Response to RC1

We sincerely thank the reviewer for the thorough and constructive evaluation of our manuscript. We have carefully considered all the comments and have substantially revised the manuscript accordingly. Below we provide point-by-point responses to all major comments, followed by responses to the minor comments.

Response to General Comments

We thank the reviewer for the overall assessment. We agree that the original manuscript did not sufficiently demonstrate novelty, lacked adequate integration with atmospheric context, and overextended some conclusions. In the revised manuscript, we have systematically addressed these issues through: (i) a clear novelty statement in the Introduction defining what is unique to 2,4-DNP beyond substituent effects; (ii) expanded literature integration covering phenolic oxidation across gas, aqueous, and interfacial phases; (iii) explicit acknowledgment of model limitations and qualification of overextended conclusions. We believe these revisions substantially strengthen the manuscript and address the reviewer's concerns.

Response to Major Comments

1. The novelty of the work is not adequately established relative to prior phenolic oxidation studies. The manuscript should more clearly define its novelty relative to the extensive literature on phenolic oxidation in gas, aqueous, and interfacial environments. At present, the core conclusions (competitive O_3 and ·OH oxidation, multiphase reactivity, interfacial processes, and formation of secondary products) overlap substantially with established studies, and it is not clear what is

fundamentally new for 2,4-DNP beyond substituent effects. The work should explicitly compare their results with relevant experimental and mechanistic studies, including interfacial and heterogeneous catechol oxidation (Pillar et al., Environ. Sci. Technol., 2014, DOI: 10.1021/es504094x; Pillar et al., J. Phys. Chem. A, 2015, DOI: 10.1021/acs.jpca.5b07914; Pillar and Guzman, Environ. Sci. Technol., 2017, DOI: 10.1021/acs.est.7b00232), phenolic-aldehyde oxidation at air-water and air-solid interfaces (Rana and Guzman, J. Phys. Chem. A, 2020, DOI: 10.1021/acs.jpca.0c05944; Rana and Guzman, ACS Earth Space Chem., 2022, DOI: 10.1021/acsearthspacechem.2c00206; Rana and Guzman, J. Phys. Chem. A, 2022, DOI: 10.1021/acs.jpca.2c04963), and aqueous ozonolysis of phenolic aldehydes producing small organic acids (Witt et al., Sci. Total Environ., 2025, DOI: 10.1016/j.scitotenv.2025.180190). The manuscript should also address multiphase NO_2/O_3 chemistry in microdroplets (Rana et al., ACS ES&T Air, 2024, DOI: 10.1021/acsestair.3c00001), particularly in relation to the discussion of $\cdot NO_2$ reactivity. The manuscript should therefore add a clear novelty statement in the introduction, explicitly identifying what mechanistic features are unique to 2,4-DNP, whether the hydration effects identified are new or an extension of known interfacial behavior, and how the predicted products differ from those observed in related phenolic systems.

Response: We thank the reviewer for this critical comment. We agree that the novelty of the work must be more clearly defined relative to the extensive phenolic oxidation literature. In the revised manuscript, we have added a clear novelty

statement at the end of the Introduction and expanded the literature comparison throughout the text. We also acknowledge the limitations of our computational approach and have qualified our conclusions accordingly.

(1) Regarding the distinction from prior studies on catechols and substituted catechols. Pillar et al. (2014, 2015) investigated catechol oxidation at the air-water and air-solid interfaces, and Pillar and Guzman (2017) examined substituted catechols with electron-donating substituents (–CH_3, –OCH_3, and additional –OH groups). In those systems, electron-donating groups increase ring electron density and promote the formation of carboxylic acids, quinones, and polyphenols. In contrast, our work examines 2,4-DNP with two strong electron-withdrawing nitro groups that suppress the rate constant by three orders of magnitude relative to mononitrocatechol. This represents a quantitative manifestation of cumulative electron-withdrawing effects that alters the reactivity regime of the compound.

(2) Regarding the distinction from studies on phenolic aldehydes. Rana and Guzman (2020, 2022a,b) studied phenolic aldehydes (syringaldehyde, vanillin, 4-hydroxybenzaldehyde) at air-water and air-solid interfaces, and Witt et al. (2025) showed that ozonolysis of these non-nitrated phenolic aldehydes produces smaller molecules such as oxalic acid, glycolic acid, formic acid, and maleic acid, which are generally considered less toxic. In contrast, our QSAR predictions indicate that ozonolysis of 2,4-DNP generates products that retain nitro groups and exhibit elevated toxicity indicators—suggesting that nitro substitution may alter the toxicity evolution direction during oxidative processing compared to non-nitrated systems. This

observation challenges the generalized assumption that oxidative degradation necessarily leads to detoxification, though we acknowledge that this conclusion is based on screening-level QSAR predictions and requires experimental validation.

(3) Regarding the hydration effects. The non-monotonic hydration-dependent adsorption behavior (first strengthening then weakening with increasing hydration) that we observed has not been explicitly reported in previous phenolic interfacial studies to our knowledge. Prior work by Pillar et al. (2015) examined humidity effects on heterogeneous oxidation kinetics and observed monotonic increases in reactivity with increasing relative humidity over the range studied. Our finding of a non-monotonic regulatory mechanism, observed within the idealized C60/water/2,4-DNP model system, suggests that hydration may play a more complex role in modulating interfacial adsorption than previously recognized. However, we acknowledge that these results are obtained from a simplified model system and may not fully represent the behavior on real aerosol surfaces.

(4) Regarding $\bullet NO_2$ reactivity. We have refined our discussion by explicitly distinguishing three levels of $\bullet NO_2$ involvement, referencing Rana et al. (2024), who demonstrated that catechol can be converted to 4-nitrocatechol in aqueous microdroplets exposed to O_3 and $\bullet NO_2$ through multiphase chemistry. This distinction clarifies that while direct $\bullet NO_2$ reaction with parent 2,4-DNP is negligible, the reaction of $\bullet NO_2$ with oxidation intermediates and multiphase $\bullet NO_2/O_3$ chemistry represent distinct pathways that may have different atmospheric relevance.

We believe these revisions adequately establish the novelty of the present work within the context of existing phenolic oxidation literature, while appropriately acknowledging the limitations of our computational approach and the need for experimental validation.

The statement on innovation has been included in the revised manuscript: "Previous studies on phenolic oxidation have focused predominantly on systems with electron-donating substituents that enhance reactivity. Pillar et al. (2014, 2015, 2017) demonstrated that electron-donating groups on catechols promote the formation of carboxylic acids, quinones, and polyphenols. Rana and Guzman (2020, 2022a,b) showed that phenolic aldehydes undergo oxidation at interfaces to produce hydroxylated methoxyphenols and multifunctional carboxylic acids. Witt et al. (2025) further showed that ozonolysis of non-nitrated phenolic aldehydes produces smaller, less toxic molecules. Rana et al. (2024) demonstrated the conversion of catechol to 4-nitrocatechol in aqueous microdroplets through multiphase $\bullet NO_2/O_3$ chemistry. In contrast, the present work examines 2,4-dinitrophenol—a system with two strong electron-withdrawing nitro groups—and reveals three features that distinguish it from prior studies: (i) the cumulative electron-withdrawing effect suppresses the rate constant by three orders of magnitude relative to mononitrocatechol; (ii) the adsorption behavior on carbonaceous surfaces exhibits a non-monotonic hydration dependence within the idealized model system; and (iii) ozonolysis products retain nitro groups and exhibit elevated toxicity indicators based on screening-level QSAR

predictions, suggesting that nitro substitution may alter the toxicity evolution direction compared to non-nitrated systems."

2. The manuscript is missing aqueous SOA, brown-carbon, and multiphase aging context. The manuscript should better connect the computed chemistry to aqueous SOA formation, brown-carbon production, and multiphase aging processes. At present, the discussion focuses on individual intermediates and QSAR toxicity predictions, without addressing the broader product distributions expected for phenolic systems. The work should incorporate relevant interfacial and multiphase literature, including oxidative oligomerization of catechol (Guzman et al., ACS Omega, 2022, DOI: 10.1021/acsomega.2c05290), which demonstrates formation of oligomeric products linked to aerosol aging and brown carbon. The manuscript should also acknowledge that particle composition and chemistry can significantly affect product formation, as shown for iron-catalyzed aerosol reactions and aminophenol-derived brown carbon (Al-Abadleh et al., Environ. Sci. Technol., 2021, DOI: 10.1021/acs.est.0c05678; Al-Abadleh et al., Commun. Chem., 2022, DOI: 10.1038/s42004-022-00732-1).

In addition, the broader framework of dynamic heterogeneous oxidation in the troposphere should be considered (Pillar-Little and Guzman, Environments, 2018, DOI: 10.3390/environments5090104) to better place the results in an atmospheric context. The manuscript should therefore expand the introduction and discussion to relate 2,4-DNP oxidation pathways to SOA formation, brown carbon, oligomerization, and experimentally observed multiphase aging mechanisms, or

explicitly limit its interpretation to molecular-scale chemistry.

Response: We thank the reviewer for this constructive comment. We fully agree that aqueous SOA, brown-carbon, and multiphase aging processes represent important atmospheric contexts for phenolic chemistry. However, we respectfully note that the present study was designed to investigate molecular-scale reaction mechanisms and interfacial adsorption behavior of 2,4-DNP within an idealized computational framework, rather than to quantify SOA formation, brown-carbon production, or multiphase aging processes. These broader atmospheric implications are inherently beyond the scope of our current model, which employs an idealized C60 surrogate and does not capture metal-catalyzed reactions, oligomerization, or the full complexity of real aerosol particles. As the reviewer suggested, we have therefore chosen to "explicitly limit its interpretation to molecular-scale chemistry."

Nevertheless, to acknowledge the broader context while maintaining the scope of our work, we have added two concise statements in the revised manuscript. First, in the Introduction, we now explicitly note that the present study focuses on the initial molecular-scale oxidation pathways and interfacial adsorption behavior, while recognizing that phenolic compounds are known to undergo further multiphase aging processes that contribute to SOA and brown-carbon formation. Second, in the Conclusions, we have added a brief statement acknowledging that downstream multiphase aging processes such as oligomerization, iron-catalyzed reactions, and SOA/brown-carbon formation pathways are beyond the scope of this work.

We believe these additions appropriately acknowledge the broader atmospheric context while maintaining the scientific rigor and scope of the present study. We have also cited the key literature suggested by the reviewer (Guzman et al., 2022; Al-Abadleh et al., 2021, 2022; Pillar-Little and Guzman, 2018) in support of these statements: "While phenolic compounds are known to undergo further multiphase aging processes that contribute to secondary organic aerosol and brown-carbon formation (Guzman et al., 2022; Al-Abadleh et al., 2021, 2022; Pillar-Little and Guzman, 2018), the present study focuses on the initial molecular-scale oxidation pathways and interfacial adsorption behavior of 2,4-DNP within an idealized model system"; "Additionally, the present study does not address downstream multiphase aging processes such as oligomerization or metal-catalyzed reactions, which would require complementary experimental and modeling approaches."

3. The atmospheric framework of the manuscript is fragmented and not quantitatively integrated. The manuscript should better integrate the DFT kinetics, MD adsorption results, and QSAR toxicity analysis into a coherent atmospheric framework. At present, these components remain disconnected and are not linked to realistic atmospheric conditions. The work should incorporate key elements required for integration, including phase partitioning or distribution estimates, a linkage between adsorption and reactivity, product-yield considerations, and exposure-relevant concentration context for toxicity. The manuscript should therefore introduce a clear conceptual or quantitative framework connecting gas-phase, aqueous-phase, and interfacial processes. At a minimum, a schematic mass-fate

diagram should be included to show how the different computational results collectively inform the atmospheric transformation and impact of 2,4-DNP.

Response: We thank the reviewer for this critical comment. We agree that the DFT kinetics, MD adsorption results, and QSAR toxicity analysis should be better integrated into a coherent atmospheric framework. In the revised manuscript, we have added a conceptual mass-fate diagram (Figure S3) in the Supplementary Information that schematically integrates the three computational components: the DFT kinetics identify the likely oxidation pathways and products; the MD results indicate the adsorption behavior on carbonaceous surfaces; and the QSAR analysis assesses the potential toxicity of the products formed. This diagram illustrates how 2,4-DNP undergoes gas-phase and aqueous-phase oxidation, partitions between phases, adsorbs onto aerosol surfaces, and generates products with predicted toxicity indicators, providing a clear visual summary of the atmospheric framework:

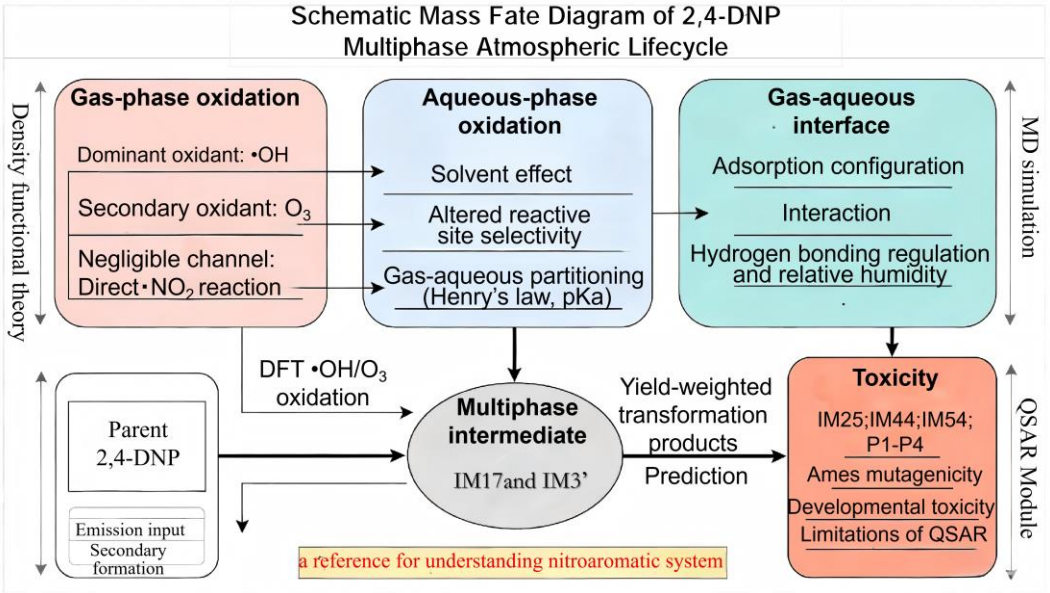

Figure 8 Integrated mass fate diagram of 2,4-DNP in the atmosphere, combining DFT kinetics, MD adsorption, and QSAR toxicity predictions.

Parent 2,4-DNP undergoes gas-aqueous partitioning controlled by Henry's law and participates in three parallel transformation pathways: gas-phase oxidation, bulk aqueous-phase oxidation, and heterogeneous reactions at the gas-aqueous interface revealed by MD simulations. Oxidation pathways calculated by DFT generate key intermediates IM3' and IM17. These intermediates further transform into a series of products, and the Ames mutagenicity and developmental toxicity of transformation products are evaluated via yield-weighted QSAR prediction. This framework establishes a coherent atmospheric fate system, which connects DFT kinetic simulation, MD interfacial adsorption analysis and QSAR toxicity assessment under realistic atmospheric conditions.

4. The manuscript should better justify the use of C60 as an aerosol surrogate and explicitly acknowledge its limitations. While useful for probing simplified π-π and dispersion interactions, C60 does not represent the chemical complexity of atmospheric particles, which can include inorganic salts, oxidized organics, soot, metals, and variable phase states. The work should add a concise limitations paragraph noting that key processes (such as metal-catalyzed reactions, acidity effects, and viscosity-dependent chemistry) are not captured in the current model.

The manuscript should also acknowledge that iron-catalyzed aerosol chemistry can strongly influence product distributions and brown-carbon formation (Al-Abadleh et al., Environ. Sci. Technol., 2021, DOI: 10.1021/acs.est.0c05678), and that aminophenol reactions can produce nitrogen-containing brown carbon in metal-containing systems (Al-Abadleh et al., Commun. Chem., 2022, DOI:

10.1038/s42004-022-00732-1). In addition, the work should note that interfacial reactivity depends on surface composition, as demonstrated for catechol on TiO_2 surfaces (Hoque et al., J. Phys. Chem. C, 2024, DOI: 10.1021/acs.jpcc.4c05777). The manuscript should therefore clearly state that C60 is an idealized surrogate, moderate generalizations to atmospheric aerosols, and include a brief limitations section describing the missing aerosol properties and their implications for atmospheric interpretation.

Response: We thank the reviewer for this important comment. We fully agree that the use of C60 as an aerosol surrogate requires clear justification and explicit acknowledgment of its limitations. In the revised manuscript, we have addressed this concern in three ways.

(1) We have added justification for the choice of C60 in the Introduction: "However, such understanding remains limited for nitrophenols on carbonaceous surfaces. While phenolic compounds are known to undergo further multiphase aging processes that contribute to secondary organic aerosol and brown carbon formation (Guzman et al., 2022; Al-Abadleh et al., 2021, 2022; Pillar-Little and Guzman, 2018), the present study focuses on the initial molecular-scale oxidation pathways and interfacial adsorption behavior of 2,4-DNP within an idealized model system. Real atmospheric carbonaceous particles, such as black carbon and soot—which are products of incomplete combustion of fossil fuels or biomass—exhibit significant complexity in both chemical composition and physical structure. Their polyaromatic (graphite-like) surfaces can form π-π electron donor-acceptor complexes with

nitroaromatic compounds, yet the adsorptive strength depends greatly on pyrolysis temperature, formation conditions, and subsequent environmental weathering. Moreover, the filling of micropores and mesopores is subject to steric effects due to size exclusion, and the adsorptive capacity becomes attenuated by fouling with natural organic matter that blocks pores and competes for adsorption sites. These factors, together with the chemical heterogeneity (oxygen-containing functional groups, defect sites, metal impurities) and morphological complexity (aggregates, pore structures) of real aerosol particles, make it extremely difficult to decouple adsorption from partitioning contributions or to identify specific non-covalent interaction types at the molecular level. Consequently, a well-defined model system is needed to isolate the specific interactions from the confounding effects of surface heterogeneity. Fullerene (C60), owing to its well-defined, stable carbon cage structure and abundant π-electron cloud, provides an ideal model for studying non-covalent interactions at organic compound-particle interfaces (Athar and Patnaik, 2022; Liu and Lu, 2024). This offers a clear platform for probing the molecular-level regulatory role of interfacial hydration."

(2) We have added a concise limitations paragraph in the Conclusions explicitly stating that C60 is an idealized surrogate and does not represent the chemical complexity of atmospheric particles, which can include inorganic salts, oxidized organics, soot, metals, and variable phase states. Key processes such as metal-catalyzed reactions, acidity effects, and viscosity-dependent chemistry are not captured in the current model: "the C60 aerosol surrogate, while useful for isolating

specific non-covalent interactions, does not capture the full chemical complexity of real atmospheric particles—particularly the presence of oxygen-containing functional groups, surface defects, heteroatoms, and transition metals that may influence reactivity and product formation. As a result, the C60 model may overestimate the contribution of π-π interactions and underestimate the role of polar interactions."

(3) We have moderated our generalizations to atmospheric aerosols throughout the manuscript, consistently referring to C60 as an "idealized model system" or "aerosol surrogate" rather than as a direct representation of real particles. We have also explicitly noted that the MD results should not be directly extrapolated to real atmospheric aerosols without considering the additional complexity of real particle surfaces.

We believe these revisions adequately justify the use of C60 as an idealized model while clearly communicating its limitations.

5. MD simulations are insufficient to support atmospheric residence-time and transport conclusions. The manuscript should restrict the interpretation of the MD results to molecular-scale adsorption behavior in the idealized C60/water/2,4-DNP system. The current conclusions regarding atmospheric residence time, long-range transport, and humidity-dependent persistence are not supported by the simulations alone.

The authors should therefore remove or substantially qualify these claims, unless they provide additional quantitative analysis (e.g., atmospheric lifetime estimates, gas–particle partitioning, uptake coefficients, or comparison with experimental/field

data). The manuscript should also clarify that key aerosol properties controlling humidity effects (such as liquid water content, ionic strength, phase behavior, viscosity, and particle morphology) are not represented in the current MD model, and discuss how this limits the atmospheric interpretation of the results.

Response: We thank the reviewer for this critical observation. In the revised manuscript, we have removed or substantially qualified all such claims and restricted the interpretation of the MD results to molecular-scale adsorption behavior in the idealized C60/water/2,4-DNP system.

Specifically, we have: (i) removed statements about atmospheric lifetime and long-range transport from the Abstract and Conclusions; (ii) revised Section 3.2 to emphasize that the MD results are limited to the idealized model system and do not account for key aerosol properties such as liquid water content, ionic strength, phase behavior, viscosity, or particle morphology: “The MD simulations presented here are limited to molecular scale adsorption behavior in the idealized C60/water/2,4-DNP system. The results provide insights into how hydration modulates specific non covalent interactions, but they do not account for key aerosol properties that control humidity effects in real atmospheric particles—including liquid water content, ionic strength, phase behavior, viscosity, and particle morphology. These properties can vary substantially with relative humidity, particle composition, and atmospheric conditions, and they collectively determine the physical state and water uptake of aerosol particles. Their absence in the current model means that the simulated hydration effects represent a simplified scenario that may not fully capture the

complexity of real aerosol surfaces. Consequently, the MD results should be interpreted as molecular-scale insights into adsorption behavior under idealized conditions, rather than as direct predictions of atmospheric persistence or humidity-dependent partitioning. Quantitative assessments of atmospheric residence time, gas-particle partitioning, or long-range transport would require additional modeling that incorporates these aerosol properties and atmospheric transport processes, and are beyond the scope of the present study."

6. The kinetic analysis requires broader validation and atmospheric context. The manuscript should strengthen the validation and interpretation of the calculated rate constants. At present, comparisons are limited and do not adequately benchmark the results against established phenolic oxidation literature. The work should incorporate relevant interfacial and heterogeneous studies (e.g., Pillar et al., Environ. Sci. Technol., 2014, DOI: 10.1021/es504094x; Pillar et al., J. Phys. Chem. A, 2015, DOI: 10.1021/acs.jpca.5b07914; Pillar and Guzman, Environ. Sci. Technol., 2017, DOI: 10.1021/acs.est.7b00232; Rana and Guzman, J. Phys. Chem. A, 2020, DOI: 10.1021/acs.jpca.0c05944) to assess whether the predicted trends for OH and O_3 are consistent with known behavior. The work should also avoid interpreting bimolecular rate constants alone as indicators of atmospheric importance.

Response: We thank the reviewer for this important comment. We have strengthened the validation and interpretation of our calculated rate constants in two ways.

(1) Regarding broader validation against established phenolic oxidation literature, our calculated rate constants show a systematic trend of decreasing reactivity with increasing nitro substitution: catechol (9.60×10^{-18}) → 4-nitrocatechol (1.48×10^{-20}) → 2,4-DNP (4.23×10^{-23} cm^3 $molecule^{-1}$ s^{-1} for O_3; 3.18×10^{-15} cm^3 $molecule^{-1}$ s^{-1} for •OH). This trend is consistent with the known electron-withdrawing effect of nitro groups, which deactivate the aromatic ring toward electrophilic attack. We have expanded the discussion in Section 3.1.2 to explicitly compare this trend with the interfacial oxidation studies of catechol (Pillar et al., 2014, 2015, 2017) and phenolic aldehydes (Rana and Guzman, 2020). In these studies, electron-donating substituents (–CH_3, –OCH_3) were shown to enhance reactivity, whereas our results demonstrate that electron-withdrawing nitro groups suppress reactivity—a trend that is consistent with the established understanding of substituent effects in phenolic oxidation: "The calculated rate constants are further validated through systematic benchmarking against available experimental and computational data for structurally related aromatic compounds, as summarized in Table 1 and Table S3. Although direct experimental measurements for the O_3 reaction with 2,4-DNP are currently unavailable, the theoretical rate constant for the mononitro analogue nitrocatechol (1.48×10^{-20} cm^3 $molecule^{-1}$ s^{-1}) (Wang et al., 2026) is approximately three orders of magnitude lower than that of catechol (9.60×10^{-18} cm^3 $molecule^{-1}$ s^{-1}) (Sun et al., 2022; Tomas et al., 2003), clearly demonstrating the strong inhibitory effect of the nitro group as an electron-withdrawing substituent on the ozone reactivity of the aromatic ring. Building on this trend, the calculated rate constant for the dinitro

compound 2,4-DNP (4.23×10^{-23} cm^3 $molecule^{-1}$ s^{-1}) is reduced by an additional three orders of magnitude, quantitatively reflecting the cumulative electron-withdrawing effect of the two nitro substituents. This trend is consistent with the established understanding of substituent effects in phenolic oxidation: electron-donating groups such as $–CH_3$ and $–OCH_3$ enhance reactivity (Pillar and Guzman, 2017; Rana and Guzman, 2020), while electron-withdrawing nitro groups deactivate the aromatic ring toward electrophilic attack."

(2) Regarding the interpretation of rate constants, we agree that bimolecular rate constants alone should not be interpreted as indicators of atmospheric importance. To address this, we have already added pseudo-first-order rate constant calculations in Section 3.1.2, using literature-reported oxidant concentrations ([OH] ≈ 10^5–10^6 molecules cm^{-3}; [NO_2] ≈ 10^{10}–10^{11} molecules cm^{-3} under nighttime conditions). We have also included a discussion in Section 3.1.3 comparing the effective rates of O_2 and $•NO_2$ for the key intermediate IM3'. Additionally, we have added a clarifying statement in Section 3.1.2 emphasizing that the reported second-order rate constants represent intrinsic reactivities, and that their actual atmospheric importance depends on oxidant concentrations, phase partitioning (Henry's law), and aerosol liquid water content. These additions ensure that our kinetic analysis is properly contextualized within realistic atmospheric conditions: "The literature review indicates that •OH concentrations typically reach $1 \times 10^6 \sim 3 \times 10^6$ molecules cm^{-3}, while $•NO_2$ levels are lower due to rapid photolysis under daytime conditions. Under heavily polluted nighttime conditions, however, •OH concentrations drop substantially. Geyer et al.

(2003) (Geyer, A., Bächmann, K., Hofzumahaus, A., Holland, F., Konrad, S., Klüpfel, T., Pätz, H. W., Perner, D., Mihelcic, D., Schäfer, H. J., and Volz-Thomas, A.: Nighttime formation of peroxy and hydroxyl radicals during the BERLIOZ campaign: Observations and modeling studies, J. Geophys. Res., 108(D4), 8249, doi:10.1029/2001JD000656, 2003.) reported nocturnal •OH concentrations of (1.85 ± 0.82) × 10^5 cm^{-3} during the BERLIOZ campaign, and in UK urban surface environments, night-time OH levels were determined to be in the range of 10^5 ~ 10^6 molecules cm^{-3} (Khan, M. A. H., Hoque, M. M. N., Alam, S. S., Ashfold, M. J., Nickless, G., and Shallcross, D. E.: Estimation and comparison of night-time •OH levels in the UK urban atmosphere using two different analysis methods, J. Environ. Sci., 23(1), 60–64, doi:10.1016/s1001-0742(10)60373-7, 2011.). Meanwhile, •NO_2 can accumulate significantly at night, with nocturnal maxima reaching 8.43 ± 0.4 ppb in Guangzhou (Qin, M., Xie, P. H., Su, H., Gu, J. W., Peng, F. M., Li, S. W., Zeng, L. M., Liu, J. G., Liu, W. Q., and Zhang, Y. H.: An observational study of the HONO–NO_2 coupling at an urban site in Guangzhou City, South China, Atmos. Environ., 43(36), 5731–5742, doi: 10.1016/j.atmosenv.2009.08.017, 2009.). Using these literature-reported concentrations, the pseudo-first-order rate constants under nighttime conditions can be estimated. For the •OH pathway, with k_{OH} = 3.18 × 10^{-15} cm^3 $molecule^{-1}$ s^{-1} and [OH] ≈ 10^5 ~ 10^6 molecules cm^{-3}, k'_{OH} ≈ 10^{-10} ~ 10^{-9} s^{-1}. For the direct •NO_2 pathway, with k_{NO2} ≈ 10^{-28} cm^3 $molecule^{-1}$ s^{-1} and [NO_2] ≈ 10^{10} ~ 10^{11} molecules cm^{-3} (corresponding to 0.4 ~ 4 ppb at 298 K and 1 atm), k'_{NO2} ≈ 10^{-18} ~ 10^{-17} s^{-1}. Even under the most favorable nighttime conditions (lowest •OH, highest

•NO_2), the direct •NO_2 pathway remains more than 7 orders of magnitude slower than the •OH pathway, corresponding to a lifetime of $>10^{10}$ s, which is negligible on atmospheric timescales. Therefore, while a full diurnal box model simulation would be required to quantify all pathways under varying pollution regimes, the quantitative analysis above confirms that the direct reaction of •NO_2 with parent 2,4-DNP is negligible even under nighttime conditions. The possible involvement of •NO_2 in subsequent reactions with primary oxidation intermediates will be discussed separately to provide a complete mechanistic picture of its environmental fate. In summary, the atmospheric degradation of 2,4-DNP is kinetically dominated by •OH, with O_3 playing a significant role in the aqueous phase, while the direct transformation contribution of •NO_2 can be neglected in environmental assessments.

It should be emphasized that the second-order rate constants presented in Figure 3d–e, even after unit conversion, represent intrinsic reactivities in each phase rather than the actual atmospheric importance of each pathway. The overall contribution of aqueous-phase reactions to the atmospheric fate of 2,4-DNP depends critically on the fraction of the compound that partitions into the aqueous phase. For 2,4-DNP, the Henry's law constant has been determined as 5.70×10^{-8} atm·m^3/mol at 5 °C (Lüttke, J. and Levsen, K.: Phase partitioning of phenol and nitrophenols in clouds, Fresenius Environ. Bull., 6, 179–184, 1997.), indicating a strong tendency to partition into the aqueous phase. The partitioning is further modulated by its acid dissociation constant (p*K*a ≈ 4.09 at 25 °C), as the deprotonated phenolate form is substantially more water-soluble than the neutral phenol. In addition, the aerosol liquid water

content—which varies widely depending on relative humidity, particle composition, and atmospheric conditions—determines the available aqueous volume for multiphase reactions. Without quantitative information on these partitioning parameters under specific atmospheric conditions, the aqueous-phase rate constants should be interpreted as intrinsic reactivity indicators rather than direct measures of atmospheric importance."

7. The treatment of NO_2 chemistry is oversimplified and should be refined. While the calculated rate constants suggest that direct NO_2 reaction with 2,4-DNP is slow, the discussion should distinguish this from NO_2 involvement in secondary and multiphase processes. The authors should incorporate relevant multiphase studies (e.g., Rana et al., ACS ES&T Air, 2024, DOI: 10.1021/acsestair.3c00001) and clarify the difference between direct reaction of the parent compound and reactions involving oxidized intermediates. This distinction is already implied by the reported low-barrier pathways for intermediate + NO_2 reactions, but is not consistently reflected in the conclusions. The manuscript should therefore clearly separate (i) direct NO_2 reaction with 2,4-DNP, (ii) NO_2 reactions with oxidation intermediates, and (iii) multiphase NO_2/O_3 chemistry, and revise the discussion accordingly to avoid overly broad statements about negligible NO_2 reactivity.

Response: We thank the reviewer for this important comment. We agree that the treatment of $\bullet NO_2$ chemistry was oversimplified and that the distinction between direct $\bullet NO_2$ reaction with the parent compound and $\bullet NO_2$ involvement in secondary and multiphase processes should be clearly articulated.

In the revised manuscript, we have explicitly separated three distinct levels of $\bullet NO_2$ involvement:

(1) Direct $\bullet NO_2$ reaction with parent 2,4-DNP. This is the reaction we characterized in Section 3.1.2, which exhibits a high energy barrier (18.48 kcal mol^{-1} for addition, 41.39 kcal mol^{-1} for HAA) and a second-order rate constant of $\sim 10^{-28}$ cm^3 $molecule^{-1}$ s^{-1}. Even under nighttime conditions with elevated $\bullet NO_2$ concentrations, the pseudo-first-order rate constant $k'_{NO2} \approx 10^{-18} \sim 10^{-17}$ s^{-1} remains more than 7 orders of magnitude slower than the •OH pathway ($k'_{OH} \approx 10^{-10} \sim 10^{-9}$ s^{-1}), corresponding to a lifetime of $>10^{10}$ s. This level is negligible.

(2) $\bullet NO_2$ reactions with oxidation intermediates. In Section 3.1.3, we showed that the key intermediate IM3′ (generated by •OH addition) reacts with $\bullet NO_2$ via HAA with a remarkably low barrier of 2.01 kcal mol^{-1} and via radical addition with a barrier of 2.78 kcal mol^{-1}. This represents a potentially important indirect nitration pathway under high-NO_2 conditions. Although O_2 dominates the fate of IM3′ due to its overwhelming concentration advantage ($\sim 10^7$ times that of $\bullet NO_2$), the low barriers suggest that $\bullet NO_2$ could play a role in nitrated product formation under certain conditions.

(3) Multiphase $\bullet NO_2/O_3$ chemistry. Rana et al. (2024) demonstrated that catechol can be converted to 4-nitrocatechol in aqueous microdroplets exposed to O_3 and $\bullet NO_2$ through three competitive pathways on the surfaces of aqueous microdroplets. This highlights that $\bullet NO_2$ can participate in multiphase processes beyond direct gas-phase reactions with the parent compound. While our study focuses on gas-phase and

aqueous-phase thermal oxidation pathways, we acknowledge that multiphase $\bullet NO_2/O_3$ chemistry represents an additional pathway not captured in our current framework.

We have revised the Conclusions to reflect this three-level distinction, avoiding overly broad statements that all $\bullet NO_2$ reactivity is negligible. Instead, we now specify that direct reaction with the parent compound is negligible, while indirect pathways involving oxidized intermediates and multiphase processes may be environmentally relevant under certain conditions: "To provide a complete picture, it is useful to distinguish three distinct levels of $\bullet NO_2$ involvement in the atmospheric chemistry of 2,4-DNP, a distinction that has been emphasized in recent multiphase studies (Rana et al., 2024). Level (i) is the direct reaction of $\bullet NO_2$ with the parent compound 2,4-DNP, which we have shown to be kinetically negligible even under nighttime conditions. Level (ii) is the reaction of $\bullet NO_2$ with primary oxidation intermediates such as IM3′ (Section 3.1.3), which exhibits a remarkably low barrier of 2.01 kcal mol^{-1} for HAA and represents a potentially important indirect nitration pathway under high-NO_2 conditions. Level (iii) is the multiphase $\bullet NO_2/O_3$ chemistry in aerosol water or microdroplets, where $\bullet NO_2$ can participate through N_2O_5 uptake and hydrolysis, leading to nitration via NO_2^+ or NO^+ species (Rana et al., 2024). This multi-level distinction clarifies that while the direct reaction of $\bullet NO_2$ with parent 2,4-DNP is negligible, the indirect pathways involving $\bullet NO_2$ and oxidized intermediates or multiphase processes may still be environmentally relevant"; "This corresponds to Level (ii) of $\bullet NO_2$ involvement as distinguished above: the reaction of $\bullet NO_2$ with a primary oxidation intermediate. While O_2 dominates the overall fate of IM3' due to its

concentration advantage (Section 3.1.2), the low barrier for the $\bullet NO_2$ + IM3' HAA pathway (2.01 kcal mol^{-1}) suggests that nitration via this indirect route could be significant under elevated $\bullet NO_2$ conditions, such as in polluted urban plumes at night"; "the direct reaction of $\bullet NO_2$ with the parent compound is kinetically unfavorable (gas-phase rate constant ~10^{-28} cm^3 $molecule^{-1}$ s^{-1}, more than 13 orders of magnitude lower than that of •OH), although reactions of $\bullet NO_2$ with oxidation intermediates (barrier as low as 2.01 kcal mol^{-1}) and multiphase $\bullet NO_2/O_3$ chemistry represent distinct pathways that may be environmentally relevant under certain conditions".

8. Photochemistry and nitrate radical chemistry are insufficiently considered in the manuscript. Therefore, the revised manuscript should acknowledge and justify the exclusion of photolysis and nitrate radical chemistry. Given that 2,4-DNP phototransformation in atmospheric water has been previously reported (Albinet et al., Chemosphere, 2010, DOI: 10.1016/j.chemosphere.2010.05.016), the work should explain why photolysis is not included in the reaction framework.

The manuscript should also incorporate relevant nitrate radical chemistry, including interfacial oxidation of catechols (Rana and Guzman, Environ. Sci. Technol., 2022, DOI: 10.1021/acs.est.2c05640) and its broader role in organic aerosol formation (Ng et al., Atmos. Chem. Phys., 2017, DOI: 10.5194/acp-17-2103-2017). The manuscript should therefore include a short limitations section addressing these excluded pathways and clarifying how their omission affects the atmospheric interpretation.

Response: We thank the reviewer for this important comment. We agree that

photolysis and nitrate radical chemistry are relevant atmospheric pathways that should be acknowledged and justified for their exclusion. In the revised manuscript, we have addressed this concern in two ways.

(1) Regarding photolysis. Albinet et al. (2010) systematically investigated the phototransformation of 2,4-DNP in atmospheric water droplets and determined the polychromatic quantum yields for photolysis in the 300–500 nm wavelength range as $(8.1 \pm 0.4) \times 10^{-5}$ for the undissociated phenol and $(3.4 \pm 0.2) \times 10^{-5}$ for the phenolate. These extremely low quantum yields indicate that direct photolysis is a relatively inefficient loss process compared to •OH oxidation, for which the second-order rate constants are $(1.76 \pm 0.05) \times 10^{9}$ M^{-1} s^{-1} and $(2.33 \pm 0.11) \times 10^{9}$ M^{-1} s^{-1} for the neutral and phenolate forms, respectively (Albinet et al., 2010). While photolysis can be a significant pathway in natural waters where •OH concentrations are limited, in the atmospheric aqueous phase where •OH concentrations are substantially higher due to photochemical production, the •OH pathway dominates 2,4-DNP loss. The present study therefore focuses on thermal oxidation pathways initiated by O_3, •OH, and $•NO_2$, which are the dominant transformation processes for 2,4-DNP under both daytime and nighttime atmospheric conditions.

(2) Regarding nitrate radical chemistry. We acknowledge that NO_3 radicals represent an important nighttime oxidation pathway for phenolic compounds. Rana and Guzman (2022) demonstrated that catechols undergo oxidation at the air-water interface by nitrate radicals, yielding products distinct from those formed in the bulk phase. Ng et al. (2017) provided a comprehensive review of NO_3-BVOC chemistry,

highlighting that NO_3 oxidation represents one of the important interactions between anthropogenic emissions and natural emissions from the biosphere, influencing air quality, climate, and visibility through regional and global budgets for reactive nitrogen and organic aerosol. While NO_3-initiated oxidation is an important nighttime process, our study focuses on thermal oxidation pathways initiated by O_3, •OH, and $•NO_2$ in the gas and aqueous phases, which represent the dominant transformation processes for 2,4-DNP under the conditions investigated. Notably, $•NO_2$ itself is included in our framework as a key oxidant; the exclusion of $•NO_3$ chemistry represents a separate nighttime pathway that merits future investigation.

We have added discussions on photolysis and $•NO_3$ chemistry in the literature review section of the introduction: "Photolysis of 2,4-DNP has been reported to occur in atmospheric water droplets, but its quantum yields are low (Albinet et al., 2010), making it a minor loss pathway compared to •OH oxidation. The present study therefore focuses on the thermal oxidation pathways initiated by O_3, •OH, and $•NO_2$. Nitrate radical ($•NO_3$) chemistry, although an important nighttime oxidation pathway for phenolic compounds (Rana and Guzman, 2022; Ng et al., 2017), was not included in the present framework because our study focuses on thermal oxidation pathways initiated by O_3, •OH, and $•NO_2$ in the gas and aqueous phases."

9. The toxicity amplification claim is overstated. The manuscript should moderate its interpretation of the toxicity results. The current claims of increased toxicity are based solely on QSAR predictions without experimental validation, product yield information, or exposure context. The revision should explicitly frame

these results as screening-level predictions and revise the language accordingly. For example, “toxicity amplification” should be replaced with more cautious phrasing such as “predicted increase in selected toxicity indicators.” The discussion should also acknowledge uncertainties associated with QSAR classification thresholds and transformation-product toxicity (e.g., Vom Eyser et al., Water Sci. Technol., 2013, DOI: 10.2166/wst.2013.452). The manuscript should either move detailed QSAR analysis to the supplement or clearly limit its role in the overall conclusions.

Response: We thank the reviewer for this critical observation. We fully agree that QSAR predictions are valuable for high-throughput hazard prioritization but should not be interpreted as definitive toxicological conclusions, and that drawing definitive conclusions about environmental risk amplification purely from in silico endpoints is indeed speculative. In the revised manuscript, we have systematically moderated the language throughout the text and explicitly framed the toxicity findings as screening-level, hypothesis-generating predictions rather than definitive conclusions. We have also expanded the discussion of QSAR uncertainties, including the inherent instability of categorical predictions with probability scores close to threshold values and the limitations of the training set chemical space, with specific reference to Vom Eyser et al. (2013). The detailed QSAR analysis remains in the main text as it provides essential context for the screening-level interpretation, but its role in the overall conclusions has been clearly limited through explicit framing language. Specific modifications made:

We have revised the title to replace “unexpected toxicity amplification” with

“Predicted Toxicity Indicators.”

We have revised the Abstract to explicitly frame the toxicity findings as screening-level predictions requiring validation: “computational toxicology predicts that certain ozonolysis products exhibit elevated Ames mutagenicity and developmental toxicity indicators relative to the parent compound... These findings provide mechanistic insights into the atmospheric transformation pathways of this specific dinitrophenol and highlight the importance of evaluating transformation product toxicity.”

In Section 3.3, we have substantially expanded the discussion of QSAR uncertainties: “The toxicity predictions presented in this section are screening-level assessments based on QSAR models. They are intended for hazard prioritization and hypothesis generation, and should not be interpreted as definitive toxicological conclusions without experimental validation. The predictive performance is fundamentally constrained by the chemical space of the training sets and the defined applicability domains. For structurally distinct species such as 2,4-DNP and its various derivatives, the confidence levels of the predictions may be diminished because these models cannot fully elucidate specific toxicological modes of action. As highlighted by the Ames/QSAR International Challenge Projects, even the best-performing models for Ames mutagenicity prediction achieve a balanced accuracy of approximately 76.9% at 100% coverage (Uesawa, 2024)(Uesawa, Y.: Progress in Predicting Ames Test Outcomes from Chemical Structures: An In-Depth Re-Evaluation of Models from the 1st and 2nd Ames/QSAR International Challenge

Projects, Int. J. Mol. Sci., 25(3), 1373, doi:10.3390/ijms25031373, 2024.), indicating that inherent uncertainties remain. In addition, categorical predictions with probability scores close to threshold are inherently unstable; as shown in Table S4, the "not detected" Ames mutagenicity signals for intermediates such as IM17, IM25, IM44, and IM54 fall within this near-threshold regime. This suggests that these signals may reflect model limitations rather than a definitive absence of toxicity. These compounds should therefore be regarded as high-priority targets for experimental validation. Furthermore, these computational frameworks necessarily simplify complex biological endpoints such as developmental toxicity. A quantitative weight-of-evidence (qWoE) approach, which combines predictions from multiple QSAR models, has been shown to achieve accuracy similar to that of the experimental Ames test (Tintó-Moliner et al., 2020) (Tintó-Moliner, A., et al.: Quantitative weight of evidence method for combining predictions of quantitative structure-activity relationship models, SAR QSAR Environ. Res., 31(4), 261–279, doi:10.1080/1062936X.2020.1725116, 2020.); however, such approaches are beyond the scope of the present screening-level assessment. Therefore, the present findings should be interpreted as hypothesis-generating rather than definitive(Vom Eyser, C., Börgers, A., Richard, J., Dopp, E., Janzen, N., Bester, K., and Tuerk, J.: Chemical and toxicological evaluation of transformation products during advanced oxidation processes, Water Sci. Technol., 68, 1976–1983, doi:10.2166/wst.2013.452, 2013.), and we recommend experimental validation through in vitro Ames tests and zebrafish embryo development assays for the high-priority compounds identified."

In the Conclusions, we have revised the language to reflect the screening-level nature of the toxicity predictions: “Additionally, the QSAR toxicity predictions are screening-level estimates requiring experimental validation.”

10. The atmospheric implications are overstated and should be revised. The manuscript should substantially revise or qualify its atmospheric implications. Current statements regarding long-range transport, humidity-dependent persistence, and underestimation in air-quality models are not supported by quantitative analysis. The revision should limit conclusions to what is directly supported by the computational results or provide additional atmospheric context (e.g., partitioning, lifetime estimates, or exposure analysis). The discussion should also acknowledge that phenolic atmospheric chemistry is governed by multiple competing pathways, including metal-catalyzed reactions, nitrate radical oxidation, and multiphase oligomerization (Al-Abadleh et al., Environ. Sci. Technol., 2021, DOI: 10.1021/acs.est.0c05678; Rana and Guzman, Environ. Sci. Technol., 2022, DOI: 10.1021/acs.est.2c05640; Guzman et al., ACS Omega, 2022, DOI: 10.1021/acsomega.2c05290; Rana et al., ACS ES&T Air, 2024, DOI: 10.1021/acsestair.3c00001). The manuscript should therefore remove or clearly qualify claims about global or regulatory implications unless supported by additional analysis.

Response: We thank the reviewer for this critical observation. In the revised manuscript, we have systematically removed or substantially qualified all such claims.

Specifically, we have: (i) removed statements about atmospheric residence time, long-range transport, and air-quality model underestimation from the Abstract and

Conclusions; (ii) restricted the interpretation of the MD adsorption results to molecular-scale behavior in the idealized C60/water/2,4-DNP system in Section 3.2; (iii) added a discussion in the Conclusions acknowledging that phenolic atmospheric chemistry is governed by multiple competing pathways—including metal-catalyzed reactions (Al-Abadleh et al., 2021), nitrate radical oxidation (Rana and Guzman, 2022; Ng et al., 2017), and multiphase oligomerization (Guzman et al., 2022; Rana et al., 2024)—that were not captured in our model; and (iv) removed claims about regulatory implications. The conclusions are now limited to what is directly supported by the computational results.

Response to Minor Comments

1. The abstract should clearly distinguish gas-phase, aqueous-phase, and interfacial results.

Response: We thank the reviewer for this suggestion. In the revised manuscript, we have restructured the Abstract to clearly distinguish the gas-phase, aqueous-phase, and interfacial results, presenting them in a logical sequence starting with gas-phase kinetics, followed by aqueous-phase kinetics, then interfacial adsorption, and finally toxicity assessment. The specific rate constants and key findings for each phase are now explicitly stated: "This study elucidates the atmospheric transformation mechanisms of 2,4-dinitrophenol (2,4-DNP) using an integrated computational framework. In the gas phase, initial oxidation by hydroxyl radicals (•OH) and ozone (O_3) is identified as the dominant pathway (kOH = 3.18×10^{-15} cm^3 $molecule^{-1}$ s^{-1}, kO_3 = 4.23×10^{-23} cm^3 $molecule^{-1}$ s^{-1}), whereas the direct reaction with nitrogen

dioxide radical (•NO_2) is kinetically hindered ($k$$NO_2$ ~10^{-28} cm^3 $molecule^{-1}$ s^{-1}). In the aqueous phase, solvation effects suppress the reaction rates, while the two nitro substituents exert a cumulative electron-withdrawing effect that reduces the rate constant by three orders of magnitude relative to mononitrocatechol. For the key radical intermediate generated by •OH addition, hydrogen atom abstraction (HAA) with O_2 represents the dominant atmospheric fate, with O_2's overwhelming concentration advantage over •NO_2 ensuring this pathway prevails. At the gas-aqueous interface, molecular dynamics simulations reveal that the adsorption of 2,4-DNP onto the C60 aerosol surrogate is non-monotonically modulated by interfacial hydration—first strengthening at moderate hydration and weakening at high hydration due to competitive solvation. Finally, computational toxicology predicts that certain ozonolysis products exhibit elevated Ames mutagenicity and developmental toxicity indicators relative to the parent compound, suggesting that oxidative processing of 2,4-DNP may not lead to simple detoxification. These findings provide mechanistic insights into the atmospheric transformation pathways of this specific dinitrophenol and highlight the importance of evaluating transformation product toxicity in the environmental risk assessment of nitrophenolic compounds."

2. Replace "governs" in the title (and elsewhere) with a weaker term such as "modulates" or "influences."

Response: We thank the reviewer for this suggestion. We have revised the title to use "modulates," which more accurately reflects the regulatory nature of the hydration

effect. We have also made this change consistently throughout the manuscript wherever the hydration effect is described.

The revised title (in full) is "Unveiling the multiphase fate of 2,4-dinitrophenol on aerosols: Interfacial hydration modulates competing oxidation pathways and predicted increase in toxicity".

3. Replace "toxicity amplification" in the title with more cautious language (e.g., "predicted increase in toxicity indicators").

Response: We thank the reviewer for this critical suggestion. We agree that "toxicity amplification" is too definitive a claim given that our toxicity assessment relies entirely on QSAR predictions without experimental validation. In the revised title, we have replaced "unexpected toxicity amplification" with "Predicted Toxicity Indicators," which more accurately reflects the screening-level, hypothesis-generating nature of the computational toxicology findings. We have also revised the Abstract and main text to use similarly cautious language throughout, consistently framing the toxicity findings as predictions rather than definitive conclusions.

The revised title (in full) is "Unveiling the multiphase fate of 2,4-dinitrophenol on aerosols: Interfacial hydration modulates competing oxidation pathways and predicted increase in toxicity".

4. Clarify the definition and context of reported rate constants, and improve discussion of Table S2.

Response: We thank the reviewer for this suggestion. In the revised manuscript, we have clarified the definition and context of the reported rate constants and improved the discussion of Table S2.

Specifically, we have: (i) explicitly defined the reported rate constants as second-order rate constants, representing the intrinsic reactivity of 2,4-DNP with each oxidant in a given phase; (ii) expanded the discussion of Table S2; and (iii) emphasized that second-order rate constants alone should not be interpreted as direct measures of atmospheric importance, as their actual contribution depends on oxidant concentrations, phase partitioning (Henry's law), and aerosol liquid water content.

A revised paragraph discussing Table S2 has been added to Section 3.1.2 of the manuscript: "First, the rate constants for both •OH and O_3 pathways decrease systematically with increasing nitro substitution: catechol (9.60×10^{-18} cm^3 $molecule^{-1}$ s^{-1}) → 4-nitrocatechol (1.48×10^{-20} cm^3 $molecule^{-1}$ s^{-1}) → 2,4-DNP (4.23×10^{-23} cm^3 $molecule^{-1}$ s^{-1}) for O_3; 3.18×10^{-15} cm^3 $molecule^{-1}$ s^{-1} for •OH. This trend quantitatively demonstrates the cumulative electron-withdrawing effect of nitro substituents on aromatic ring reactivity. Second, aqueous-phase rate constants for 2,4-DNP are consistently lower than their gas-phase counterparts, reflecting the inhibitory effect of solvation on these reactions. Third, the •OH pathway exhibits rate constants that are 7–8 orders of magnitude higher than the O_3 pathway in the gas phase and 6–7 orders of magnitude higher in the aqueous phase, confirming •OH as the dominant atmospheric oxidant for 2,4-DNP. The direct $•NO_2$ pathway, with rate constants on the order of 10^{-28} cm^3 $molecule^{-1}$ s^{-1}, is more than 13 orders of magnitude

slower than the •OH pathway. It should be noted that these second-order rate constants represent intrinsic reactivities; their actual atmospheric importance depends on oxidant concentrations, phase partitioning, and aerosol liquid water content, as discussed below through pseudo-first-order calculations. As shown in Figure 3d–e, the rate constants of all major channels increase with temperature over the range of 200–400 K, exhibiting a characteristic Arrhenius-type temperature dependence.

The literature review indicates that •OH concentrations typically reach $1 \times 10^6 \sim 3 \times 10^6$ molecules cm^{-3}, while $•NO_2$ levels are lower due to rapid photolysis under daytime conditions. During heavily polluted nighttime conditions, however, •OH concentrations drop substantially. Geyer et al. (2003) reported a nocturnal •OH concentration of $(1.85 \pm 0.82) \times 10^5$ cm^{-3} during the BERLIOZ campaign, and in UK urban surface environments, night-time OH levels were determined to be in the range of $10^5 \sim 10^6$ molecules cm^{-3}. Meanwhile, $•NO_2$ can accumulate significantly at night, with nocturnal maxima reaching 8.43 ± 0.4 ppb in Guangzhou. Using these literature-reported concentrations, the pseudo-first-order rate constants under nighttime conditions can be estimated. For the •OH pathway, with kOH = 3.18×10^{-15} cm^3 $molecule^{-1}$ s^{-1} and [OH] ≈ $10^5 \sim 10^6$ molecules cm^{-3}, k'OH ≈ $10^{-10} \sim 10^{-9}$ s^{-1}. For the direct $•NO_2$ pathway, with $k$$NO_2$ ≈ 10^{-28} cm^3 $molecule^{-1}$ s^{-1} and [NO_2] ≈ $10^{10} \sim 10^{11}$ molecules cm^{-3} (corresponding to 0.4 ~ 4 ppb at 298 K and 1 atm), k'NO_2 ≈ $10^{-18} \sim 10^{-17}$ s^{-1}. Even under the most favorable nighttime conditions (lowest •OH, highest $•NO_2$), the direct $•NO_2$ pathway remains more than 7 orders of magnitude slower than the •OH pathway, corresponding to a lifetime of $>10^{10}$ s, which is negligible on

atmospheric timescales. Therefore, while a full diurnal box model simulation would be required to quantify all pathways under varying pollution regimes, the quantitative analysis above confirms that the direct reaction of $\bullet NO_2$ with parent 2,4-DNP is negligible even under nighttime conditions. The possible involvement of $\bullet NO_2$ in subsequent reactions with primary oxidation intermediates will be discussed separately to provide a complete mechanistic picture of its environmental fate. In summary, the atmospheric degradation of 2,4-DNP is kinetically dominated by •OH, with O_3 playing a significant role in the aqueous phase, while the direct transformation contribution of $\bullet NO_2$ can be neglected in environmental assessments.

The overall contribution of aqueous-phase reactions to the atmospheric fate of 2,4-DNP depends critically on the fraction of the compound that partitions into the aqueous phase. For 2,4-DNP, the Henry's law constant has been determined as 5.70×10^{-8} atm·m^3/mol at 5 °C (Lüttke and Levsen, 1997), indicating a strong tendency to partition into the aqueous phase. The partitioning is further modulated by its acid dissociation constant (pKa ≈ 4.09 at 25 °C), as the deprotonated phenolate form is substantially more water-soluble than the neutral phenol. In addition, the aerosol liquid water content—which varies widely depending on relative humidity, particle composition, and atmospheric conditions—determines the available aqueous volume for multiphase reactions. Without quantitative information on these partitioning parameters under specific atmospheric conditions, the aqueous-phase rate constants should be interpreted as intrinsic reactivity indicators rather than direct measures of atmospheric importance."

5. Add pseudo-first order loss estimates or limit interpretation to relative trends.

Response: We thank the reviewer for this important suggestion. We have added pseudo-first-order calculations in the revised manuscript and have refined our interpretation to emphasize that second-order rate constants alone should not be interpreted as direct measures of atmospheric importance, limiting conclusions to relative trends where quantitative loss estimates are not available.

In Section 3.1.2, we have added a quantitative comparison of the pseudo-first-order rate constants for the •OH and direct $•NO_2$ pathways under nighttime conditions: "The literature review indicates that •OH concentrations typically reach $1 \times 10^6 \sim 3 \times 10^6$ molecules cm^{-3}, while $•NO_2$ levels are lower due to rapid photolysis under daytime conditions. During heavily polluted nighttime conditions, however, •OH concentrations drop substantially. Geyer et al. (2003)(Geyer, A., Bächmann, K., Hofzumahaus, A., Holland, F., Konrad, S., Klüpfel, T., Pätz, H. W., Perner, D., Mihelcic, D., Schäfer, H. J., and Volz-Thomas, A.: Nighttime formation of peroxy and hydroxyl radicals during the BERLIOZ campaign: Observations and modeling studies, J. Geophys. Res., 108(D4), 8249, doi:10.1029/2001JD000656, 2003.) reported a nocturnal •OH concentration of $(1.85 \pm 0.82) \times 10^5$ cm^{-3} during the BERLIOZ campaign, and in UK urban surface environments, night-time OH levels were determined to be in the range of $10^5 \sim 10^6$ molecules cm^{-3} (Khan, M. A. H., Hoque, M. M. N., Alam, S. S., Ashfold, M. J., Nickless, G., and Shallcross, D. E.: Estimation and comparison of night-time OH levels in the UK urban atmosphere using two different analysis methods, J. Environ.

Sci., 23(1), 60–64, doi:10.1016/s1001-0742(10)60373-7, 2011.). Meanwhile, •NO_2 can accumulate significantly at night, with nocturnal maxima reaching 8.43 ± 0.4 ppb in Guangzhou (Qin, M., Xie, P. H., Su, H., Gu, J. W., Peng, F. M., Li, S. W., Zeng, L. M., Liu, J. G., Liu, W. Q., and Zhang, Y. H.: An observational study of the HONO–NO_2 coupling at an urban site in Guangzhou City, South China, Atmos. Environ., 43(36), 5731–5742, doi:10.1016/j.atmosenv.2009.08.017, 2009.) Using these literature-reported concentrations, the pseudo-first-order rate constants under nighttime conditions can be estimated. For the •OH pathway, with kOH = 3.18×10^{-15} cm^3 $molecule^{-1}$ s^{-1} and [OH] ≈ 10^5 ~ 10^6 molecules cm^{-3}, k'OH ≈ 10^{-10} ~ 10^{-9} s^{-1}. For the direct •NO_2 pathway, with $k$$NO_2$ ≈ 10^{-28} cm^3 $molecule^{-1}$ s^{-1} and [NO_2] ≈ 10^{10} ~ 10^{11} molecules cm^{-3} (corresponding to 0.4 ~ 4 ppb at 298 K and 1 atm), k'NO_2 ≈ 10^{-18} ~ 10^{-17} s^{-1}. Even under the most favorable nighttime conditions (lowest •OH, highest •NO_2), the direct •NO_2 pathway remains more than 7 orders of magnitude slower than the •OH pathway, corresponding to a lifetime of >10^{10} s, which is negligible on atmospheric timescales. Therefore, while a full diurnal box model simulation would be required to quantify all pathways under varying pollution regimes, the quantitative analysis above confirms that the direct reaction of •NO_2 with parent 2,4-DNP is negligible even under nighttime conditions. The possible involvement of •NO_2 in subsequent reactions with primary oxidation intermediates will be discussed separately to provide a complete mechanistic picture of its environmental fate. In summary, the atmospheric degradation of 2,4-DNP is kinetically dominated by •OH,

with O_3 playing a significant role in the aqueous phase, while the direct transformation contribution of $\bullet NO_2$ can be neglected in environmental assessments."

In Section 3.1.3, we have added a quantitative effective rate comparison for the reaction of the key intermediate IM3' with O_2 versus $\bullet NO_2$: "It should be emphasized that the competition between O_2 and $\bullet NO_2$ for IM3' must be evaluated based on effective rates (k × [oxidant]) rather than second-order rate constants alone. The atmospheric concentration of O_2 is 5.4×10^{18} molecules cm^{-3} (0.21 atm). For the reaction of IM3' with O_2 via HAA (barrier = 2.86 kcal mol^{-1}), the barrier height indicates that the reaction is near the gas-kinetic limit, with rate constants for alkyl radical + O_2 reactions typically in the range of $10^{-12} \sim 10^{-11}$ cm^3 $molecule^{-1}$ s^{-1} (Miyoshi et al., 1990 (Miyoshi, A., Matsui, H., and Washida, N.: Rates of reaction of hydroxyalkyl radicals with molecular oxygen, J. Phys. Chem., 94, 3016–3019, 1990). Taking a conservative estimate of $kO_2 \approx 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1}, the effective rate is $k'O_2 \approx 10^{-12} \times 5.4 \times 10^{18} \approx 5.4 \times 10^6$ s^{-1}, corresponding to a lifetime of 0.2 microseconds—consistent with the well-established behavior that alkyl radicals react with O_2 on timescales of 10 ~ 100 nanoseconds (Vereecken and Francisco, 2012 Vereecken, L. and Francisco, J. S.: Theoretical studies of atmospheric reaction mechanisms in the troposphere, Chem. Soc. Rev., 41, 6259–6293, 2012.; Calvert et al., 2015 Calvert, J. G., Orlando, J. J., Stockwell, W. R., and Wallington, T. J.: The Mechanisms of Reactions Influencing Atmospheric Ozone, Oxford University Press, 2015.). For the reaction of IM3' with $\bullet NO_2$ via HAA (barrier = 2.01 kcal mol^{-1}), even under the most favorable nighttime conditions with $[\bullet NO_2] \approx 10^{10} \sim 10^{11}$ molecules

cm^{-3}, and taking $kNO_2 \approx 10^{-11}$ cm^3 $molecule^{-1}$ s^{-1}, the effective rate is $k'NO_2 \approx 10^{-1} \sim 1$ s^{-1}, corresponding to a lifetime of 1 ~ 10 seconds. Thus, $k'O_2$ is more than 6 orders of magnitude faster than $k'NO_2$. The overwhelming concentration advantage of O_2—more than 10^7 times that of $\bullet NO_2$—ensures that the reaction of IM3' with O_2 is the dominant atmospheric fate of this intermediate. This is fully consistent with the established behavior that addition of O_2 is essentially the sole atmospheric fate of organic radicals formed during the oxidation of organic compounds (Calvert et al., 2015)."

6. Clearly state that C60 is an idealized surrogate and not representative of real aerosols.

Response: We thank the reviewer for this important suggestion. We agree that the idealized nature of C60 as an aerosol surrogate must be stated explicitly. In the revised manuscript, we have added clear statements to ensure this limitation is properly communicated: "The results obtained with this surrogate provide molecular-level insights into specific interaction mechanisms, but should not be directly extrapolated to real atmospheric aerosols without considering the additional complexity of real particle surfaces"; "the C60 aerosol surrogate, while useful for isolating specific non-covalent interactions, does not capture the full chemical complexity of real atmospheric particles—particularly the presence of oxygen-containing functional groups, surface defects, and heteroatoms that may enhance polar interactions. As a result, the C60 model may overestimate the contribution of π-π interactions and underestimate the role of polar interactions.

Future complementary simulations using more realistic carbon models, such as amorphous carbon clusters or graphene with functional groups, would be valuable to validate the trends identified here".

7. Justify the MD timescale or reduce the strength of related conclusions.

Response: We thank the reviewer for this thoughtful comment. We fully acknowledge that longer simulations would be desirable. However, we respectfully argue that the current 1 ns simulations are scientifically justified for this specific system, for the following reasons.

First, the 1 ns production run is sufficient because the key observable—the adsorption energy of 2,4-DNP on the C60 surface—converged rapidly. As shown in Figure 6c, the interaction energies stabilized within the first 500 ps and remained stable throughout the remaining trajectory. For small molecule adsorption on rigid surfaces, convergence is typically achieved on the sub-nanosecond timescale. Second, the non-monotonic hydration-dependent adsorption trend, which is the central finding of our MD study, was consistently reproduced across four independent replicas at each hydration level. As emphasized in best practice guidelines for MD simulations (Reliability and reproducibility checklist for molecular dynamics simulations. *Commun Biol* 6, 268 (2023). https://doi.org/10.1038/s42003-023-04653-0), partial equilibrium may be sufficient if the properties of interest have converged. The consistency across replicas, rather than the absolute simulation length, provides the statistical confidence for our conclusions. Third, we have added a limitation statement in the Conclusions noting that "the 1 ns MD timescale is sufficient for the rigid

C60/small molecule system studied here, but longer simulations may be needed to capture slower dynamical processes on more complex surfaces".

8. Explain why photolysis is not included in the reaction framework.

Response: We thank the reviewer for this important question. Photolysis of 2,4-dinitrophenol was not included in the reaction framework because its atmospheric significance is substantially lower than that of •OH and O_3 oxidation under the conditions relevant to this study.

Albinet et al. (2010) (Albinet, A., Minero, C., and Vione, D.: Phototransformation processes of 2,4-dinitrophenol, relevant to atmospheric water droplets, Chemosphere, 80, 753–758, doi:10.1016/j.chemosphere.2010.05.016, 2010.) systematically investigated the phototransformation of 2,4-DNP in atmospheric water droplets and determined the polychromatic quantum yields for photolysis in the 300–500 nm wavelength range as $(8.1 \pm 0.4) \times 10^{-5}$ for the undissociated phenol and $(3.4 \pm 0.2) \times 10^{-5}$ for the phenolate. These extremely low quantum yields indicate that direct photolysis is a relatively inefficient loss process for 2,4-DNP compared to its reactions with •OH and O_3. In contrast, the second-order rate constants for •OH oxidation are $(1.76 \pm 0.05) \times 10^9$ M^{-1} s^{-1} and $(2.33 \pm 0.11) \times 10^9$ M^{-1} s^{-1} for the neutral and phenolate forms, respectively (Albinet et al., 2010), making •OH-driven oxidation the dominant daytime loss pathway. Furthermore, the present study focuses on thermal (dark) oxidation pathways initiated by O_3, •OH, and $•NO_2$, which are relevant both day and night. While photolysis is an important process for some nitrophenols,

its contribution to the overall transformation of 2,4-DNP is minor compared to the oxidation pathways investigated here.

9. Acknowledge nitrate radical chemistry as a relevant but excluded pathway.

Response: We thank the reviewer for this important suggestion. We agree that nitrate radical ($\bullet NO_3$) chemistry is a relevant nighttime oxidation pathway for phenolic compounds and should be acknowledged. In the revised manuscript, we have added this acknowledgment directly in Introduction: "Nitrate radical ($\bullet NO_3$) chemistry, although an important nighttime oxidation pathway for phenolic compounds that contributes to secondary organic aerosol and brown carbon formation at the air-water interface (Rana and Guzman, 2022; Ng et al., 2017)(Rana, M. S. and Guzman, M. I.: Oxidation of Catechols at the Air-Water Interface by Nitrate Radicals, Environ. Sci. Technol., 56(22), 15437–15448, doi:10.1021/acs.est.2c05640, 2022.; Ng, N. L., Brown, S. S., Archibald, A. T., et al.: Nitrate radicals and biogenic volatile organic compounds: oxidation, mechanisms, and organic aerosol, Atmos. Chem. Phys., 17(3), 2103–2162, doi:10.5194/acp-17-2103-2017, 2017.), was not included in the present framework because our study focuses on thermal oxidation pathways initiated by O_3, $\bullet OH$, and $\bullet NO_2$ in the gas and aqueous phases."

10. Correct the formatting error in Table S3 (next to the rate constant of nitrophenol).

Response: We thank the reviewer for pointing out this error. We have carefully checked Table S3 and corrected the rate constant for nitrophenol from "10^{-116}" to the

proper superscript format "10^{-11}". We have also reviewed the entire table to ensure all exponents are consistently formatted as superscripts.

11. Improve figure clarity and ensure all pathways, phases, and units are clearly labeled.

Response: We thank the reviewer for this suggestion. We have systematically reviewed all figures to ensure: (i) all axes labels include the physical quantity and units; (ii) legends are placed in positions that do not overlap with data; (iii) font sizes have been uniformly increased to ensure readability in print; (iv) all subpanel titles are consistently formatted as "(a)", "(b)", etc.

12. Move detailed mechanistic/geometric descriptions to the supplement where appropriate.

Response: We thank the reviewer for this suggestion. In the revised manuscript, we have streamlined the main text by moving detailed mechanistic and geometric descriptions to the Supplementary Information, while retaining only the key mechanistic conclusions and structural trends in the main text.

Specifically, we have: (i) moved detailed bond lengths, bond angles, and dihedral angles for all transition states and intermediates to a new Table S5 in the Supplement; (ii) summarized the O_3, •OH, and •NO_2 reaction pathways in Section 3.1.2 with concise descriptions of the key bond-breaking and bond-forming events, without listing every geometric parameter; (iii) similarly, for the IM3' subsequent reactions in Section 3.1.3, retained only the essential structural features that support the mechanistic conclusions. The main text now focuses on mechanistic interpretations,

while all supporting geometric data are available in the Supplement for readers who wish to examine them in detail.

13. Expand discussion of QSAR uncertainty and threshold limitations (Table S4).

Response: We thank the reviewer for this suggestion. In the revised manuscript, we have expanded the discussion of QSAR uncertainty and threshold limitations in Section 3.3, with specific reference to Table S4.

Specifically, we have added: (i) a clearer explanation of the applicability domain limitations of the T.E.S.T. models, noting that the training set chemical space may not fully cover nitroaromatic compounds; (ii) an explicit discussion of the instability of categorical predictions with probability scores close to the classification threshold, explaining why compounds such as IM17, IM25, IM44, and IM54 showed "not detected" Ames mutagenicity signals that may reflect model limitations rather than a definitive absence of toxicity; (iii) a quantitative reference to the performance of QSAR models for Ames mutagenicity prediction, acknowledging that even the best-performing models achieve a balanced accuracy of approximately 76.9% at 100% coverage; and (iv) a recommendation that these compounds be considered high-priority targets for experimental validation. These additions are now included in Section 3.3, and the expanded discussion is cross-referenced with Table S4, which presents the detailed prediction results and threshold values.

The manuscript has been revised as follows: "The QSAR models utilized in this study provide valuable preliminary information for risk prioritization; however, the

inherent uncertainties associated with in silico predictions must be acknowledged. The predictive performance is fundamentally constrained by the chemical space of the training sets and the defined applicability domains. For structurally distinct species such as 2,4-DNP and its various derivatives, the confidence levels of the predictions may be diminished because these models cannot fully elucidate specific toxicological modes of action. As highlighted by the Ames/QSAR International Challenge Projects, even the best-performing models for Ames mutagenicity prediction achieve a balanced accuracy of approximately 76.9% at 100% coverage (Uesawa, 2024)(Uesawa, Y.: Progress in Predicting Ames Test Outcomes from Chemical Structures: An In-Depth Re-Evaluation of Models from the 1st and 2nd Ames/QSAR International Challenge Projects, Int. J. Mol. Sci., 25(3), 1373, doi:10.3390/ijms25031373, 2024.), indicating that inherent uncertainties remain. In addition, categorical predictions with probability scores close to threshold are inherently unstable; as shown in Table S4, the "not detected" Ames mutagenicity signals for intermediates such as IM17, IM25, IM44, and IM54 fall within this near-threshold regime. This suggests that these signals may reflect model limitations rather than a definitive absence of toxicity. These compounds should therefore be regarded as high-priority targets for experimental validation. Furthermore, these computational frameworks necessarily simplify complex biological endpoints such as developmental toxicity. A quantitative weight-of-evidence (qWoE) approach, which combines predictions from multiple QSAR models, has been shown to achieve accuracy similar to that of the experimental Ames test (Tintó-Moliner et al., 2020)

(Tintó-Moliner, A., et al.: Quantitative weight of evidence method for combining predictions of quantitative structure-activity relationship models, SAR QSAR Environ. Res., 31(4), 261–279, doi:10.1080/1062936X.2020.1725116, 2020.); however, such approaches are beyond the scope of the present screening-level assessment. Therefore, the present findings should be interpreted as hypothesis-generating rather than definitive, and we recommend experimental validation through in vitro Ames tests and zebrafish embryo development assays for the high-priority compounds identified."

14. Revise the conclusions to clearly separate computational results from atmospheric implications and avoid unsupported claims.

Response: We thank the reviewer for this important suggestion. In the revised manuscript, we have substantially reorganized the Conclusions to clearly separate the computational results from the atmospheric implications, and we have removed or qualified all unsupported claims:

"This study systematically investigated the chemical transformation mechanisms, multiphase interfacial behavior, and toxicity evolution of 2,4-DNP in the atmosphere using an integrated computational framework combining DFT, MD simulations, and QSAR models. The main quantitative findings are: the atmospheric degradation of 2,4-DNP is dominated by the •OH pathway in the gas phase, while O_3 plays a significant role in the aqueous phase; direct reaction with $•NO_2$ is kinetically unfavorable (gas-phase rate constant 10^{-28} cm^3 $molecule^{-1}$ s^{-1}, more than 13 orders of magnitude lower than that of •OH); solvation effects and the electron-withdrawing

nitro groups suppress the initial reaction rates; the key radical intermediate from •OH addition reacts with O_2 and $•NO_2$ predominantly via HAA; MD simulations reveal that the adsorption behavior of 2,4-DNP on the idealized C60 aerosol surrogate is regulated non-monotonically by the degree of interfacial hydration, with enhanced solute-particle interactions under low-hydration conditions and weakened adsorption under high-hydration conditions; and QSAR predictions indicate that certain ozonolysis products exhibit elevated Ames mutagenicity and developmental toxicity indicators relative to the parent compound. Compared to previous studies that focused on gas-phase photolysis and assumed oxidative detoxification, our work quantifies the cumulative electron-withdrawing effect of two nitro groups (rate constant three orders lower than mononitrocatechol) and predicts that ozonolysis products may exhibit increased toxicity indicators, challenging conventional assumptions that oxidative degradation necessarily leads to detoxification. While the quantitative conclusions apply specifically to 2,4-DNP, the qualitative framework established here—linking substituent electronic effects to reaction kinetics, interfacial behavior, and toxicity indicators—may serve as a reference for understanding related nitroaromatic systems.

Several limitations should be noted: the C60 aerosol surrogate, while useful for isolating specific non-covalent interactions, does not capture the full chemical complexity of real atmospheric particles—particularly the presence of oxygen-containing functional groups, surface defects, and heteroatoms that may enhance polar interactions. As a result, the C60 model may overestimate the contribution of π-π interactions and underestimate the role of polar interactions.

Future complementary simulations using more realistic carbon models, such as amorphous carbon clusters or graphene with functional groups, would be valuable to validate the trends identified here. The 1 ns MD timescale is sufficient for the rigid C60/small molecule system studied here, but longer simulations may be needed to capture slower dynamical processes on more complex surfaces. Additionally, the QSAR toxicity predictions are screening-level estimates requiring experimental validation; and a full diurnal box model simulation incorporating temporally resolved oxidant concentrations, Henry's law partitioning, and aerosol liquid water content would be needed to fully quantify the atmospheric importance of each pathway under realistic conditions.

Based on these findings, we recommend the following directions for future research: (i) Experimental validation of predicted kinetics: Advanced kinetic techniques such as laser-induced fluorescence or cavity ring-down spectroscopy should be employed to measure the rate constants for the reactions of 2,4-DNP with O_3 and •OH, providing direct experimental confirmation of the theoretical trends. (ii) In vitro toxicity testing: The high-priority ozonolysis products identified in this study (IM54, P1, and P2) should be subjected to Ames mutagenicity assays and zebrafish embryo developmental toxicity tests to validate the QSAR predictions. (iii) Refined interfacial models: Complementary MD simulations using more realistic carbonaceous models, such as functionalized graphene or amorphous carbon clusters, would help assess the influence of surface functional groups and defects on the adsorption behavior of 2,4-DNP. (iv) Diurnal box model simulations: Full diurnal

chemical box models incorporating temporally resolved oxidant concentrations, Henry's law partitioning, and aerosol liquid water content are needed to fully quantify the atmospheric importance of each oxidation pathway under different pollution regimes. Despite these caveats, the mechanistic insights into the molecular-level reactivity and interfacial behavior of 2,4-DNP provide a foundation for future experimental and modeling studies on the multiphase fate of nitrophenolic compounds."