to the influence of urban air, although, butanal was significantly lower in comparison to the observed values in the golf course area, suggesting that carbonyl levels might be influenced by temperature and transportation of polluted air masses from remote areas, then, Rome could be a potential emission source.

As described by Zhou et al., 2020 [46], aldehydes can be produced through both anthropogenic and biological pathways, as they serve as intermediates in the synthesis of biochemicals or are derived from biomass via bio- and chemocatalysis.

The most prevalent BVOCs are terpenoids, alcohols and carbonyls [7], and they can be emitted by plants and animals and the degradation of microorganisms. According to Kesselmeier and Staudt [47], there are biogenic sources and sinks that influence short-chain aldehydes levels in the area. Hexanal and nonanaldehyde constitute some of the most typical biogenic carbonyl emissions. Both aldehydes could be generated from several plant species [48,49]. However, nonanaldehyde has also been found in Mediterranean natural environments as one of the most abundant carbonyls [49], and as hexanal, emissions from Sweet Olive (*Osmanthus fragrans*) and camphor tree (*Cinnamomum camphora*) were detected at similar levels to that of formaldehyde and acetaldehyde [43]. These two carbonyl compounds were also detected under fuming ozone conditions in sunflower emissions [50]. Among biogenic emissions, nonanaldehyde has also been identified as the most abundant carbonyl compound, alongside acetaldehyde and formaldehyde in food-processing sites [51], cooking oil [52] and exhaust systems of commercial restaurants [53].

α,β-unsaturated aldehydes, such as acrolein and crotonaldehyde, are known to be more toxic than their saturated counterparts [54]. In our work, neither acrolein nor crotonaldehyde (among other aldehydes) was detected in September/October by HPLC-DAD (Table 2). Hence, further studies are needed to monitor the seasonal variation of unsaturated carbonyl compounds in the golf course. In addition, alternative instrumentation, like gas chromatography coupled to mass spectrometry (GC-MS), capable of analyzing lower VOCs concentrations, should be used. Additionally, different sampling devices might also need to be evaluated (i.e., thermal desorption).

Further studies are needed to monitor seasonal variation in both butanal levels and the other carbonyl compounds detected in this area, as well as different sampling locations in the golf course and the surrounding area. Even though, as described above, the main source of butanal emission in these environments is grassland. As described previously, this study did not analyze carbonyl samples outside the golf course; therefore, there is no possible comparison between sampling points to consider the influence of a different environment on butanal levels. Furthermore, VOCs studies, including benzene, toluene, ethylbenzene, xylene isomers (BTEX) and nitrogen oxides ($NO_x$), are needed for a better understanding of the impact on the golf course air quality driven by urban (including traffic) and industrial pollution sources.

The International Agency for Research on Cancer (IARC) has established a classification where formaldehyde and acetaldehyde [55], both identified in this study, are included as Group 1 (carcinogenic to humans) and Group 2B (possibly carcinogenic to humans), respectively. No other carbonyl compounds measured in this research were included in this list. As reported by Okada et al., 2012 [56] and Huang et al., 2019 [57], the estimated inhalation unit risk (IUR) for formaldehyde is $1.3 \times 10^{-5}$ and $2.2 \times 10^{-6}$ units per $\mu g\ m^{-3}$, respectively, following Environmental Protection Agency (EPA) USA indications. These values are also included within the inhalation reference concentration (RfC) for acetaldehyde as $0.009\ mg\ m^{-3}$, according to IRIS (Integrated Risk Information System). However, no respiratory intake data were provided for formaldehyde [58]. Therefore, the comparison of estimated values by WHO and EPA with those obtained in this research suggests an inhalation cancer risk attributable to outdoor formaldehyde and acetaldehyde in this area for an estimated exposure frequency of 24h/7 days.

### 3.2. Diagnostic Ratios

Formaldehyde ($C_1$)/acetaldehyde ($C_2$) and acetaldehyde/propionaldehyde ($C_2/C_3$) diagnostic ratios were discussed to provide information about the main emissions sources of the carbonyl compound concentrations observed in the golf course. According to previous studies, formaldehyde has been associated with biogenic sources [43,59–61]. High $C_1/C_2$ ratios are correlated with biogenic emissions, whereas low ratios are linked to anthropogenic sources. On the other hand, the $C_2/C_3$ ratio serves as an indicator of anthropogenic activity since propionaldehyde mainly originates from industrial emissions, while acetaldehyde is associated with both biogenic and anthropogenic sources [62]. High values of $C_1/C_2$ and $C_2/C_3$ ratios (approximately 10) are related to areas with dense vegetation, whereas low ratios (values close to 1) are linked to urban areas.

In this study, the $C_1/C_2$ ratio was 0.76. Therefore, this ratio indicates that carbonyl levels in the golf course are mainly associated with anthropogenic hydrocarbon emissions, mostly related to traffic, industrial activities and urban areas.

The $C_2/C_3$ ratio yielded a value of 2.29 in this campaign, which might suggest that anthropogenic sources could prevail as the main attributable source. High temperatures were reached during the sampling period. This could affect the acetaldehyde photooxidation, leading to variations in acetaldehyde levels and, consequently, influencing the $C_2/C_3$ ratio. Table 3 summarizes the concentration ratios of the present study and others in urban, rural and forest sites.

**Table 3.** Minimum, maximum and average (in parenthesis) formaldehyde, acetaldehyde and propionaldehyde mixing ratios and $C_1/C_2$ and $C_2/C_3$ concentration ratios in the present study and other sites. Data are given in $\mu g\ m^{-3}$.

| Location | Sampling Period | Formaldehyde | Acetaldehyde | Propionaldehyde | $C_1/C_2$ | $C_2/C_3$ | Reference |
|---|---|---|---|---|---|---|---|
| *Forest and rural sites* | | | | | | | |
| Golf Ciudad Real (Spain) | September–October 2023 | 2.13–2.63 (2.37) | 3.01–3.28 (3.11) | 1.34–1.37 (1.36) | 0.76 | 2.29 | This work |
| Cabañeros National Park (Spain) | August–November 2010<br>February–August 2011 | ND-2.56 (0.96) | 0.13–1.89 (0.79) | ND-1.04 (0.52) | 1.51 | 1.65 | Villanueva et al., 2014 [26] |
| Tijuca Forest (Brazil) | January–August 2008 | ND-29.1 (4.68) | ND-8.42 (1.96) | 0.74–4.83 (2.73) | 2.39 | 0.72 | Custódio et al., 2010 [44] |
| Montelibretti (Italy) | July–September 2005<br>February 2006 | 2.9–11.8 (4.89) | 0.9–4.1 (1.87) | 0.20–1.27 (0.55) | 2.61 | 3.4 | Possanzini et al., 2007 [45] |
| Lota (Portugal) | June–July 2001, 2002 | 0.04–1.16 (0.43) | 0.06–3.05 (0.52) | 0.02–0.21 (0.09) | 0.83 | 5.78 | Evtyugina et al., 2006 [63] |
| Covelo (Portugal) | June–July 2001, 2002 | 0.22–2.51 (1.13) | 0.35–1.31 (0.70) | 0.03–0.40 (0.17) | 1.61 | 4.12 | Evtyugina et al., 2006 [63] |
| Sangalhos (Portugal) | June–July 2001, 2002 | 0.13–1.54 (0.58) | 0.08–1.01 (0.44) | ND-1.97 (0.15) | 1.32 | 2.93 | Evtyugina et al., 2006 [63] |
| *Urban sites* | | | | | | | |
| Hyogo Prefecture (Japan) | 2005–2009 | 2.3–4.3 (3.08) | 2.8–4.5 (3.5) | N/A | 0.88 | - | Okada et al., 2012 [56] |
| Hong Kong (China) | April–April 1999–2000 | 0.98–5.92 (4.64) | 0.69–2.67 (2.09) | 0.28–0.63 (0.33) | 2.22 | 6.33 | Ho et al., 2002 [62] |
| Shanghai (China) | January–October 2007 | 2.64–49.54 (19.84) | 4.39–100.49 (16.31) | ND–14.19 (2.07) | 1.22 | 7.88 | Huang et al., 2008 [43] |

ND: Not Detected. N/A: Not Assessed.

Previous studies developed in Tijuca forest [44], an urban forest in the city of Rio de Janeiro, observed an average $C_2/C_3$ ratio of 1.88 for different sampling periods. Since the selected sampling locations were mostly influenced by anthropogenic activities, this could provide a reasonable explanation for the values observed in Golf Ciudad Real. However, the average $C_1/C_2$ ratios calculated were 2.13 for each sampling period, which could be related to the abundant vegetation of the forest; thus, biogenic volatile organic compounds (BVOCs) could also play a pivotal role in carbonyl levels of the area.

Mean values of $C_1/C_2$ and $C_2/C_3$ ratios estimated during October in ambient air of Shanghai by Huang et al., 2008 [43] were 0.83 and 5.09, respectively. These values are in accordance with the ones observed on the golf course. As a matter of fact, both results show the same trend in terms of biogenic emissions and as expected, a higher influence on anthropogenic sources since Shanghai constitutes one of the most populated cities in the world.

Evtyugina et al., 2006 [63] conducted a study in three different locations in north-central Portugal and obtained $C_1/C_2$ ratios of 1.32, 0.83 and 1.65 and $C_2/C_3$ ratios of 2.93, 5.78 and 4.12 in Sangalhos, Lota and Covelo, respectively. Sangalhos is the most affected by anthropogenic pollutant emissions, which could be a consequence of the high industrial activity in the area since some of the most important cities in Portugal, Porto, Coimbra and Aveiro are situated nearby. Although Lota (an open area located in the northwest of Aveiro) shows a similar $C_1/C_2$ ratio to the one observed in the golf course, butanal was not monitored, so it has not been possible to compare it with the values obtained in Golf Ciudad Real.

As previously described, acetaldehyde levels could change in different seasons as temperature variations could contribute to photooxidative processes of VOCs and influence $C_1/C_2$ and $C_2/C_3$ diagnostic ratios. As carbonyl compound concentrations were analyzed in September/October, further carbonyl measurement studies are needed to characterize the seasonal concentration trends of these compounds and evaluate the contribution of anthropogenic and biogenic sources on carbonyl levels in Golf Ciudad Real.

### 3.3. Ozone Levels

Ozone is one of the major constituents of photochemical smog on the ground and it is released as a result of reactions between gases in the presence of sunlight. WHO updated the Air Quality Guidelines in 2021, indicating that ozone concentrations at ground levels are about 100 $\mu g\ m^{-3}$ at an 8 h average. In comparison, peak season (average $O_3$ concentration of daily maximum 8 h) is 60 $\mu g\ m^{-3}$ in the six consecutive months with the highest six-month running average.

Ozone values measured at the different sampling locations are displayed in Table 4. Mean ozone concentration levels during July campaign were 70.63 ± 2.52 $\mu g\ m^{-3}$, whereas September and October average measures were 51.09 ± 1.91 $\mu g\ m^{-3}$. However, in July, ozone values trend upwards, peaking and then stabilizing by the end of the month; the levels observed in the first week of July and in September/October show similar values.

**Table 4.** Ambient air ozone levels ($\mu g\ m^{-3}$) and ± standard deviations at the different sampling locations.

| | **Period (Days of the Month)** | | | | | |
|---|---|---|---|---|---|---|
| **Ozone Sampling Locations** | **July (3–11)** | **July (11–18)** | **July (18–25)** | **September/October (25–02)** | **July (Average)** | **September/October (Average)** |
| C1-P1 | 56.17 ± 2.05 | 74.27 ± 2.64 | 81.94 ± 2.82 | 53.16 ± 1.99 | 70.63 ± 2.52 | 51.09 ± 1.91 |
| C2-P2 | N/A | N/A | N/A | 49.40 ± 1.85 | | |
| C3-P3 | N/A | N/A | N/A | 50.69 ± 1.88 | | |
| C4-P4 | N/A | N/A | 70.13 ± 2.55 | 51.12 ± 1.90 | | |

N/A: Not Assessed.

Results obtained for the monitored seasonal period are in accordance with the ones observed by Notario et al., 2012 [64] and Villanueva et al., 2014 [26]. Ozone seasonal behavior shows higher values in July than in September/October. Specifically, by the end of the summer, a temperature decrease could lead to fewer photochemical reactions and, consequently, a decrease in ozone chemical release. This behavior has also been detected in other studies [57], wherein ozone levels decrease due to a decrease in temperature, and the greatest concentration has been observed in July.

According to MITECO, following WHO Guidelines, ozone concentrations in the golf course during July 2023 are in good agreement with the Spanish Royal Decree 102/2011 on the improvement of air quality. Levels detected in the present study are lower than the alert threshold (240 $\mu g\ m^{-3}$), and WHO advised outdoor long-term goal (120 $\mu g\ m^{-3}$) for human health protection.

Ozone levels were analyzed by sampling 24 h/7 days; however, further studies are needed to monitor ozone seasonal trend levels as described in detail elsewhere [26,64] to determine the impact on WHO-advised long-term goals. Also, the European Directive 2008/50/EC advised long-term goal on ozone for vegetation protection is given by AOT40 (Accumulated Ozone exposure over a Threshold) and is 40 ppb (80 $\mu g\ m^{-3}$), which constitutes the accumulated excess of ozone concentrations above 80 $\mu g\ m^{-3}$ hourly from 8 a.m. to 10 p.m. (Central European Time) from May to July (growth season). This indicator is designed to protect crops and (semi)natural vegetation. The European target value is 18,000 $\mu g\ m^{-3}$ h averaged over a five-year period, and the long-term goal is 6000 $\mu g\ m^{-3}$ h. In our study, ozone level threshold AOT40 was exceeded once by the end of July in sampling point C1-P1, though this value was obtained by sampling 24 h/7 days.

### *3.4. ProtoPRED Predictions*

Carbonyl compounds, such as aldehydes and ketones, are chemicals to which humans are exposed continuously in different indoor and outdoor environments and constitute a potential health risk. Therefore, understanding the mechanisms of (eco)toxicity is essential for accurate environmental risk assessment. There have been previous studies to evaluate the toxicity of several aldehydes by QSAR models [65,66] in aquatic organisms and protozoans based on LC50 parameter using the DCW descriptor.

LC50 values usually refer to the concentration of a substance in air but in environmental studies, it can also mean the concentration of a chemical in water. More QSAR data for the related carbonyl compounds analyzed in this study could be found in European Chemicals Agency (ECHA) dossiers [67].

QSAR predictions were performed using the ProtoPRED online server (https://protopred.protoqsar.com/, accessed on 10 September 2024), a reliable and efficient tool for computational predictions of various physicochemical and (eco)toxicological properties. The server is organized into different modules, each designed to predict specific endpoints. For this study, several modules were employed. The ProtoTOX module, focused on human toxicity, was utilized to predict endpoints such as in vivo skin irritation, in vivo eye irritation, developmental toxicity, carcinogenicity, and neurotoxicity. Additionally, the ProtoECO module, aimed at ecotoxicological endpoints, provided predictions for environmental persistence in water, soil, and sediment, as well as adsorption/desorption behavior and bioconcentration factors. The GenoITS module was used for in vitro gene mutation studies in mammalian cells, further expanding the scope of the predictions.

Predictions were obtained by submitting the list of studied molecules as input into their respective modules. The results were analyzed using both the tables of results and the QSAR Prediction Reporting Format (QPRF) generated by the ProtoPRED tool, which provided a structured and detailed report of the predictions. This comprehensive approach allowed a robust assessment of the predicted properties, ensuring a reliable foundation for further analysis and comparison with experimental data.

All data obtained by running all the tests mentioned previously in ProtoPRED are shown in Table 5.

**Table 5.** QSAR modules and models performed using ProtoPRED online server.

| | ProtoECO | | | | | ProtoTOX | | | | | GenoITS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Carbonyl Compound** | **Persistence in Water (Days)** | **Persistence in Soil (Days)** | **Persistence in Sediment (Days)** | **Adsorption/ Desorption (L $kg^{-1}$)** | **Bioconcentration Factor (L $kg^{-1}$)** | **In Vivo Skin Irritation** | **In Vivo Eye Irritation** | **Developmental Toxicity** | **Carcinogenicity** | **Neurotoxicity (mg $kg^{-1}$) (LD50)** | **In Vitro Gene Mutation Study in Mammalian Cells (Hprt Assay)** |
| Formaldehyde | 3.6 | 6.5 ** | 25.7 | 7.4 | 2.9 | Irritant | Irritant | Non-toxic * | N/A [a] | 300.7 ** | Genotoxic |
| Acetaldehyde | 3.5 | 6.7 | 21.6 | 7.4 | 3.5 | Irritant | Irritant | Non-toxic * | Non-carcinogen | 382.3 | Non-genotoxic |
| Acetone | 4.3 | 7.7 | 22.2 | 5.8 | 3.7 | Irritant * | Irritant * | Non-toxic | Carcinogen | 389.5 | Non-genotoxic |
| Propionaldehyde | 2.3 * | 2.3 * | 7.1 * | 7.6 | 4.1 | Irritant | Irritant * | Non-toxic | Non-carcinogen | 353.4 ** | Non-genotoxic |
| Butanal | 5.0 | 4.2 | 22.9 | 17.4 | 4.4 | Irritant | Irritant * | Non-toxic | Non-carcinogen | 341.8 | Non-genotoxic |
| Valeraldehyde | 5.2 | 4.8 | 24.4 | 21.1 | 3.3 | Irritant | Irritant * | Toxic | Non-carcinogen | 308.8 | Non-genotoxic |
| m-tolualdehyde | 6.8 | 5.7 | 21.8 | 84.7 | 9.3 | Irritant | Irritant | Non-toxic | Non-carcinogen | 395.6 | Non-genotoxic |
| p-tolualdehyde | 6.7 | 5.6 | 23.1 | 95.7 | 9.7 | Irritant | Irritant | Toxic | Non-carcinogen | 394.9 | Non-genotoxic |
| Hexanal | 6.5 | 5.3 | 24.4 | 32.9 | 6.8 | Irritant | Irritant * | Non-toxic | Non-carcinogen | 290.0 | Non-genotoxic |

* This value is experimental (from the method development dataset). ** This value has low reliability because it is out of the Applicability Domain (AD) of the model. For GenoITS test, Applicability Domain (AD) includes Tanimoto, Leverage, Euclidean distance and R descriptor range for each compound evaluated. [a] No possibility to use the molecular descriptors on this molecule using ProtoPRED server.

As the descriptors for carcinogenicity by ProtoTOX module in formaldehyde could not be estimated, N/A outcome was obtained, as shown in Table 5. The descriptors used in this module cannot be calculated for this molecule, preventing the prediction using the ProtoPRED server.

Concerning data analyzed by ProtoECO, m-tolualdehyde and p-tolualdehyde present high values compared to the other carbonyl compounds studied, thereby suggesting that benzene groups could have an impact on adsorption/desorption and bioconcentration factors.

Neurotoxicity was analyzed by median lethal dose (LD50), which is used in toxicology to determine the dose of a substance that is required to cause death in 50% of a test population, usually in laboratory animals. It is used to assess the acute toxicity of a substance and provides a standardized method of comparing the relative toxicities of different substances. A lower LD50 value indicates a more toxic substance, while a higher LD50 suggests a less toxic one. As can be seen in Table 5, based on the LD50 parameter, hexanal shows the highest toxicity among all compounds tested by ProtoTOX. Formaldehyde and valeraldehyde showed similar values compared to hexanal, although formaldehyde LD50 has questionable reliability as it represents an outlier in the model. ProtoTOX identified acetone as the only carcinogenic carbonyl compound analyzed.

GenoITS was used to evaluate in vitro gene mutation and outcomes were identified to be genotoxic or non-genotoxic. If the chemical compound is genotoxic, it could induce cancer by altering the genetic material of target cells, while non-genotoxic might use a secondary mechanism unrelated to direct gene damage to produce cancer. Of all tested compounds, only formaldehyde was found to be genotoxic using the GenoITS module.

## 4. Conclusions

Carbonyl compounds (including aldehydes and acetone) and ozone were sampled and analyzed in July and September-October in the 2023 campaign on a golf course in Ciudad Real. Carbonyl compound analyses show butanal as the most abundant—about 40% of the total carbonyl compounds measured. Also, formaldehyde, acetaldehyde, acetone, propionaldehyde, valeraldehyde, isomers m- and p-tolualdehyde and hexanal were identified in all analyzed samples.

The diagnostic ratios, $C_1/C_2$ and $C_2/C_3$, indicate that anthropogenic emissions may play a significant role in the airborne carbonyl concentrations of the area, probably by transport of pollutant air masses from cities nearby, traffic and industrial activities. These results are in good agreement with data described from previous studies observed in rural and urban areas.

As ozone is considered one of the Air Quality Guideline target pollutants by WHO, it could have an impact on human health. Its monitoring throughout the campaign showed results under long-term goals marked by European Directive 2008/50/EC Spanish Royal Decree RD 102/2011 on the improvement of air quality. Moreover, AOT40 was exceeded once in C1-P1, thereby compromising the long-term goal of ozone to protect vegetation.

ProtoPRED online server was used to evaluate (eco)toxicity of the identified carbonyl compounds, and its GenoITS model indicated that formaldehyde was the only genotoxic compound as suggested by the Hprt assay.

Values extremely higher than the other carbonyls were found on m-tolualdehyde and p-tolualdehyde for adsorption/desorption and bioconcentration factors analysis by the ProtoECO module, thereby suggesting that benzene groups may affect these parameters.

ProtoTOX identified acetone as the only carcinogenic carbonyl compound studied. Hexanal, formaldehyde (exhibiting low reliability), and valeraldehyde displayed the lowest LD50, constituting the most toxic identified compounds in this work.

Long-term studies in these areas could lead to a better understanding of seasonal variability on the measured VOCs, as well as monitoring other pollutants (isoprene, benzene or toluene) and ozone that could have a remarkable impact on the air quality of the golf course due to the influence from urban areas or traffic. Moreover, monitoring in distinct seasons among different sampler positions could shed some light on the health of the vegetation and its evolution, which can also be influenced by photochemical reactions that lead to ozone formation.

Furthermore, VOCs' short-term real-time monitoring, including carbonyl, ketones, and other species on the air quality of the area, would elucidate the impact of day and night chemistry of the gas-phase pollutants.

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## References

1. Finlayson-Pitts, B.J.; Pitts, J.N., Jr. *Chemistry of the Upper and Lower Atmosphere: Theory, Experiments and Applications*; John Wiley & Sons: Hoboken, NJ, USA, 2000; ISBN 978-0-12-257060-5.
2. Seinfeld, J.H.; Pandis, S.N. *Atmospheric Chemistry and Physics: From Air Pollution to Climate Change*, 2nd ed.; John Wiley & Sons: Hoboken, NJ, USA, 2006; ISBN 978-0-471-72018-8.
3. Environmental Protection Agency. Report on the Environment. Air | US EPA. 2023. Available online: https://www.epa.gov/report-environment/air (accessed on 3 June 2024).
4. World Health Organization. Ambient (Outdoor) Air Pollution. Ambient (Outdoor) Air Pollution (who.int). 2022. Available online: https://www.who.int/news-room/fact-sheets/detail/ambient-(outdoor)-air-quality-and-health (accessed on 20 May 2024).
5. Singh, Y.; Singla, A.; Singh, N.K.; Sharma, A. Production and feasibility characterization of bio-oil from jojoba seed-based biomass through solar thermal energy pyrolysis process. *Biomass Convers. Biorefin.* **2024**, *14*, 5225–5237. [CrossRef]
6. Rumchev, K.; Brown, H.; Spickett, J. Volatile organic compounds: Do they present a risk to our health? *Rev. Environ. Health* **2007**, *22*, 39–55. [CrossRef]
7. Epping, R.; Koch, M. On-Site Detection of Volatile Organic Compounds (VOCs). *Molecules* **2023**, *28*, 1598. [CrossRef]
8. Soni, V.; Singh, P.; Shree, V.; Goel, V. Effects of VOCs on human health. In *Air Pollution and Control*; Springer: Berlin, Germany, 2017; pp. 119–142. ISBN 879-981-10-7185-0.

9. Xiong, Y.; Du, K.; Huang, Y. One-third of global population at cancer risk due to elevated volatile organic compounds levels. *Clim. Atmos. Sci.* **2024**, *7*, 54. [CrossRef]
10. Sexton, K.; Adgate, J.L.; Church, T.R.; Ashley, D.L.; Needham, L.L.; Ramachandran, G.; Fredrickson, A.L.; Ryan, A.D. Children's Exposure to Volatile Organic Compounds as Determined by Longitudinal Measurements in Blood. *Environ. Health Perspect.* **2005**, *113*, 342–349. [CrossRef]
11. Adgate, J.L.; Church, T.R.; Ryan, A.D.; Ramachandran, G.; Fredrickson, A.L.; Stock, T.H.; Morandi, M.T.; Sexton, K. Outdoor, indoor, and personal exposure to VOCs in children. *Environ. Health Perspect.* **2004**, *112*, 1386–1392. [CrossRef]
12. Zhong, L.; Su, F.-C.; Batterman, S. Volatile Organic Compounds (VOCs) in conventional and High Performance school buildings in the U.S. *Int. J. Environ. Res. Public Health* **2017**, *14*, 100. [CrossRef] [PubMed]
13. Villanueva, F.; Tapia, A.; Lara, S.; Amo-Salas, M. Indoor and outdoor air concentrations of volatile organic compounds and $NO_2$ in schools of urban. industrial and rural areas in Central-Southern Spain. *Sci. Total Environ.* **2018**, *622*, 222–235. [CrossRef] [PubMed]
14. Sonne, C.; Xia, C.; Dadvand, P.; Targino, A.C.; Lam, S.S. Indoor volatile and semivolatile organic toxic compounds: Need for global action. *J. Build. Eng.* **2022**, *62*, 105344. [CrossRef]
15. Bergomi, A.; Mangia, C.; Fermo, P.; Genga, A.; Comité, V.; Guadagnini, S.; Ielpo, P. Outdoor trends and indoor investigations of volatile organic compounds in two high schools of southern Italy. *Air Qual. Atmos. Health* **2024**, *17*, 1325–1340. [CrossRef]
16. Mishra, N.; Bartsch, J.; Ayoko, G.A.; Salthammer, T.; Morawska, L. Volatile organic compounds: Characteristics, distribution and sources in urban schools. *Atmos. Environ.* **2015**, *106*, 485–491. [CrossRef]
17. Atkinson, R.; Arey, J. Atmospheric degradation of volatile organic compounds. *Chem. Rev.* **2003**, *103*, 4605–4638. [CrossRef]
18. Liu, Q.; Gao, Y.; Huang, W.; Ling, Z.; Wang, Z.; Wang, X. Carbonyl compounds in the atmosphere: A review of abundance, source and their contributions to $O_3$ and SOA formation. *Atmos. Res.* **2022**, *274*, 106184. [CrossRef]
19. Saiz-Lopez, A.; Borge, R.; Notario, A.; Adame, J.A.; de la Paz, D.; Querol, X.; Artíñano, B.; Gómez-Moreno, F.J.; Cuevas, C.A. Unexpected increase in the oxidation capacity of the urban atmosphere of Madrid, Spain. *Sci. Rep.* **2017**, *7*, 45956. [CrossRef] [PubMed]
20. O'Brien, P.J.; Siraki, A.G.; Shangari, N. Aldehyde sources. metabolism. molecular toxicity mechanisms and possible effects on human health. *Crit. Rev. Toxicol.* **2005**, *35*, 609–662. [CrossRef]
21. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Formaldehyde. 2-Butoxyethanol and 1-Tert-Butoxypropan-2-ol*; IARC Publications: Lyon, France, 2006; Volume 88.
22. International Agency for Research on Cancer (IARC). *Chemical Agents and Related Occupations. A Review of Human Carcinogens. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans*; IARC Publications: Lyon, France, 2012; Volume 100F.
23. Matsuda, T.; Yabushita, H.; Kanaly, R.A.; Shibutani, S.; Yokoyama, A. Increased DNA damage in ALDH2-deficient alcoholics. *Chem. Res. Toxicol.* **2006**, *19*, 1374–1378. [CrossRef]
24. Chen, C.H.; Ferreira Batista, J.C.; Gross, E.R.; Mochly-Rosen, D. Targeting aldehyde dehydrogenase 2: New therapeutic opportunities. *Physiol. Rev.* **2014**, *94*, 1–34. [CrossRef]
25. Kim, S.-Y.; Jiang, X.; Lee, M.; Tumipseed, A.; Guenther, A.; Kim, J.-C.; Lee, S.-J.; Kim, S. Impact of biogenic volatile organic compounds on ozone production at the Taehwa Research Forest near Seoul, South Korea. *Atmos. Environ.* **2013**, *70*, 447–453. [CrossRef]
26. Villanueva, F.; Tapia, A.; Notario, A.; Albaladejo, J.; Martinez, E. Ambient levels and temporal trends of VOCs, including carbonyl compounds, and ozone at Cabañeros National Park border, Spain. *Atmos. Environ.* **2014**, *85*, 256–265. [CrossRef]
27. Patokoski, J.; Ruuskanen, T.M.; Kajos, M.K.; Taipale, R.; Rantala, P.; Aalto, J.; Ryyppö, T.; Nieminen, T.; Hakola, H.; Rinne, J. Sources of long-lived atmospheric VOCs at the rural boreal forest site, SMEAR II. *Atmos. Chem. Phys.* **2015**, *15*, 13413–13432. [CrossRef]
28. Wu, J.; Wang, Q.; Xu, C.; Lun, X.; Wang, L.; Gao, Y.; Huang, L.; Zhang, Q.; Li, L.; Liu, B.; et al. Biogenic volatile organic compounds in forest therapy base: A source of air pollutants or a healthcare function? *Sci. Total Environ.* **2024**, *931*, 172944. [CrossRef]
29. Yong, J.; Guo, H.; Li, Y.; Sun, S. Unraveling the influence of biogenic volatile organic compounds and their constituents on ozone and SOA formation within the Yellow River Basin, China. *Chemosphere* **2024**, *353*, 141549. [CrossRef] [PubMed]
30. Matsunaga, S.N.; Guenther, A.B.; Potosnak, M.J.; Apel, E.C. Emission of sunscreen salicylic esters from desert vegetation and their contribution to aerosol formation. *Atmos. Chem. Phys.* **2008**, *8*, 7367–7371. [CrossRef]
31. Gozalbes, R.; de Julián-Ortiz, J.D. Applications of chemoinformatics in Predictive Toxicology for Regulatory Purposes, especially in the context of the EU REACH Legislation. *Int. J. Quant. Struct. Prop. Rel.* **2018**, *3*, 1–24. [CrossRef]
32. Blázquez, M.; Andreu-Sáncez, O.; Ballesteros, A.M.; Fernández-Cruz, M.L.; Fito, C.; Gómez-Ganau, S.; Gozalbes, R.; Hernández-Moreno, D.; de Julián-Ortiz, J.V.; Lombardo, A.; et al. Computational Tools for the Assessment and Substitution of Biocidal Active Substances of Ecotoxicological Concern. In *Chemometrics and Cheminformatics in Aquatic Toxicology*; John Wiley & Sons: Hoboken, NJ, USA, 2021.
33. Carpio, L.E.; Sanz, Y.; Gozalbes, R.; Barigye, S.J. Computational strategies for the discovery of biological functions of the health foods, nutraceuticals and cosmeceuticals: A review. *Mol. Divers.* **2021**, *25*, 1425–1438. [CrossRef]

34. Fondazione Salvatore Maugeri. Instruction Manual for Radiello Sampler. Available online: http://www.radiello.com (accessed on 24 September 2024).
35. Uchiyama, S.; Aoyagi, S.; Ando, M. Evaluation of a diffusive sampler for measurement of carbonyl compounds in air. *Atmos. Environ.* **2004**, *38*, 6319–6326. [CrossRef]
36. ProtoPRED Online Server. ProtoPRED. Available online: https://protoqsar.com (accessed on 10 September 2024).
37. Tabershaw, I.R.; Utidjian, H.M.D.; Kawahara, B.L. *Occupational Diseases: A Guide to Their Recognition*; Department of Health, Education, and Welfare: Washington, DC, USA, 1977; pp. 131–439.
38. Ziemann, P.J.; Atkinson, R. Kinetics, products, and mechanisms of secondary organic aerosol formation. *Chem. Soc. Rev.* **2012**, *41*, 6582–6605. [CrossRef]
39. Wayne, R.P.; Barnes, I.; Biggs, P.; Burrows, J.P.; Canosa-Mas, C.E.; Hjorth, J.; Le Bras, G.; Moortgat, G.K.; Perner, D.; Poulet, G.; et al. The nitrate radical: Physics, chemistry, and the atmosphere. *Atmos. Environ. Part A Gen. Top.* **1991**, *25*, 1–203. [CrossRef]
40. Luttrell, W.E.; Tyler, J.W. Butyraldehyde. *J. Chem. Health Saf.* **2011**, *18*, 25–26. [CrossRef]
41. König, G.; Brunda, M.; Puxbaum, H.; Hewitt, C.N.; Duckham, S.C.; Rudolph, J. Relative contribution of oxygenated hydrocarbons to the total biogenic VOC emission of selected mid-European agricultural and natural plant species. *Atmos. Environ.* **1995**, *29*, 861–874. [CrossRef]
42. Notario, A.; Bravo, I.; Adame, J.A.; Díaz-de-Mera, Y.; Aranda, A.; Rodríguez, A.; Rodríguez, D. Variability of oxidants (OX = O3 + NO2), and preliminary study on ambient levels of ultrafine particles and VOCs, in an important ecological area in Spain. *Atmos. Environ.* **2013**, *128*, 35–45. [CrossRef]
43. Huang, J.; Feng, Y.; Li, J.; Xiong, B.; Feng, J.; Wen, S.; Sheng, G.; Fu, J.; Wu, M. Characteristics of carbonyl compounds in ambient air of Shanghai, China. *J. Atmos. Chem.* **2008**, *61*, 1–20. [CrossRef]
44. Custódio, D.; Guimaraes, C.S.; Varandas, L.; Arbilla, G. Pattern of volatile aldehydes and aromatic hydrocarbons in the largest urban rainforest in the Americas. *Chemosphere* **2010**, *79*, 1064–1069. [CrossRef]
45. Possanzini, M.; Tagliacozzo, G.; Cecinato, A. Ambient Levels and Sources of Lower Carbonyls at Montelibretti, Rome (Italy). *Water Air Soil Pollut.* **2007**, *183*, 447–454. [CrossRef]
46. Zhou, J.; Chen, Z.; Wang, Y. Bioaldehydes and beyond: Expanding the realm of bioderived chemicals using biogenic aldehydes as platforms. *Curr. Opin. Chem. Biol.* **2020**, *59*, 37–59. [CrossRef] [PubMed]
47. Kesselmeier, J.; Staudt, M. Biogenic volatile organic compounds (VOC): An overview on emission, physiology and ecology. *J. Atmos. Chem.* **1999**, *33*, 23–88. [CrossRef]
48. Ciccioli, P.; Brancaleoni, E.; Frattoni, M.; Cecinato, A.; Brachetti, A. Ubiquitous occurrence of semi-volatile carbonyl compounds in tropospheric samples and their possible source. *Atmos. Environ.* **1993**, *27A*, 1891–1901. [CrossRef]
49. Owen, S.; Boissard, C.; Street, R.A.; Duckham, S.C. Screening of 18 Mediterranean plant species for volatile organic compounds emissions. *Atmos. Environ.* **1997**, *31*, 101–117. [CrossRef]
50. Wildt, J.; Kobel, K.; Schuh-Thomas, G.; Heiden, A.C. Emissions of oxygenated volatile organic compounds from plants. Part II: Emissions of saturated aldehydes. *J. Atmos. Chem.* **2003**, *45*, 173–196. [CrossRef]
51. Ho, S.S.H.; Ip, H.S.S.; Ho, K.F.; Ng, L.P.T.; Chan, C.S.; Dai, W.T.; Cao, J.J. Hazardous airborne carbonyls emissions in industrial workplaces in China. *J. Air Waste Manag. Assoc.* **2013**, *63*, 864–877. [CrossRef]
52. Schauer, J.J.; Kleeman, M.J.; Cass, G.R.; Simoneit, B.R.T. Measurement of emissions from air pollution sources. 4. C1–C27 organic compounds from cooking with seed oils. *Environ. Sci. Technol.* **2000**, *36*, 567–575. [CrossRef] [PubMed]
53. Ho, S.S.H.; Yu, J.Z.; Chu, K.W.; Yeung, L.L. Carbonyl emissions from commercial cooking sources in Hong Kong. *J. Air Waste Manag. Assoc.* **2006**, *56*, 1091–1098. [CrossRef] [PubMed]
54. LoPachin, R.M.; Gavin, T. Molecular Mechanisms of aldehyde toxicity: A chemical perspective. *Chem. Res. Toxicol.* **2014**, *27*, 1081–1091. [CrossRef]
55. Agents Classified by the IARC Monographs, Volumes 1–136–IARC. Monographs on the Identification of Carcinogenic Hazards to Humans (who.int). Available online: https://monographs.iarc.who.int/agents-classified-by-the-iarc/ (accessed on 15 July 2024).
56. Okada, Y.; Nakagoshi, A.; Tsurukawa, M.; Matsumura, C.; Eiho, J.; Nakano, T. Environmental risk assessment and concentration trend of atmospheric volatile organic compounds in Hyogo Prefecture, Japan. *Environ. Sci. Pollut. Res.* **2012**, *19*, 201–213. [CrossRef] [PubMed]
57. Huang, Y.; Su, T.; Wang, L.; Wang, N.; Xue, Y.; Dai, W.; Lee, S.C.; Cao, J.; Ho, S.S.H. Evaluation and characterization of volatile air toxics indoors in a heavy polluted city of northwestern China in wintertime. *Sci. Total Environ.* **2019**, *662*, 470–480. [CrossRef]
58. Chemical Search | IRIS | US EPA. Available online: https://www.epa.gov/iris (accessed on 27 June 2024).
59. Shepson, P.; Hastie, D.; Schiff, H.; Polizzi, M.; Bottenheim, J.; Anlauf, K.; Mackay, G.; Karecki, D. Atmospheric concentrations and temporal variations of C1–C3 carbonyl compounds at two rural sites in central Ontario. *Atmos. Environ.* **1991**, *25*, 2001–2015. [CrossRef]
60. Feng, Y.; Wen, S.; Chen, Y.; Wang, X.; Lu, H.; Bi, X.; Sheng, G.; Fu, J. Ambient levels of carbonyl compounds and their sources in Guangzhou, China. *Atmos. Environ.* **2005**, *39*, 1789–1800. [CrossRef]

61. Ochs, S.d.M.; Albuquerque, F.C.; Pontes Massa, M.C.G.; Pereira Netto, A.D. Evaluation of C1–C13 carbonyl compounds by RRLC-UV in the atmosphere of Niterói City, Brazil. *Atmos. Environ.* **2011**, *45*, 5183–5190. [CrossRef]
62. Ho, K.; Lee, S.; Louie, P.K.; Zou, S. Seasonal variation of carbonyl compound concentrations in Urban Area of Hong Kong. *Atmos. Environ.* **2002**, *36*, 1259–1265. [CrossRef]
63. Evtyugina, M.G.; Nunes, T.; Pio, C.; Costa, C.S. Photochemical pollution under sea breeze conditions, during summer, at the Portuguese West Coast. *Atmos. Environ.* **2006**, *40*, 6277–6293. [CrossRef]
64. Notario, A.; Diaz de Mera, Y.; Aranda, A.; Adame, J.A.; Parra, A.; Romero, E.; Parra, J.; Muñoz, F. Surface ozone comparison conducted in two rural areas in central-southern Spain. *Environ. Sci. Pollut. Res.* **2012**, *19*, 186–200. [CrossRef] [PubMed]
65. Toropov, A.A.; Benfenati, E. QSAR modelling of aldehyde toxicity by means of optimization of correlation weights of nearest neighbouring codes. *J. Mol. Struct.* **2004**, *676*, 165–169. [CrossRef]
66. Toropov, A.A.; Benfenati, E. QSAR modelling of aldehyde toxicity against a protozoan, Tetrahymena pyriformis by optimization of correlation weights of nearest neighboring codes. *J. Mol. Struct.* **2004**, *679*, 225–228. [CrossRef]
67. ECHA REACH Dossiers Registered Substances-ECHA. Available online: https://echa.europa.eu/information-on-chemicals/registered-substances (accessed on 4 December 2024).