

A Large-Scale Dataset for Molecular Structure-Language Description via a Rule-Regularized Method

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Abstract

Molecular function is largely determined by structure. Accurately aligning molecular structure with natural language is therefore essential for enabling large language models (LLMs) to reason about downstream chemical tasks. However, the substantial cost of human annotation makes it infeasible to construct large-scale, high-quality datasets of structure-grounded descriptions. In this work, we propose a fully automated annotation framework for generating precise molecular structure descriptions at scale. Our approach builds upon and extends a rule-based chemical nomenclature parser to interpret IUPAC names and construct enriched, structured XML metadata that explicitly encodes molecular structure. This metadata is then used to guide LLMs in producing accurate natural-language descriptions. Using this framework, we curate a large-scale dataset of approximately 163k molecule-description pairs. A rigorous validation protocol combining LLM-based and expert human evaluation on a subset of 2,000 molecules demonstrates a high description precision of 98.6%. The resulting dataset provides a reliable foundation for future molecule-language alignment, and the proposed annotation method is readily extensible to larger datasets and broader chemical tasks that rely on structural descriptions.

1. Introduction

By aligning other modalities with language, the strong reasoning capabilities and flexibility of large language models (LLMs) can be transferred to multimodal settings, allowing for interpretation and inference beyond text. This paradigm has proven particularly successful in vision-language models (VLMs). For example, VLMs are now widely used for

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image recognition and analysis (OpenAI, 2025b), as well as for conditional image generation and editing based on user instructions (OpenAI, 2025c). Similarly, aligning molecular representations with language could enable chemical reasoning that are currently not possible for traditional unimodal models (Cai et al., 2025b; Irwin et al., 2022), thereby providing new opportunities for diverse chemical tasks such as property prediction (Wu et al., 2018), molecular and drug discovery (Brown et al., 2019; Polykovskiy et al., 2020), and synthesis prediction and planning (Lowe, 2017).

Early attempts to bridge molecular representations with language include the curation of molecule-description datasets (Edwards et al., 2021; 2024) and subsequent models that translate between the two modalities (Edwards et al., 2021; 2022). With the emergence of LLMs, research efforts have shifted toward leveraging them for downstream chemical tasks, including direct capability benchmarking (Guo et al., 2023), training chemistry- or science-specific LLMs (Taylor et al., 2022; Zhang et al., 2024), and building multimodal models (Su et al., 2022; Jablonka et al., 2024; Liu et al., 2025). However, these approaches remain far from practical use and still lag behind specialized unimodal chemical models on nearly all downstream tasks.

These models, along with curated datasets, bypass alignment between language and the underlying molecular structure. Instead, they attempt to directly bridge the molecular representations with downstream objectives that require higher-level, domain-specific reasoning. However, as illustrated in Fig. 2, a molecule’s function, including physicochemical properties and reaction mechanisms, is fundamentally determined by its structure. Whether performing property inference, molecular design, or reaction planning, chemists always rely on an explicit understanding of molecular structure, and so should AI models. This gap has been systematically highlighted by the recent MolLangBench benchmark (Cai et al., 2025a), which evaluates molecule-language interface tasks such as molecular structure recognition, structure generation, and structure editing from language. The results show that even advanced general-purpose AI systems, perform far from perfectly on these tasks, while chemistry-specific multimodal models fail almost entirely. Without

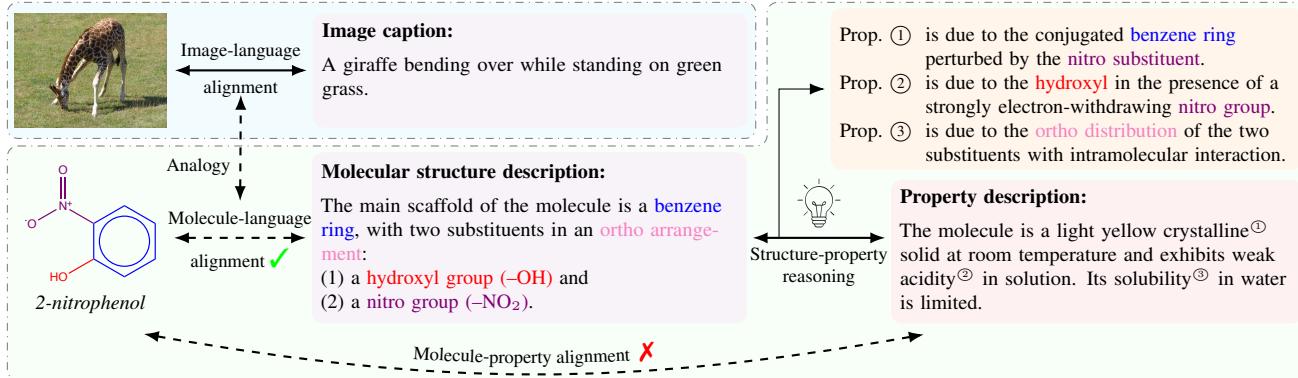


Figure 1. An illustrative example motivating this work. Existing approaches align molecular representations with high-level objectives, while we argue molecule-language alignment should be structure-grounded, with higher-level reasoning handled by the LLM backbone, analogous to image-language alignment. Real molecular descriptions in this work are substantially more complex than this example.

these foundational capabilities, success on more complex chemical reasoning tasks is unlikely.

We therefore argue that *molecular representations should first be aligned with structure-grounded language descriptions*. More advanced chemical knowledge and functional reasoning should then be encoded and learned within the language model through large-scale external knowledge training. This resonates with vision-language modeling: image descriptions typically focus on faithfully describing the *observed visual content*, as illustrated in Fig. 2, with the visual module serving primarily as a perception or generation component, while deeper interpretation and reasoning are delegated to the LLM backbone (Zhou et al., 2025).

Molecule-language alignment thus demands a large volume of structure-grounded descriptions, analogous to those used in VLMs (Schuhmann et al., 2022). However, curating molecular description datasets presents fundamentally different challenges. First, subtle changes in molecular structure can lead to dramatic changes in properties (Eichelbaum et al., 2012; Smith, 2020), requiring descriptions to be complete and unambiguous. Second, unlike the image domain, no readily available large-scale molecular structure descriptions exist. Given the inherent complexity of molecular structures, including intricate ring topologies, multiple and nested substituents, stereochemical configurations, human annotation at scale is also impractical: annotating and validating a single complete structure description can require approximately 1 hour of expert effort (Cai et al., 2025a).

In this work, we address this challenge by developing an automated annotation framework. Building upon and extending OPSIN (Lowe et al., 2011), a rule-based tool that parses systematic IUPAC names into molecular structure representations, we perform substantial engineering to construct enriched, structured XML metadata that explicitly encodes molecular structure. The resulting metadata captures ring topology, substituents, attachment relationships, and labeling semantics, and is injected into LLMs to regularize

accurate molecular structure description generation. Using this pipeline, we curate 163,085 molecule-description pairs, with a rigorous validation on a 2,000-sample subset demonstrating a high annotation precision of 98.6%. Together, this annotation pipeline and the resulting large-scale dataset establish a scalable and reliable foundation for molecule-language alignment prior to advancing chemical reasoning.

2. Task Formulation and Challenges

Motivated by the premise that effective molecule-language alignment should be grounded at the structural level, in this paper we consider the task of generating a large-scale dataset of molecular structure descriptions. Specifically, we aim to construct a dataset in which each entry consists of a molecular structure and a corresponding structural description text, denoted as a pair $(\mathcal{M}, \mathcal{T})$. The description \mathcal{T} is precise and unambiguous, such that the molecular structure \mathcal{M} can be uniquely determined from it. Conversely, while a given molecular structure may admit multiple valid natural-language descriptions due to linguistic and chemical terminology variation, all such descriptions should be semantically equivalent. However, generating such a dataset at scale presents several challenges:

Challenge 1: Appropriate Level of Structural Detail

At one extreme, a description could enumerate all atoms, bond types, connectivities, and stereochemical relationships. Although such descriptions can be generated by traversing molecular graph, they become verbose even for molecules of moderate size. More importantly, molecular properties and chemical reactions are often associated with specific functional groups and scaffold-level motifs rather than individual atoms in isolation. Purely atom-level descriptions therefore fail to align structure with the abstractions most useful for downstream reasoning. At the other extreme, descriptions that only summarize functional groups or scaffold types may omit critical structural details. Subtle differences in ring topologies, attachment positions, or

stereochemistry can substantially change physicochemical properties, biological activity, or toxicity (Eichelbaum et al., 2012; Smith, 2020), and thus cannot be ignored. An effective description must therefore balance sufficient structural specificity with chemically meaningful abstractions.

Challenge 2: Scalability of Dataset Construction

Molecule-language modeling typically requires datasets containing hundreds of thousands to millions of molecule-description pairs. According to MolLangBench (Cai et al., 2025a), annotating and validating a single structure description can require up to 1 hour of expert effort. Even hybrid pipelines that combine LLM-assisted generation with human validation remain impractical at this scale. Dataset construction must therefore rely on fully automated generation while maintaining high description accuracy.

Challenge 3: Insufficient Structural Information

LLMs are increasingly used to scale annotation (Tan et al., 2024), but accurate molecular structure descriptions generation depends heavily on the complete and precise structural information provided as input, which is not conveyed by commonly used molecular representations. Linear representations such as SMILES (Weininger, 1988) specify atom-wise connectivity through grammar rules and traversal order, but they do not directly represent structural information. LLMs must infer these abstractions from atom-level sequences, which we and prior work (Cai et al., 2025a) find to be error-prone, particularly for molecules with complex ring topologies and long side chains.

IUPAC nomenclature more closely reflects how chemists describe molecular structures. However, directly converting IUPAC names into accurate structural descriptions is non-trivial. Correct interpretation requires extensive knowledge of complex nomenclature rules, including tokenization conventions, locant assignment, ring labeling schemes, and fusion, bridged, and spiro descriptors. For example, in the illustrative example shown in Fig.2, interpreting the IUPAC name requires understanding how to tokenize, where and in what order to start parsing, what fusion letters mean (e.g., the ‘e’ in fused-ring notation), and how to handle numerical locants after complex ring fusion, bridging, and spiro structures. Indeed, the IUPAC Blue Book (Favre & Powell, 2013) takes over 1,100 pages to provide guidance for IUPAC nomenclature of organic compounds. Consequently, directly generating descriptions from IUPAC remains unreliable for precise structure description generation, as we demonstrate in ablation study (Sec. 4.3).

3. Methodology of Dataset Generation

Building on OPSIN (Lowe et al., 2011), a rule-based system for interpreting chemical nomenclature and reconstructing molecular structures, we develop an automated pipeline

that substantially adapts and extends its intermediate representations to produce complete, structured XML metadata encoding molecular structure. This metadata is used to guide LLMs in generating accurate and unambiguous molecular structure descriptions. Below, we first briefly introduce OPSIN and analyze the limitations of its native parse tree for description generation, then present our approach for constructing enriched structural metadata, and finally describe the prompt design and filtering strategies used to improve generation accuracy.

3.1. Limitations of OPSIN for Description Generation

Given a chemical name, OPSIN performs grammatical tokenization (e.g., *propan-2-ol* → [prop, an, -, 2-, ol]) and assigns each token a semantic role from grammar-defined 98 classes (e.g., root structures, substituents, locants, suffixes, stereochemistry). The tokens and their associated attributes are organized into an XML parse tree representing intermediate structural interpretations. The tree is then operated through a staged pipeline in which structural components are generated, processed, and assembled into a complete molecular graph, output in formats such as CML (Chemical Markup Language) (Murray-Rust & Rzepa, 1999), InChI (Heller et al., 2013), or SMILES (Weininger, 1988).

However, OPSIN’s XML parse tree is designed as an internal processing representation rather than an explicit and complete encoding of molecular structure, making it unsuitable for guiding molecular structure description generation. Specifically, (i) structural elements such as substituents, locants, prefixes, suffixes, and stereochemical descriptors are often not positioned to reflect their true attachment or affiliation in the final molecular structure; (ii) many intermediate elements are discarded once they have served their role, leaving the final XML representation incomplete; (iii) critical topological relationships, such as fused-ring connectivity, bridged and spiro junctions, implicit locants, and atom labeling schemes, are handled internally and never recorded in the parse tree; and (iv) some nomenclature components (e.g., von Baeyer spiro systems) are resolved directly into SMILES, which provide limited guidance for description generation, as LLMs struggle to reliably interpret molecular structure from SMILES alone. These limitations motivate the construction of enriched structural metadata tailored specifically for molecular structure description generation.

3.2. Enriched Structural Metadata Construction

We fully leverage OPSIN’s grammatical tokenization and initial XML parse tree construction. We perform substantial engineering to transform the parse tree into a complete and explicit structural metadata representation suitable for guiding molecular structure description generation. Importantly, these modifications do not alter OPSIN’s native

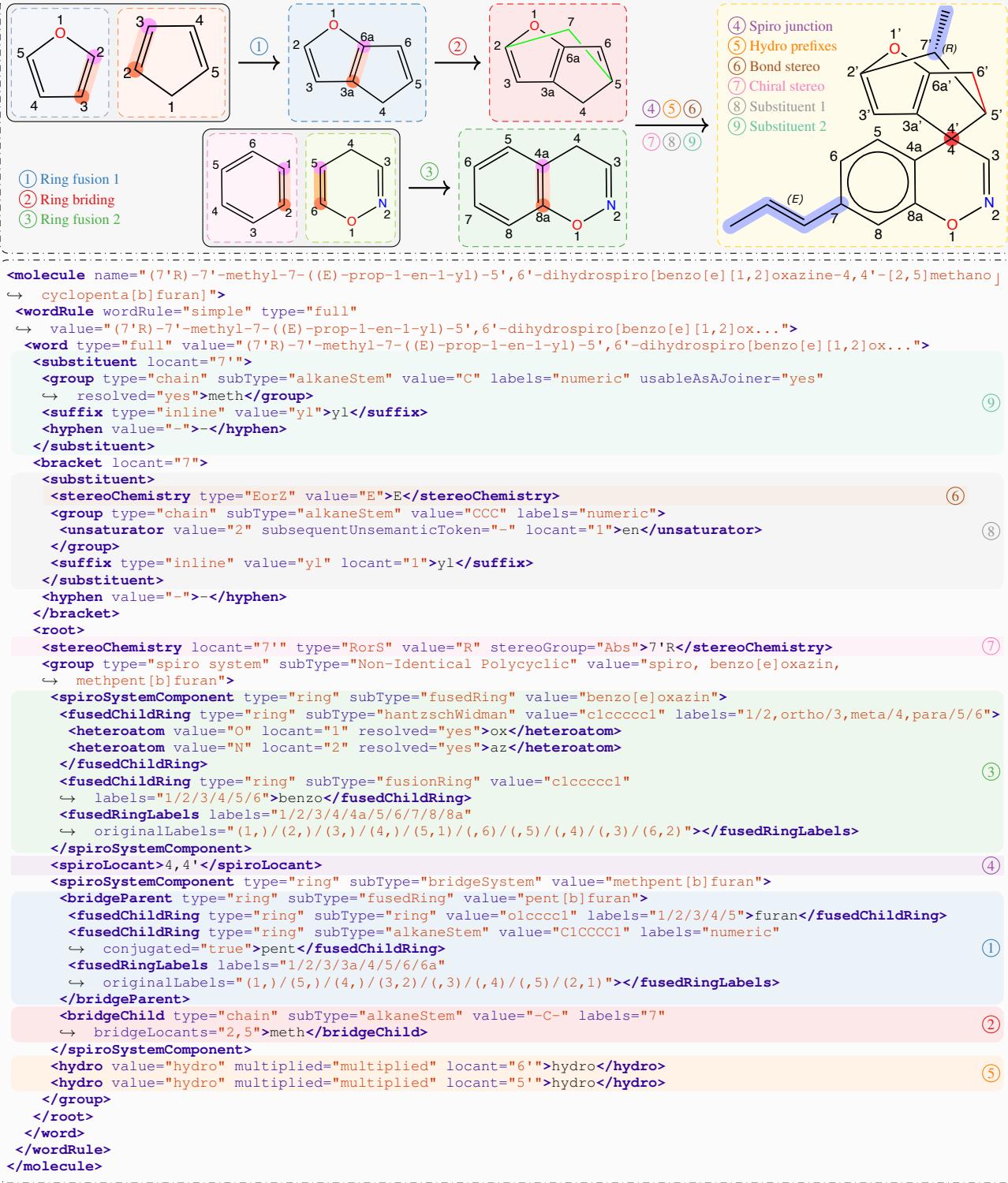


Figure 2. Illustrative example of the molecule $(7'R)-7'$ -methyl-7-((E)-prop-1-en-1-yl)-5',6'-dihydrospiro[benzo[e][1,2]oxazine-4,4'-(2,5)methanocyclopenta[b]furan]. The top shows the decomposition from basic components to the complete structure. The bottom presents the structure metadata constructed by our approach; the corresponding native OPSIN XML output is shown in Appendix Fig.S2 for comparison. The natural-language structural description generated from this metadata is provided in Appendix Fig.S1.

structure reconstruction process. Our tool serves as an adaptive extension of OPSIN, preserving full compatibility with

chemical name-to-structure conversion while providing a semantically complete and well-organized structural repre-

sentation. This design facilitates compatibility with future OPSIN updates and a principled sanity check by comparing reconstructed structures with those from the native OPSIN pipeline, ensuring the reliability of generated metadata.

A systematic redesign of OPSIN is impractical, as both IUPAC nomenclature and the OPSIN system itself are highly complex; despite being actively developed and maintained for over a decade, OPSIN continues to encounter unresolved special cases. We therefore adopt a trial-and-error engineering strategy. Our metadata construction procedure is iteratively tested and refined on over 2000 molecules covering diverse and challenging cases, including but not limited to, complex fused, bridged, and spiro ring systems; Hantzsch-Widman heterocycles; multiple stereochemical configurations; amino acid derivatives; and a wide range of prefixes, infixes, and suffixes. Using representative example in Fig. 2, and the corresponding native OPSIN XML shown in Fig. S2 of the Appendix, we summarize the key modifications:

Augment topology and labeling information. Molecules containing complex ring systems, such as fused, bridged, and spiro topologies, comprise over 30% of entries in public repositories such as PubChem (Kim et al., 2016). In native OPSIN, information describing ring construction and the resulting atom labeling schemes, is handled internally and not explicitly encoded in the parse tree. This missing information is critical not only for accurately describing ring topology, but also for correctly determining the attachment locants for subsequent substituents, prefixes, and suffixes. We therefore augment the XML metadata to encode the missing topology and atom labeling information.

For fused rings, we first record each constituent base ring as a `fusedChildRing` element, storing its atom set (`value` attribute) and original atom labels (`labels` attribute). A `fusedRingLabels` structure is then introduced to specify both the fusion junctions between the base rings (`originalLabels` attribute) and the new atom labeling scheme of the fused system (`labels` attribute). Taking the *benzo[e][1,2]oxazine* fusion (process ③) as an example, the *benzo* and *oxazine* rings are fused by sharing two atom pairs, (3, 2) and (2, 1). These indicate that the third atom of the *benzo* is fused with the second atom of the *oxazine*, and the second atom of the *benzo* is fused with the first atom of the *oxazine*. After fusion, these junction atoms are relabeled as 3a and 6a. The complete fusion process is thus fully represented in the augmented metadata. Bridged and spiro ring systems are handled analogously. These representations naturally support cascaded multi-ring fusions as well as nested topologies, as illustrative example. Semantic definitions for fused, bridged, and spiro systems are provided in Prompts 2, 3, and 4 in the Appendix.

Retain critical elements. We modify OPSIN to retain structurally meaningful elements that are otherwise discarded

during component generation and structure assembly. Taking Fig. 2 as an example, stereochemical information (⑥ and ⑦), unsaturation descriptors such as the *en* modifier of the *prop* substituent (⑧), hydro prefixes (⑤), and core ring descriptors, including heteroatom information in the *oxazine* ring (③), are removed in the native OPSIN parse tree but explicitly retained in our metadata. In addition, information related to fused, bridged, and spiro ring systems, which is never created in native OPSIN and is reduced to a generic systematic scaffold name, is fully augmented in our XML representation (①–④), as described above. All retained elements are further marked and post-processed to prevent re-interpretation or unintended modification in subsequent OPSIN processing stages.

Rearrange elements to reflect affiliation and connectivity. The native OPSIN XML organizes elements according to IUPAC token order, whereas actual modification and attachment relationships are resolved through rule-based inference during structure assembly. Thus, locants, prefixes, and stereochemical descriptors may appear detached from the structural components they actually modify. For example, in *(E)-5-(prop-1-en-1-yl)non-3-ene*, the ‘*E*’ descriptor applies to the *non-3-ene* backbone, whereas in *(E)-5-(prop-1-en-1-yl)non-1-ene*, it instead applies to the *prop-1-en-1-yl* substituent. A similar issue arises in the illustrative example, where prefixes such as hydrogenation modifiers should apply to the fully resolved fused or spiro scaffold rather than to early name fragments. However, the native OPSIN parse tree does not encode these relationships. We systematically relocate prefixes, locants, stereochemical descriptors, and substituents in the XML tree so that each element is attached to the structural component it modifies in the final molecular graph.

Miscellaneous corner cases. Beyond the major structural deficiencies discussed above, our practical implementation required substantial engineering effort to address many additional corner cases where native OPSIN metadata is incomplete or difficult for LLMs to interpret. For example, explicit heteroatom positions in Hantzsch-Widman systems (e.g., *1,2-oxazole*) are not encoded in the native XML representation. Similarly, for von Baeyer spiro systems, OPSIN directly resolves name fragments into SMILES strings via rule-based functions, which are effective for structure reconstruction but provide limited and unreliable guidance for LLM-based description generation.

Although corner cases inevitably remain, our iterative refinement process enables the construction of complete and structured metadata for the vast majority of molecules encountered in practice. This is supported by our dataset validation results, which show that no description errors source from incomplete or incorrect metadata construction.

3.3. Prompt Design and Atom-Matching Filtering

In addition to the enriched structural metadata, the LLM is provided with the corresponding SMILES string and IUPAC name as reference, and is instructed to generate a self-contained, natural-language molecular structure description. The prompt used for description generation is given in Prompt 1 in the Appendix. The generated description is required to be sufficiently complete and precise that someone with basic organic chemistry knowledge can reconstruct the molecular structure exactly and unambiguously from the description alone. The prompt includes explicit guidance on describing molecular backbones, connectivity, substituents, functional groups, and stereochemistry. When fused, spiro, or bridged ring systems are present, additional semantic specifications are automatically injected to guide the interpretation of complex ring topologies.

Despite with detailed structural information, preliminary experiments show that the LLM occasionally omits atoms in long side chains or chain linkers. To mitigate this, we incorporate an automated atom-matching filtering step during description generation. In addition to producing the structural description, the LLM is prompted to count the total number of the non-hydrogen atoms based solely on its generated description. Descriptions whose reported atom counts do not match the ground truth are automatically discarded.

More rigorous self-checking mechanisms are possible, such as prompting the LLM to reconstruct the SMILES from the generated description and performing full structure matching. However, this strategy is not suited for large-scale dataset construction. First, including SMILES reconstruction within the same prompt introduces an additional non-trivial task that can interfere with the primary objective of structural description generation; alternatively, performing reconstruction in a separate LLM call substantially increases cost, making impractical for large-scale curation. Second, single-pass reconstruction checking suffers from high false rejection rates: even strong models (e.g., GPT-5.2) can reject a large fraction of otherwise correct descriptions, resulting in very low annotation efficiency despite near-zero description errors. We therefore adopt this lightweight yet effective atom-matching filtering mechanism that improves description accuracy while preserving scalability, as demonstrated by the ablation study in Sec. 4.3.

4. Dataset Collection and Validation

4.1. Dataset Collection

Chemical space is extremely large (Reymond, 2015); even much smaller public molecule repositories contain hundreds of millions to billions of molecules (Kim et al., 2016; Irwin et al., 2020). We select PubChem (Kim et al., 2016) as the molecule pool for dataset construction, and randomly

sample 200,000 molecules as candidates for description generation. We then apply an initial filtering to remove molecules that would not yield reliable structure metadata. Specifically, we exclude molecules for which (i) an IUPAC name is not provided by PubChem, (ii) the entry corresponds to multiple disconnected molecular components, with dot ‘.’ separators in the SMILES, (iii) OPSIN raises warnings or errors when parsing the IUPAC name, such as ambiguity, unsupported or rare chemical patterns, or parsing failures, or (iv) the SMILES string parsed by OPSIN from the IUPAC name does not match the SMILES provided by PubChem. After filtering, 167,416 molecules remain as final candidates and are passed to the LLMs for description generation.

While structural metadata provide sufficient information for molecular structure description, accurate generation still depends strongly on the capacity of the generation model. The task requires the LLM to faithfully interpret and integrate detailed structural information into precise textual descriptions. Based on the difficulty of generation, we therefore categorize molecules into three difficulty levels (easy, medium, and hard) and route them to different LLMs accordingly.

- **Easy:** Molecules contain no fused ring systems and consist only of isolated rings and/or acyclic chains, including cases where two isolated rings meet at a single spiro atom.
- **Medium:** Molecules contain exactly one fused ring system composed of two rings and do not exhibit spiro or bridged junctions within the fused system.
- **Hard:** Molecules exhibit complex fused-ring topology, including fused systems with more than two rings, multiple fused ring systems within a molecule, or fused systems involving spiro or bridged connectivity.

We emphasize that *the difficulty level does not necessarily reflect overall molecular complexity*; molecules in the easy category may still be structurally intricate, as illustrated in Appendix Fig. S4b . The generation models and reasoning effort used for each category is listed in Table 1, with the corresponding model snapshots provided in Appendix A.2. We select generation models for each difficulty level based on a trade-off between generation quality and practical budget constraints. While higher-capacity models, such as GPT-5.2 Pro (OpenAI, 2025b), can yield more reliable and accurate descriptions, but it requires approximately 12× the cost of GPT-5.2, which we use for dataset generation.

As discussed, in addition to generating structural descriptions, we prompt the LLM to count the non-hydrogen atoms to filter out potentially erroneous descriptions. After filtering, the final dataset consists of 163,085 molecule-description pairs, with 106,379, 41,412, and 15,294 samples in the easy, medium, and hard categories, respectively, as summarized in Table 1. Since molecules are randomly sampled from the PubChem pool, the resulting dataset follows the underlying distribution of PubChem. The gener-

Table 1. Generation models and their reasoning effort, along with dataset statistics across different generation difficulty levels, including the number of collected samples, validation subset size, and validation precision (%). For collected and validation samples, each entry is reported as the sample count with its proportion (%) relative to the total dataset or total validation set, respectively.

Generation difficulty	Model (reasoning)	Collected samples	Validated samples	Validation precision
Easy	GPT-5.2 (high)	106,379 (65.2%)	1,317 (65.8%)	1,300 (98.7%)
Medium	GPT-5.2 (xhigh)	41,412 (25.4%)	496 (24.8%)	492 (99.2%)
Hard	GPT-5.2 (xhigh)	15,294 (9.4%)	187 (9.4%)	180 (98.3%)
Overall	–	163,085	2,000	1,972 (98.6%)

ated descriptions have an average length of 261 words and provide complete structural information. Representative examples are shown in Appendix A.7, and additional dataset statistics are provided in Appendix A.4.

4.2. Dataset Validation

To provide quantitative evidence of the dataset’s reliability, we conduct rigorous validation on a randomly drawn subset of 2,000 samples from the full generated dataset that pass the atom-matching check, comprising 1,317, 496, and 187 easy, medium, and hard samples, respectively.

Validation Process Human validation of molecular descriptions is highly time-consuming. Based on our records, validating a single sample requires approximately 11.7 min on average, slightly higher than the 10 min reported by MolLangBench (Cai et al., 2025a). As a result, fully validating even the 2,000-sample subset would require approximately 390 human-hours for a single round, excluding additional validation needed for later ablation studies.

To evaluate more samples and ensure sufficient statistical power under a fixed human validation budget, we adopt a hybrid validation strategy combining LLM-based and human validation. For each sample, we first employ an LLM validator (GPT-5.2 (OpenAI, 2025b) with medium reasoning effort), prompting it to reconstruct the molecule in SMILES format from the generated description. We use the prompt from Appendix A.21.3 of MolLangBench for this evaluation. If the LLM produces an exactly matching SMILES string within three attempts (`pass@3`), the molecule sample is accepted as correctly described. This criterion is motivated by the near-zero likelihood of false positives: reconstructing an exact molecular structure from an incorrect or ambiguous description is highly unlikely. Using this approach, the LLM validator successfully validates 85.7% of samples, reducing the number requiring human validation to 287.

However, LLM validation may produce false negatives. All samples failing LLM validation undergo human validation. Each such sample is independently evaluated by up to two expert validators. Validators are provided only with the textual description and reconstruct the molecule using chemical drawing software. Their reconstructed structure are submitted to an internal validation application that automatically checks against the ground truth. Each validator is allowed up to three attempts. A sample is considered valid if either expert confirms that the description is *unambiguous* and successfully reconstructs the *exact* molecular structure. Only samples that fail reconstruction by both validators are labeled as incorrect. Using two validators helps mitigate the risk of individual oversight or error.

Validation Results We report description precision on the validation set across difficulty levels in Table 1, with additional validation statistics provided in Appendix A.3. The validated descriptions achieve an overall precision of 98.6%, with 98.7%, 99.2%, and 98.3% for the easy, medium, and hard categories, respectively.

We manually examine all incorrect descriptions and confirm that structure parsing and metadata construction are correct; errors therefore arise solely from the LLM’s description generation. In nearly all incorrect cases, the errors are minor: the descriptions contain all scaffolds and substituents, with most structural elements correctly connected and only localized issues, such as misplaced substituents or imprecise ring fusion descriptions. Overall, the low error rate and minor errors in the incorrect cases demonstrate the reliability of both the generation pipeline and the resulting dataset.

4.3. Ablation Study

We perform a set of ablation studies to analyze the impact of major design choices in our data generation pipeline.

Effect of Atom-Matching Filtering To evaluate this effect, we validate 2,000 samples with the same difficulty-level distribution as the main validation set. This set largely overlaps with the previously validated samples; the final validation set earlier consists of samples from this ablation study that pass the atom-matching check, supplemented with additional passing samples. Among these samples, 97.7% pass the atom-matching check, indicating that the filter preserves the vast majority of generated data and does not significantly reduce generation efficiency.

We then apply the same hybrid validation procedure described above to both the passing and failing subsets, with results reported in Table 2. For samples that pass the atom-matching filter, description precision remains comparable to the main validation results, achieving an overall precision of 98.6%. In contrast, precision drops sharply to 27.7% for the small subset that fail the filter, demonstrating that atom-

Table 2. Validation precision under structural metadata and atom-matching ablations across generation difficulty levels. Each entry is reported as passed / total evaluated samples (precision %).

	With metadata		Without metadata (atom match)
	Atom match	Atom mismatch	
Easy	1,275/1,292 (98.7%)	8/25 (32.0%)	1,191/1,242 (95.9%)
Medium	472/476 (99.2%)	5/20 (25.0%)	427/457 (93.4%)
Hard	178/185 (96.2%)	0/2 (0.00%)	142/172 (82.6%)
Overall	1,925/1,953 (98.6%)	13/47 (27.7%)	1,761/1,871 (94.1%)

matching effectively removes incorrectly labeled samples.

Effect of Structure Metadata We ablate the use of structural metadata to evaluate whether injecting this information improves description precision. Specifically, we regenerate descriptions for the same set of molecules used in the atom-matching filtering study, using identical generation models but providing only the SMILES string and IUPAC name, without structural metadata (see Prompt 5 in the Appendix).

Removing structural metadata reduces sampling efficiency, as reflected by a decrease in the fraction of molecules passing the atom-matching check, from 97.7% to 93.6%. We then apply the same hybrid validation procedure to samples that pass atom matching, with results reported in Table 2. Although descriptions generated without structural metadata still achieve a relatively high precision of 94.1%, this performance is consistently lower by approximately 4.5% than the baseline with structural metadata. The performance gap becomes more pronounced as difficulty level increases. This is because, for medium- and hard-level molecules, the structure metadata explicitly encode ring fusion, bridged and spiro relationships, as well as ring system labeling information that is not captured by IUPAC names or SMILES strings, thereby guiding more accurate and unambiguous description generation. During validation, we observed that descriptions generated without structural metadata often omit fusion-ring information and labeling schemes. Such descriptions are not necessarily incorrect, since expert validators can infer the intended structure using their knowledge of chemical nomenclature and labeling conventions. However, they are less suitable for structure-language alignment.

Sensitivity to Generation Model This generation process demands LLMs both strong chemical domain understanding and the ability to reason over long and information-dense contexts. To study model sensitivity, we replace the GPT-5.2 series with GPT-5 models (OpenAI, 2025a) for description generation, using high reasoning effort on the same molecule set as in prior ablations. To reduce human validation cost, we rely solely on LLM validation in this

study, continuously using GPT-5.2 as the validator and applying validation only to descriptions that pass the atom-matching check. Compared to GPT-5.2, the LLM validation precision for GPT-5-generated descriptions decreases consistently across difficulty levels by 0.6%, 18.0%, and 20.7% for the easy, medium, and hard categories, respectively. This indicates sensitivity of description reliability to generation model capacity, particularly for complex structures. Detailed results are reported in Table S1 in the Appendix. We expect that other commercial LLMs, such as Gemini (Comanici et al., 2025) and Claude (Anthropic, 2025), may exhibit different performance depending on their chemical reasoning capabilities, as the evaluation in MolLangBench.

5. Discussion and Conclusion

This work opens new opportunities for molecule-language modeling. The proposed annotation pipeline provides an accurate one-way mapping from molecular structures to language descriptions. For tasks requiring only structure information as input, such as property prediction, the descriptions can be generated on demand and used directly, potentially without prior molecule-language alignment. As shown in MolLangBench, prompting LLMs to generate structure descriptions before property prediction improves performance even with imperfect descriptions. For tasks requiring structural outputs or precise structure-level reasoning, such as reaction mechanisms or molecular design, cross-modal training remains necessary. One practical challenge is that generated descriptions are typically much longer than image captions (see statistics in Appendix A.4) due to the inherent complexity of molecular structures and lack of explicit verbosity control. An open question is whether models should be trained on raw descriptions or condensed versions obtained through linguistic simplification or selectively removing structural details. Fortunately, LLM-based condensation is both methodologically and economically feasible based on our generated datasets.

This work may also facilitate progress in broader multimodal modeling beyond vision-language, particularly in graph-language modeling. While recent LLMs show improving accuracy in recognizing and generating molecular structures from textual inputs such as SMILES or chemical names, substantial gaps remain. LLMs currently spend considerable reasoning effort on these simple interface tasks: we observed that generating complete structure descriptions for complex molecules can require over 30 min. Structural perception and manipulation should be efficient, reserving the majority of reasoning capacity for downstream chemical reasoning tasks. In summary, we hope this work highlights the importance of structure-grounded tasks and that the proposed pipeline and dataset contribute to continued progress in molecule-language modeling.

Software and Data

The Java source code for the structural metadata generation tool, along with a compiled executable and example scripts demonstrating how to generate structural metadata and incorporate it into the description generation prompt, is publicly available at <https://github.com/TheLuofengLab/MolLangData>. The complete dataset of generated molecular descriptions, including the validation dataset, is available at <https://huggingface.co/datasets/ChemFM/MolLangData>

Impact Statement

This paper presents work whose goal is to advance the field of Machine Learning. There are many potential societal consequences of our work, none which we feel must be specifically highlighted here.

References

- Anthropic. Claude opus 4 / claude sonnet 4 system card. <https://www-cdn.anthropic.com/4263b940cabb546aa0e3283f35b686f4f3b2ff47.pdf>, 2025.
- Brown, N., Fiscato, M., Segler, M. H., and Vaucher, A. C. Guacamol: benchmarking models for de novo molecular design. *Journal of chemical information and modeling*, 59(3):1096–1108, 2019.
- Cai, F., Bai, J., Tang, T., He, G., Luo, J., Zhu, T., Pilla, S., Li, G., Liu, L., and Luo, F. Mollangbench: A comprehensive benchmark for language-prompted molecular structure recognition, editing, and generation. *arXiv preprint arXiv:2505.15054*, 2025a.
- Cai, F., Zacour, K., Zhu, T., Tzeng, T.-R., Duan, Y., Liu, L., Pilla, S., Li, G., and Luo, F. Chemfm as a scaling law guided foundation model pre-trained on informative chemicals. *Communications Chemistry*, 2025b.
- Comanici, G., Bieber, E., Schaekermann, M., Pasupat, I., Sachdeva, N., Dhillon, I., Blstein, M., Ram, O., Zhang, D., Rosen, E., et al. Gemini 2.5: Pushing the frontier with advanced reasoning, multimodality, long context, and next generation agentic capabilities. *arXiv preprint arXiv:2507.06261*, 2025.
- Edwards, C., Zhai, C., and Ji, H. Text2mol: Cross-modal molecule retrieval with natural language queries. In *Conference on Empirical Methods in Natural Language Processing*, 2021.
- Edwards, C., Lai, T., Ros, K., Honke, G., Cho, K., and Ji, H. Translation between molecules and natural language. In *Conference on Empirical Methods in Natural Language Processing*, 2022.
- Edwards, C., Wang, Q., Zhao, L., and Ji, H. L+ m-24: Building a dataset for language+ molecules@ acl 2024. In *Proceedings of the 1st Workshop on Language+ Molecules (L+ M 2024)*, 2024.
- Eichelbaum, M. F., Testa, B., and Somogyi, A. *Stereochemical aspects of drug action and disposition*, volume 153. Springer Science & Business Media, 2012.
- Favre, H. A. and Powell, W. H. *Nomenclature of organic chemistry: IUPAC recommendations and preferred names 2013*. Royal Society of Chemistry, 2013.
- Guo, T., Guo, K., Nan, B., Liang, Z., Guo, Z., Chawla, N. V., Wiest, O., and Zhang, X. What can large language models do in chemistry? a comprehensive benchmark on eight tasks. In *37th Conference on Neural Information Processing Systems Datasets and Benchmarks Track*, 2023.
- Heller, S., McNaught, A., Stein, S., Tchekhovskoi, D., and Pletnev, I. Inchi—the worldwide chemical structure identifier standard. *Journal of cheminformatics*, 5(1):7, 2013.
- Irwin, J. J., Tang, K. G., Young, J., Dandarchuluun, C., Wong, B. R., Khurelbaatar, M., Moroz, Y. S., Mayfield, J., and Sayle, R. A. Zinc20—a free ultralarge-scale chemical database for ligand discovery. *Journal of chemical information and modeling*, 60(12):6065–6073, 2020.
- Irwin, R., Dimitriadis, S., He, J., and Bjerrum, E. J. Chemformer: a pre-trained transformer for computational chemistry. *Machine Learning: Science and Technology*, 3(1):015022, 2022.
- Jablonka, K. M., Schwaller, P., Ortega-Guerrero, A., and Smit, B. Leveraging large language models for predictive chemistry. *Nature Machine Intelligence*, 6(2):161–169, 2024.
- Kim, S., Thiessen, P. A., Bolton, E. E., Chen, J., Fu, G., Gindulyte, A., Han, L., He, J., He, S., Shoemaker, B. A., et al. Pubchem substance and compound databases. *Nucleic acids research*, 44(D1):D1202–D1213, 2016.
- Liu, G., Sun, M., Matusik, W., Jiang, M., and Chen, J. Multimodal large language models for inverse molecular design with retrosynthetic planning. In *13th International Conference on Learning Representations*, 2025.
- Lowe, D. Chemical reactions from us patents. <https://doi.org/10.6084/m9.figshare.5104873.v1>, 2017.

- Lowe, D. M., Corbett, P. T., Murray-Rust, P., and Glen, R. C. Chemical name to structure: Opsin, an open source solution, 2011.
- Murray-Rust, P. and Rzepa, H. S. Chemical markup, xml, and the worldwide web. 1. basic principles. *Journal of Chemical Information and Computer Sciences*, 39(6): 928–942, 1999.
- OpenAI. Introducing gpt-5. <https://openai.com/index/introducing-gpt-5/>, 2025a.
- OpenAI. Introducing gpt-5.2. <https://openai.com/index/introducing-gpt-5-2/>, 2025b.
- OpenAI. The new chatgpt images is here. <https://openai.com/index/new-chatgpt-images-is-here/>, 2025c.
- Polykovskiy, D., Zhebrak, A., Sanchez-Lengeling, B., Golovanov, S., Tatanov, O., Belyaev, S., Kurbanov, R., Artyamonov, A., Aladinskiy, V., Veselov, M., Kadurin, A., Johansson, S., Chen, H., Nikolenko, S., Aspuru-Guzik, A., and Zhavoronkov, A. Molecular Sets (MOSES): A Benchmarking Platform for Molecular Generation Models. *Frontiers in Pharmacology*, 11:565644, 2020.
- Reymond, J.-L. The chemical space project. *Accounts of chemical research*, 48(3):722–730, 2015.
- Schuhmann, C., Beaumont, R., Vencu, R., Gordon, C., Wightman, R., Cherti, M., Coombes, T., Katta, A., Mullis, C., Wortsman, M., et al. Laion-5b: An open large-scale dataset for training next generation image-text models. 2022.
- Smith, M. *March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure*. Wiley, 2020. ISBN 9781119371809.
- Su, B., Du, D., Yang, Z., Zhou, Y., Li, J., Rao, A., Sun, H., Lu, Z., and Wen, J.-R. A molecular multimodal foundation model associating molecule graphs with natural language. *arXiv preprint arXiv:2209.05481*, 2022.
- Tan, Z., Li, D., Wang, S., Beigi, A., Jiang, B., Bhattacharjee, A., Karami, M., Li, J., Cheng, L., and Liu, H. Large language models for data annotation and synthesis: A survey. In *Conference on Empirical Methods in Natural Language Processing*, 2024.
- Taylor, R., Kardas, M., Cucurull, G., Scialom, T., Hartshorn, A., Saravia, E., Poulton, A., Kerkez, V., and Stojnic, R. Galactica: A large language model for science. *arXiv preprint arXiv:2211.09085*, 2022.
- Weininger, D. Smiles, a chemical language and information system. 1. introduction to methodology and encoding rules. *Journal of chemical information and computer sciences*, 28(1):31–36, 1988.
- Wu, Z., Ramsundar, B., Feinberg, E. N., Gomes, J., Geenesse, C., Pappu, A. S., Leswing, K., and Pande, V. Moleculenet: a benchmark for molecular machine learning. *Chemical science*, 9(2):513–530, 2018.
- Zhang, D., Liu, W., Tan, Q., Chen, J., Yan, H., Yan, Y., Li, J., Huang, W., Yue, X., Ouyang, W., et al. Chemllm: A chemical large language model. *arXiv preprint arXiv:2402.06852*, 2024.
- Zhou, C., Wang, M., Ma, Y., Wu, C., Chen, W., Qian, Z., Liu, X., Zhang, Y., Wang, J., Xu, H., et al. From perception to cognition: A survey of vision-language interactive reasoning in multimodal large language models. *arXiv preprint arXiv:2509.25373*, 2025.

A. Appendix

A.1. Additional Information for the Illustrative Example in Figure 2

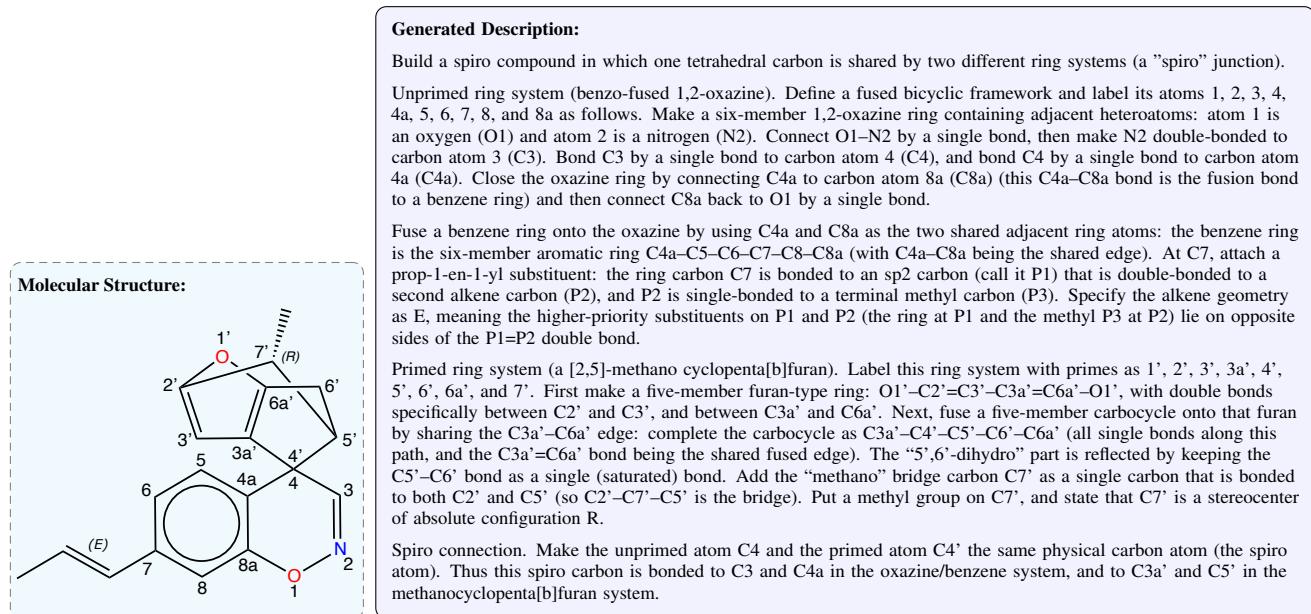


Figure S1. Molecular structure and generated natural-language structural description for the illustrative example shown in Fig.2. The structured metadata provided as input to the LLM are illustrated in Fig.2.

Native OPSIN-Generated XML Parse Tree for the Illustrative Example:

```

<molecule name="(7'R)-7'-methyl-7-((E)-prop-1-en-1-yl)-5',6'-dihydrospiro[benzo[e][1,2]oxazine-4,4'-[2,5]methanoc
  <wordRule wordRule="simple" type="full"
  <value="(7'R)-7'-methyl-7-((E)-prop-1-en-1-yl)-5',6'-dihydrospiro[benzo[e][1,2]ox...">
  <word type="full" value="(7'R)-7'-methyl-7-((E)-prop-1-en-1-yl)-5',6'-dihydrospiro[benzo[e][1,2]ox...">
  <substituent locant="7'">
    <group type="chain" subType="alkaneStem" value="C" labels="numeric">meth</group>
    <suffix type="inline" value="yl">yl</suffix>
    <hyphen value="-">>-</hyphen>
  </substituent>
  <bracket locant="7">
    <substituent>
      <group type="chain" subType="alkaneStem" value="CCC" labels="numeric">prop</group>
      <suffix type="inline" value="yl" locant="1">yl</suffix>
    </substituent>
    <hyphen value="-">>-</hyphen>
  </bracket>
  <root>
    <group type="ring" subType="ring" value="pent[b]furan"
      <labels="1/2/3/4/5">spirobenzo[e]oxazinpent[b]furan</group>
  </root>
  </word>
</wordRule>
</molecule>
```

Figure S2. Molecular structure XML parse tree produced by the native OPSIN tool (Lowe et al., 2011) after the structure assembly for the illustrative example shown in Fig.2. The corresponding XML representation generated by our approach is shown in Fig.2 for comparison.

A.2. Model Snapshots

All experiments and data collection in this work are conducted using model APIs provided through Azure AI Foundry. We use GPT-5 with model snapshot 2025-08-07 and GPT-5.2 with model snapshot 2025-12-11.

A.3. Validation Statistics

We report validation statistics for a subset of 2,000 samples across easy, medium, and hard difficulty levels. Among 1,317/496/187 samples in the easy/medium/hard categories, 1,181/415/117 samples pass automatic LLM validation, while the remaining samples require human validation. Of these, 112/77/63 samples are approved by the first human validator, and the remaining cases are forwarded to a second validator. The second validator largely agree with the first: only 7 additional easy samples are passed after secondary validation, while no additional medium or hard samples are confirmed.

The validation time for a single human annotator is 13.5 min/8.3 min/12.2 min for the easy, medium, and hard categories, respectively, with an overall average of 11.7 min across all validated samples. This is slightly longer than the approximately 10 min reported in MolLangBench (Cai et al., 2025a). We note that these times are collected automatically by our internal validation application and are intended as a coarse reference rather than a precise measure of annotation efficiency.

A.4. Dataset Statistics

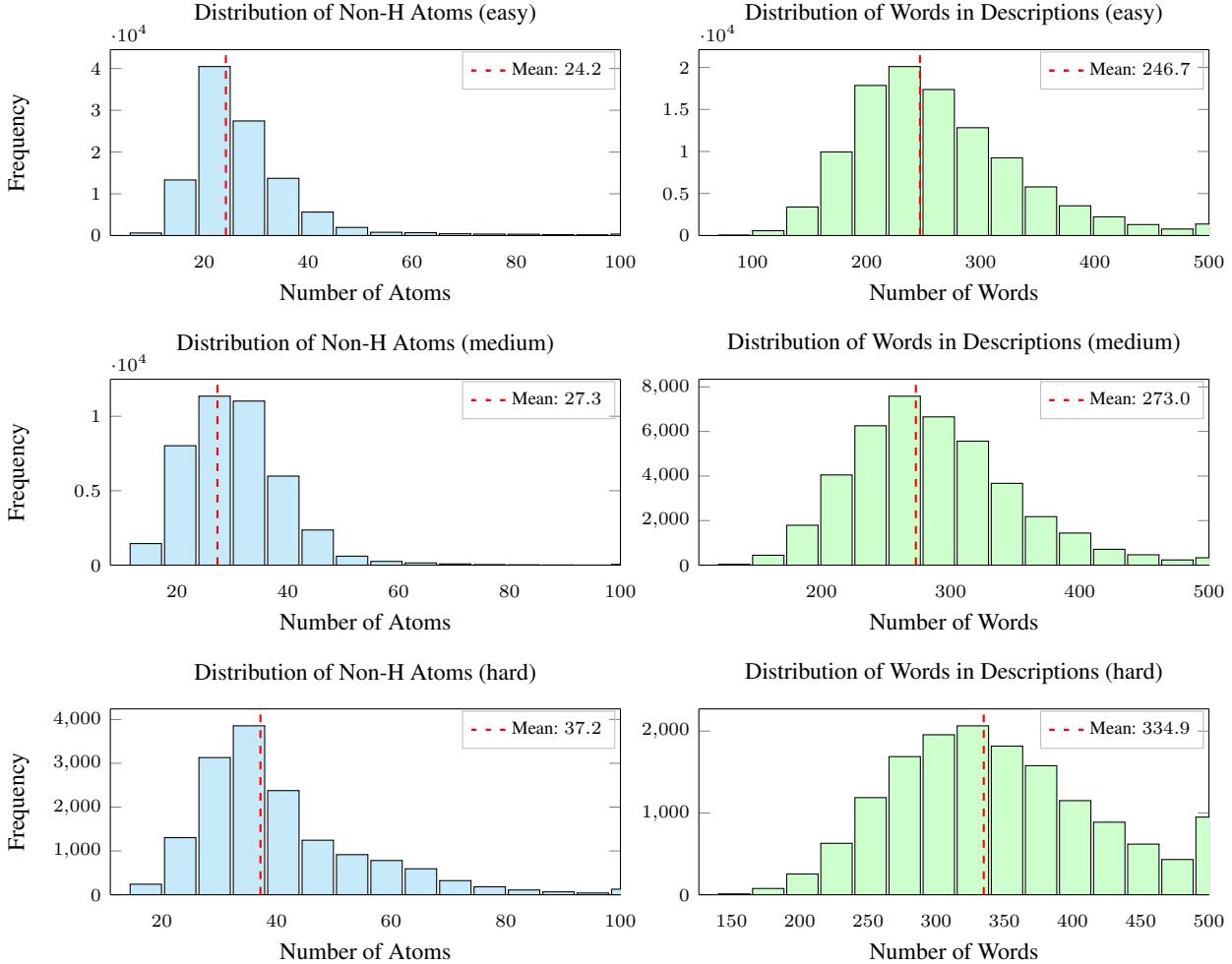


Figure S3. Distribution statistics of the entire generated dataset, including non-hydrogen atom counts and description word counts, across easy, medium, and hard categories.

We summarize the distribution statistics of the entire generated dataset across easy, medium, and hard difficulty levels in Fig. S3. For the easy category, molecules span from 2 to 335 non-hydrogen atoms (mean 24.2), with description lengths ranging from 53 to 1308 words (mean 246.7). The medium category covers molecules with 8 to 274 atoms (mean 27.3) and descriptions of 105 to 981 words (mean 273.0). The hard category exhibits the highest structural and linguistic complexity, with atom counts ranging from 11 to 414 (mean 37.2) and description lengths from 126 to 1358 words (mean 334.9).

A.5. Additional Results for Ablation Study

Table S1. Ablation study on model sensitivity. Pass rates (%) of the LLM-based validator for descriptions generated by GPT-5 and GPT-5.2 across different difficulty levels.

Model	Easy	Medium	Hard
GPT-5	88.9%	66.0%	42.5%
GPT-5.2	89.5%	84.0%	63.2%

A.6. Description Generation Prompts and Complex-Ring XML Semantics

Prompt 1: Molecular Description Generation from SMILES, IUPAC Names, and Structural Metadata

Task:

You are provided with the **IUPAC name**, **SMILES string**, and **rule-based hierarchical metadata** describing the molecular structure. Generate a **detailed and accurate structural description** that would allow a person with **basic organic chemistry knowledge** to reconstruct the exact molecule using only your structural description text. The description should be **natural, diverse**, and **chemically precise**, clearly conveying the molecular skeleton, substituents, and stereochemistry.

In addition, after completing the description, report the total number of non-hydrogen atoms implied by your description, computed **only from the information explicitly stated in the description itself**.

Guidelines:

1. Purpose and Independence

- The description must be **self-contained** and **sufficient for reconstruction**.
- Assume the reader only has your final text—they will **not see** the SMILES, IUPAC name, or metadata.
- You may use all input data internally to reason about the molecule, but the final description must read as a stand-alone, human-readable explanation.

2. Freedom of Description

You may begin from any perspective—the main skeleton, a key ring system, or an important substituent. Combine information freely from the IUPAC name, SMILES, and metadata to capture the complete structure.

3. Backbone and Connectivity

Describe how rings, chains, and substituents are connected. Indicate branching positions, linkages, and overall topology so that the structure can be reconstructed accurately.

4. Functional Groups and Substituents

Identify all key functional groups and substituents. Specify their type (e.g., hydroxyl, amine, halogen, carbonyl), location, and bonding pattern relative to the molecular framework.

5. Simple or Isolated Rings

For common rings (benzene, pyridine, cyclohexane), you may name them directly or briefly describe their composition and bonding.

6. Fused, Bridged, or Spiro Ring Systems — explicit, structured, and verified

It is **strongly recommended to follow the guidance below** when describing complex ring topologies:

When interpreting fused, bridged, or spiro ring systems, you should explicitly refer to the corresponding ring-system semantics described later. These semantics are essential for correctly understanding atom labeling, fusion points, bridge connections, and spiro locants as derived from the provided metadata.

- Define and label atoms/rings.** Explicitly assign ring labels and atom labels to each ring in the ring system (e.g., “Ring A: C1–C6 clockwise starting at the junction with ring B”; include heteroatoms like O1/N5 as needed). For complex fused or multi-ring systems, it is recommended to align the atom labeling by the structure metadata to maintain chemical accuracy. If there are multiple distinct fused systems, assign separate, non-overlapping label sets to avoid confusion.
- Describe internal ring features.** State ring size, aromaticity/saturation, heteroatoms, and bonding patterns (alternation, single/double).
- Explain how rings are connected.** Specify **exact shared atoms or edges** (e.g., “Ring B shares the C5–C6 edge with ring A”). Describe **fusion geometry** (linear, angular, bridged, spiro).

Required verification (before finalizing your description):

- **Label consistency:** Each label you introduced is used consistently; no duplicate or skipped numbering within a ring.
- **Ring labeling check:** Verify that the atom labeling and numbering sequence are correct, and that the shared atoms or edges described for each fusion correspond accurately to your own ring definitions and orientations. The metadata should be treated as the **gold standard** for validating both labeling and fusion topology.
- **Orientation sanity-check:** The shared atoms/edge and the named orientation (linear vs angular; inner vs outer edge) match the topology. Do not accidentally mirror or rotate the fusion.
- **Cross-consistency check:** Ensure that substituent positions and stereochemical designations correspond correctly to the atom labels and numbering scheme you defined for each ring.

7. Stereochemistry

Include stereochemical information such as (R/S) or (E/Z) when available, and describe how these configurations relate to surrounding atoms or bonds.

8. Rational Use of Metadata

- Treat the metadata as **accurate structural evidence**, but express its meaning in **your own words**.
- The metadata is not shown to the reader, so do not include or reference any of its raw contents directly.
- Only mention atoms, labels, or locants (e.g., “C9,” “N5”) **after you have introduced them** in your own description.
- When metadata provides **partial or shorthand notations**, infer and expand these to their complete, chemically correct forms.

9. Use of Chemical Shorthand

- **Avoid full structural formulas** written as continuous symbolic notations.
- Short fragments like “–OH,” “–CH₃,” or “–NH₂” are acceptable when helpful.

10. Balance and Readability

Aim for a **balanced level of detail**.

11. Descriptive Diversity

Use varied styles and sentence structures.

12. Do Not Include

- The full IUPAC name, SMILES string, or XML tags verbatim.
- Long symbolic chemical formulas for the entire molecule.
- Brand names, trivial comments, or unrelated metadata.
- Unintroduced atom labels or locants.

13. Non-hydrogen atom count

- After completing the description, report the **total number of non-hydrogen atoms**.
- Do **not** use the SMILES to perform this count.
- Do **not** include the counting process in your description.

Output Format:

```
<description>
[Concise, varied, and chemically precise structural description]
</description>
<non_hydrogen_atom_count>
[integer]
</non_hydrogen_atom_count>
```

This section of the prompt specifies semantics for *fused*, *spiro*, and *bridged* ring systems, which are automatically injected when required. Detailed prompt specifications for these semantics are provided in prompts 2, 3, and 4, respectively.

Inputs:

- **IUPAC Name:** {IUPAC}

- SMILES String: {SMILES}
- Molecular Metadata (XML Hierarchy):
{XML_METADATA}

Prompt 2: Fused Ring Semantics (XML)

A fused ring system is represented in the XML by **incrementally constructing new ring identities** from simpler rings. Each fusion step introduces a **new global labeling scheme**, which replaces all previous ones and is used for any subsequent fusion and structural references.

Core semantics

1. Local ring definition

- Each ring is described by a value attribute containing its **SMILES representation**; in some fused ring systems, this SMILES value may be omitted.
- A labels attribute assigns **atom labels** for the ring; when a SMILES value is present, the labels follow the **atom order in the SMILES**.
 - If labels is **explicitly provided**, those labels define the atom labeling scheme.
 - If labels is **omitted** or set to numeric, atoms are implicitly labeled from 1 to n , where n is the number of atoms in the ring, following SMILES order.
- Atom indices **start from 1**.

2. Fusion via originalLabels

- originalLabels maps **each atom of the newly fused system** to atom indices in the component rings.
- Each entry corresponds to **one atom in the fused system**.
- Multiple indices in an entry indicate a **fusion point**.
- A blank position indicates that the fused-system atom does not belong to that ring.

3. Label propagation

- After fusion, the fused system receives a new labels list.
- This labeling scheme **replaces all previous local labels**.
- All subsequent structural references—including further fusions, bridged connections, spiro connections, substituent attachment positions, and stereochemical descriptors—**must reference this new labeling scheme**.

Worked Example: indeno[5,6-b]furan

```
<group type="ring" subType="fusedRing" value="indeno[5,6-b]furan">
  <fusedChildRing
    type="ring"
    subType="ring"
    value="o1cccc1"
    labels="1/2/3/4/5">
  furan
  </fusedChildRing>
  <fusedChildRing
    type="ring"
    subType="fusionRing"
    value="[cH2]1ccc2cccc12"
    labels="1/2/3/3a/4/5/6/7/7a"
    fusedRing1="[cH2]1cccc1"
    fusedRing2="c1cccc1"
    originalLabels="(1,)/(2,)/(3,)/(4,1)/(2,)/(3,)/(4,)/(5,)/(5,6)">
  indeno
  </fusedChildRing>
  <fusedRingLabels
    labels="1/2/3/3a/4/4a/5/6/7/7a/8/8a"
    originalLabels="(1,)/(5,)/(4,)/(3, 6)/(7,)/(7a)/(1,)/(2,)/(3,)/(3a,)/(4,)/(2,5)">
  </fusedRingLabels>
</group>
```

Step-by-step interpretation

Step 1: Ring A (furan)

- SMILES: o1cccc1
- Labels: 1/2/3/4/5
- Label assignment follows SMILES order:
 - O → 1
 - Carbons → 2–5

Step 2: Ring B (indeno)

Ring B is formed by fusing two sub-rings:

- fusedRing1: [cH2]1cccc1 → atoms 1–5
- fusedRing2: c1ccccc1 → atoms 1–6

Fusion is defined by:

```
originalLabels = (1,)/(2,)/(3,)/(4,1)/(,2)/(,3)/(,4)/(,5)/(5,6)
```

Fusion points:

- atom 4 of fusedRing1 ↔ atom 1 of fusedRing2
- atom 5 of fusedRing1 ↔ atom 6 of fusedRing2

After fusion, Ring B receives a **new labeling scheme**:

```
labels = 1/2/3/3a/4/5/6/7/7a
```

From this point onward, **indeno is treated as a single ring**.

Step 3: Fuse Ring A with Ring B

The final fused system (indeno[5,6-b]furan) is created by fusing:

- Ring A (labels 1/2/3/4/5)
- Ring B (labels 1/2/3/3a/4/5/6/7/7a)

The final system receives a **new global labeling scheme**:

```
labels = 1/2/3/3a/4/4a/5/6/7/7a/8/8a
```

Fusion is defined by:

```
(1,)/(5,)/(4,)/(3,6)/(,7)/(,7a)/(,1)/(,2)/(,3)/(,3a)/(,4)/(2,5)
```

Fusion points:

- atom 3 of Ring A ↔ atom 6 of Ring B
- atom 2 of Ring A ↔ atom 5 of Ring B

Prompt 3: Bridged Ring Semantics (XML)

A bridged ring system is represented by defining a **parent ring system** and a **bridge fragment** that connects two atoms of the parent ring.

For a bridged ring system, the XML normally provides:

- A **parent ring system**, defined by its value (SMILES, when provided) and `labels`. The parent ring may itself be a fused ring system, following the fused-ring semantics.
- A **bridge fragment**, defined by its own value (SMILES) and `labels`.
- A **bridgeLocants** attribute, which specifies the **two atom labels of the parent ring** that are connected by the bridge.

The `bridgeLocants` are ordered and define the **direction along the bridge**. The labels of the bridge fragment are assigned **from the first locant to the second locant**, following the order of the bridge fragment's SMILES.

Worked Example: 4a,8a-propanoquinoline

```

<group type="ring" subType="bridgeSystem" value="propanoquinoline">
  <brIDGEparent
    type="ring"
    subType="ring"
    value="n1cccc2cccc12"
    labels="1/2/3/4/4a/5/6/7/8a"
    fusedRing1="n1ccccc1"
    fusedRing2="c1ccccc1"
    originalLabels="(1,) / (2,) / (3,) / (4,) / (5,1) / (,2) / (,3) / (,4) / (,5) / (6,6)">
  quinoline
  </brIDGEparent>
  <brIDGEchild
    type="chain"
    subType="alkaneStem"
    value="-CCC-"
    labels="11/10/9"
    usableAsAJoiner="yes"
    bridgeLocants="4a,8a">
    prop
  </brIDGEchild>
</group>

```

Interpretation:

- Parent ring labels: 1/2/3/4/4a/5/6/7/8a
- Bridge locants: 4a, 8a
- Bridge labels: 11/10/9

The bridge is incorporated directionally as: **4a – 11 – 10 – 9 – 8a**

The resulting structure uses a **single combined labeling scheme**, consisting of the parent-ring labels extended by the bridge labels. All subsequent references (including further fusions, substituents, and stereochemistry) must use this combined labeling scheme.

Prompt 4: Spiro Ring Semantics (XML)

For a spiro ring system, the XML normally provides:

- One or more `spiroSystemComponent` entries, each describing a **complete ring system**.
 - Each component has a `value` (SMILES) and a `labels` attribute.
 - If `labels` is **explicitly provided**, those labels are used; if `labels` is **omitted** or set to `numeric`, atoms are implicitly labeled from 1 to n , following the **SMILES atom order**.
 - A component may itself be a fused ring system, following the fused-ring semantics.
- A `spiroLocant`, which specifies the **spiro atom in each ring system**.

Each ring system **retains its own labeling scheme**. To distinguish atoms belonging to different ring systems, **prime notation** (', ', ...) is used.

The locants in `spiroLocant` are listed in the same order as the `spiroSystemComponent` entries and identify the single atom in each ring system that represents the same physical atom.

Worked Example: spiro[cyclopentane-1,1'-indene]

```

<group type="spiro system" subType="Polycyclic" value="spiro,pent,inden">
  <spiroSystemComponent
    type="ring"
    subType="alkaneStem"
    value="C1CCCC1"
    labels="numeric">
    pent
  </spiroSystemComponent>
  <spiroLocant>1,1'</spiroLocant>
  <spiroSystemComponent
    type="ring"
    subType="ring"
    value="[cH2]1ccc2ccccc12"
    labels="1/2/3/3a/4/5/6/7/7a"
    fusedRing1="[cH2]1cccc1"
    fusedRing2="c1cccc1"
    originalLabels="(1,)/(2,)/(3,)/(4,1)/(2,)/(3,)/(4,)/(5,)/(5,6)">
    inden
  </spiroSystemComponent>
</group>

```

Interpretation:

- Cyclopentane uses labels 1–5; the spiro atom is 1.
- Indene uses its own labeling scheme; the spiro atom is 1'.
- Atoms 1 and 1' refer to the **same physical atom**.

All other atoms are referenced using their **component-specific labels with primes**, consistent with the XML.

Prompt 5: Molecular Description Generation from SMILES and IUPAC Names**Task:**

You are provided with the **IUPAC name** and **SMILES string**, generate a **detailed and accurate structural description** that would allow a person with **basic organic chemistry knowledge** to reconstruct the exact molecule using only your structural description text. The description should be **natural**, **diverse**, and **chemically precise**, clearly conveying the molecular skeleton, substituents, and stereochemistry.

In addition, after completing the description, report the total number of non-hydrogen atoms implied by your description, computed **only from the information explicitly stated in the description itself**.

Guidelines:**1. Purpose and Independence**

- The description must be **self-contained** and **sufficient for reconstruction**.
- Assume the reader only has your final text—they will **not see** the SMILES or IUPAC name.
- You may use all input data internally to reason about the molecule, but the final description must read as a stand-alone, human-readable explanation.

2. Freedom of Description

You may begin from any perspective—the main skeleton, a key ring system, or an important substituent. Combine information freely from the IUPAC name and SMILES to capture the complete structure.

3. Backbone and Connectivity

Describe how rings, chains, and substituents are connected. Indicate branching positions, linkages, and overall topology so that the structure can be reconstructed accurately.

4. Functional Groups and Substituents

Identify all key functional groups and substituents. Specify their type (e.g., hydroxyl, amine, halogen, carbonyl), location, and bonding pattern relative to the molecular framework.

5. Simple or Isolated Rings

For common rings (benzene, pyridine, cyclohexane), you may name them directly or briefly describe their composition and bonding.

6. Fused, Bridged, or Spiro Ring Systems — explicit, structured, and verified

It is **strongly recommended to follow the guidance below** when describing complex ring topologies:

- (a) **Define and label atoms/rings.** Explicitly assign ring labels and atom labels to each ring in the ring system (e.g., “Ring A: C1–C6 clockwise starting at the junction with ring B”; include heteroatoms like O1/N5 as needed). For complex fused or multi-ring systems, it is recommended to align the atom labeling by the structure metadata to maintain chemical accuracy. If there are multiple distinct fused systems, assign separate, non-overlapping label sets to avoid confusion.
- (b) **Describe internal ring features.** State ring size, aromaticity/saturation, heteroatoms, and bonding patterns (alternation, single/double).
- (c) **Explain how rings are connected.** Specify **exact shared atoms or edges** (e.g., “Ring B shares the C5–C6 edge with ring A”). Describe **fusion geometry** (linear, angular, bridged, spiro).

Required verification (before finalizing your description):

- **Label consistency:** Each label you introduced is used consistently; no duplicate or skipped numbering within a ring.
- **Ring labeling check:** Verify that the atom labeling and numbering sequence are correct, and that the shared atoms or edges described for each fusion correspond accurately to your own ring definitions and orientations.
- **Orientation sanity-check:** The shared atoms/edge and the named orientation (linear vs angular; inner vs outer edge) match the topology. Do not accidentally mirror or rotate the fusion.
- **Cross-consistency check:** Ensure that substituent positions and stereochemical designations correspond correctly to the atom labels and numbering scheme you defined for each ring.

7. Stereochemistry

Include stereochemical information such as (R/S) or (E/Z) when available, and describe how these configurations relate to surrounding atoms or bonds.

8. Use of Chemical Shorthand

- **Avoid full structural formulas** written as continuous symbolic notations.
- Short fragments like “–OH,” “–CH₃,” or “–NH₂” are acceptable when helpful.

9. Balance and Readability

Aim for a **balanced level of detail**.

10. Descriptive Diversity

Use varied styles and sentence structures.

11. Do Not Include

- The full IUPAC name or SMILES tags verbatim.
- Long symbolic chemical formulas for the entire molecule.
- Brand names, trivial comments, or unrelated metadata.
- Unintroduced atom labels or locants.

12. Non-hydrogen atom count

- After completing the description, report the **total number of non-hydrogen atoms**.
- **Do not** use the SMILES to perform this count.
- **Do not** include the counting process in your description.

Output Format:

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<description>
[Concise, varied, and chemically precise structural description]
</description>
<non_hydrogen_atom_count>
[integer]
</non_hydrogen_atom_count>
```

Inputs:

- **IUPAC Name:** {IUPAC}
- **SMILES String:** {SMILES}

A.7. Representative Samples

We present representative molecule–description pairs from each generation difficulty level (easy, medium, and hard), with two examples per category. For each level, we select one molecule with a relatively simple structure and one with a more complex structure. For the structurally simpler examples, we additionally include the structured XML metadata constructed by our method.

Molecular Structure:

Generated Description:

The molecule is a substituted phosphinic acid built around a tetra-coordinate phosphorus atom. At the phosphorus center, place one oxo group (a P=O double bond) and one hydroxyl group (a single P–O–H bond), giving the phosphinic acid functionality. The remaining two substituents on phosphorus are: (1) a methyl group (–CH₃) directly bonded to phosphorus, and (2) a two-carbon alkyl chain (–CH₂–CH₂–) also directly bonded to phosphorus.

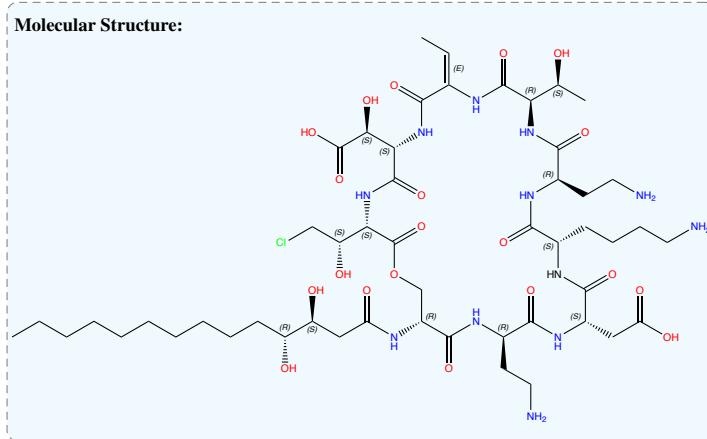
From the end of that phosphorus-bound ethyl chain, connect a sulfur atom as a thioether (so the chain continues as –CH₂–CH₂–S–). From sulfur, attach another ethyl linker (–CH₂–CH₂–) that terminates at an oxygen atom (–O–). That oxygen is the single-bond (alkoxy) oxygen of an ester: it is bonded to the carbonyl carbon of a prop-2-enoyl (acryloyl) group. Complete the acyl fragment as an α,β -unsaturated carbonyl: the carbonyl carbon is double-bonded to one oxygen, and single-bonded to a vinyl group so that the chain is –C(=O)–CH=CH₂ (terminal alkene).

```

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```

(a) Easy category example 1 (simple structure): *methyl-[2-(2-prop-2-enyloxyethylsulfanyl)ethyl]phosphinic acid*

**Generated Description:**

Begin with a 2-hydroxyacetic acid (glycolic acid) unit: a carboxylic acid group ($-\text{C}(=\text{O})\text{OH}$) whose adjacent (α) carbon bears a hydroxyl group ($-\text{OH}$) and is stereogenic with S configuration. This stereogenic α carbon is bonded directly (by a C-C single bond) to a large macrocyclic substituent described next.

Construct a **28-membered macrocycle** and label the ring atoms consecutively **1→28** as follows (then close the ring by bonding atom 28 back to atom 1):

- **Atom 1:** an oxygen (an ether/ester oxygen) in the ring.
- **Atom 2:** a carbonyl carbon attached to atom 1; atom 2 is $\text{C}(=\text{O})$ (the carbonyl oxygen is outside the ring), and atom 2 is also bonded to atom 3. (Thus, atoms 1–2–3 form an ester linkage: $\text{O}-\text{C}(=\text{O})-\text{C}$.)
- **Atom 3:** a stereogenic carbon with S configuration, bonded to atom 2 and to atom 4.
- **Atom 4:** an amide nitrogen ($-\text{NH}-$) bonded to atom 3 and to atom 5.
- **Atom 5:** a carbonyl carbon ($\text{C}(=\text{O})$) bonded to atom 4 and atom 6.
- **Atom 6:** a stereogenic carbon with S configuration, bonded to atom 5 and atom 7; this is the **attachment point to the glycolic acid α carbon** described at the beginning (the glycolic acid stereocenter is directly bonded to ring atom 6).
- **Atom 7:** an amide nitrogen ($-\text{NH}-$) bonded to atom 6 and atom 8.
- **Atom 8:** a carbonyl carbon ($\text{C}(=\text{O})$) bonded to atom 7 and atom 9.
- **Atom 9:** a vinylic ring carbon bonded to atom 8 and atom 10, and double-bonded to an **exocyclic ethylenic group**: atom 9 is double-bonded to an external carbon that bears one hydrogen and one **methyl** substituent (i.e., $=\text{CH}-\text{CH}_3$). The $\text{C}=\text{C}$ (exocyclic) double bond has E geometry.
- **Atom 10:** an amide nitrogen ($-\text{NH}-$) bonded to atom 9 and atom 11.
- **Atom 11:** a carbonyl carbon ($\text{C}(=\text{O})$) bonded to atom 10 and atom 12.
- **Atom 12:** a stereogenic carbon with R configuration, bonded to atom 11 and atom 13.
- **Atom 13:** an amide nitrogen ($-\text{NH}-$) bonded to atom 12 and atom 14.
- **Atom 14:** a carbonyl carbon ($\text{C}(=\text{O})$) bonded to atom 13 and atom 15.
- **Atom 15:** a stereogenic carbon with R configuration, bonded to atom 14 and atom 16.
- **Atom 16:** an amide nitrogen ($-\text{NH}-$) bonded to atom 15 and atom 17.
- **Atom 17:** a carbonyl carbon ($\text{C}(=\text{O})$) bonded to atom 16 and atom 18.
- **Atom 18:** a stereogenic carbon with S configuration, bonded to atom 17 and atom 19.
- **Atom 19:** an amide nitrogen ($-\text{NH}-$) bonded to atom 18 and atom 20.
- **Atom 20:** a carbonyl carbon ($\text{C}(=\text{O})$) bonded to atom 19 and atom 21.
- **Atom 21:** a stereogenic carbon with S configuration, bonded to atom 20 and atom 22.
- **Atom 22:** an amide nitrogen ($-\text{NH}-$) bonded to atom 21 and atom 23.
- **Atom 23:** a carbonyl carbon ($\text{C}(=\text{O})$) bonded to atom 22 and atom 24.
- **Atom 24:** a stereogenic carbon with R configuration, bonded to atom 23 and atom 25.
- **Atom 25:** an amide nitrogen ($-\text{NH}-$) bonded to atom 24 and atom 26.
- **Atom 26:** a carbonyl carbon ($\text{C}(=\text{O})$) bonded to atom 25 and atom 27.
- **Atom 27:** a stereogenic carbon with R configuration, bonded to atom 26 and atom 28.
- **Atom 28:** a methylene carbon ($-\text{CH}_2-$) bonded to atom 27 and back to atom 1 to close the macrocycle.

Add the substituents on the ring carbons (all other ring nitrogens are the secondary amide $-\text{NH}-$ described above):

1. At **ring atom 3** (the S stereocenter): attach a **2-chloro-1-hydroxyethyl** group in which the carbon directly attached to ring atom 3 is itself stereogenic with S configuration and bears $-\text{OH}$; that carbon is bonded to a terminal $-\text{CH}_2\text{Cl}$ group.
2. At **ring atom 12** (R): attach a **1-hydroxyethyl** group where the carbon attached to ring atom 12 is stereogenic with S configuration and bears $-\text{OH}$ and a **methyl** group (i.e., $-\text{CH}(\text{OH})-\text{CH}_3$).
3. At **ring atom 15** (R): attach a **2-aminoethyl** substituent, $-\text{CH}_2-\text{CH}_2-\text{NH}_2$.
4. At **ring atom 18** (S): attach a **4-aminobutyl** substituent, $-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{NH}_2$.
5. At **ring atom 21** (S): attach a **carboxymethyl (acetic acid)** substituent, $-\text{CH}_2-\text{C}(=\text{O})\text{OH}$.
6. At **ring atom 24** (R): attach a second **2-aminoethyl** substituent, $-\text{CH}_2-\text{CH}_2-\text{NH}_2$.
7. At **ring atom 27** (R): attach an **amide side chain** via an $-\text{NH}-$ group directly bonded to ring atom 27 (so ring atom 27 bears a substituent $-\text{NH}-\text{C}(=\text{O})-\dots$). This amide nitrogen is acylated by a **tetradecanoyl** chain (14 carbons counting the carbonyl carbon) that is linear and unbranched and contains two hydroxyl groups at the 3- and 4-positions from the carbonyl: $-\text{C}(=\text{O})-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}(\text{OH})-(\text{CH}_2)_9-\text{CH}_3$, with the hydroxyl-bearing carbons having **3S** and **4R** configurations (counting from that side-chain carbonyl carbon as position 1).

This completes the full connectivity and stereochemistry (including the E ethylenic double bond at ring atom 9 and the stated absolute configurations at every stereocenter).

(b) Easy category example 2 (complex structure): (2S)-2-[(3S,6S,9E,12R,15R,18S,21S,24R,27R)-18-(4-azanylbutyl)-15,24-bis(2-azanylethyl)-27-[[3S,4R]-3,4-bis(oxidanyl)tetradecanoyl]amino]-3-[(1S)-2-chloranyl-1-oxidanyl-ethyl]-9-ethylidene-21-(2-hydroxy-2-oxoethyl)-12-[(1S)-1-oxidanyl-ethyl]-2,5,8,11,14,17,20,23,26-nonakis(oxidanylidene)-1-oxa-4,7,10,13,16,19,22,25-octazacyclooctacos-6-yl]-2-oxidanyl-ethanoic acid

Molecular Structure:

Generated Description:

The molecule is a diaryl ketone (a “benzophenone-type” structure): a single carbonyl group ($\text{C}=\text{O}$) whose carbon is bonded to two aromatic substituents.

First build the fused bicyclic aryl substituent (a benzene fused to a 7-membered dioxacycle). Define it with these atom labels:

- Ring A (benzene): six aromatic carbons arranged as $\text{C5a}-\text{C6}-\text{C7}-\text{C8}-\text{C9}-\text{C9a}$ -(back to C5a).
- Ring B (seven-membered heterocycle): fuse this ring to Ring A by sharing the $\text{C5a}-\text{C9a}$ bond. Ring B is $\text{C9a}-\text{O1}-\text{C2}-\text{C3}-\text{C4}-\text{O5}-\text{C5a}$ -(back to C9a), where O1 and O5 are ether oxygens and C2 , C3 , and C4 are three consecutive saturated methylene carbons ($-\text{CH}_2-$ units).

At aromatic carbon C7 of Ring A, attach the carbonyl carbon of the ketone (the carbonyl oxygen is double-bonded to this carbonyl carbon).

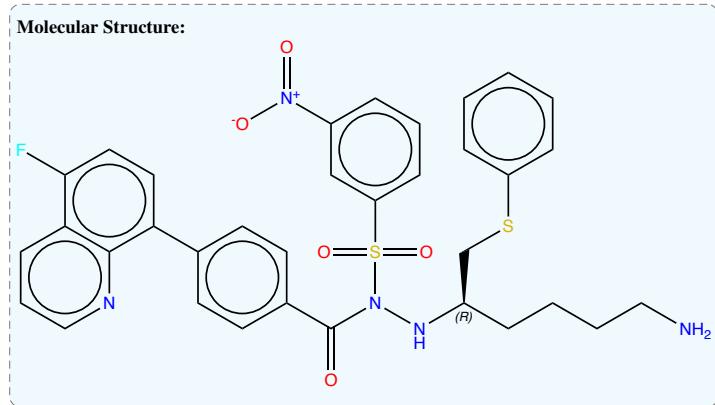
The other substituent on the carbonyl carbon is a phenyl ring. Label the phenyl carbon bonded directly to the carbonyl as $\text{C1}'$; place a fluorine atom on the adjacent ring carbon $\text{C2}'$ (i.e., ortho to the carbonyl attachment). The remaining four phenyl positions are unsubstituted.

```

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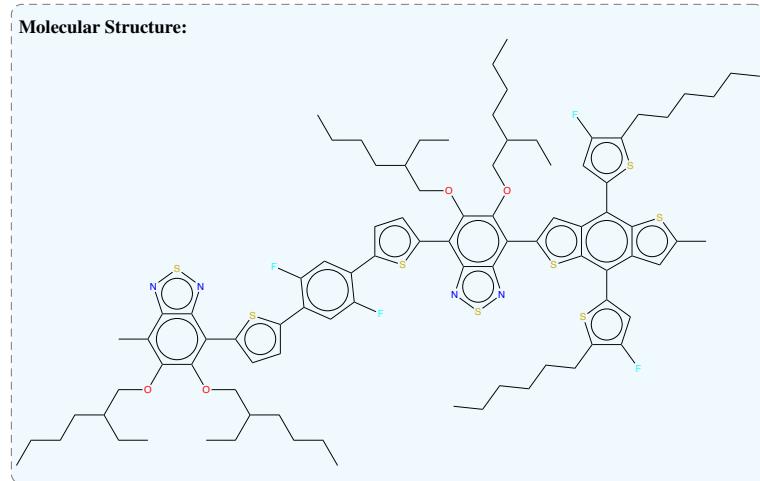
(c) Medium category example 1 (simple structure): 3,4-dihydro-2H-1,5-benzodioxepin-7-yl-(2-fluorophenyl)methanone

**Generated Description:**

Start from an acyl hydrazide core derived from a para-substituted benzoic acid.

1. Define Ring A as a benzene ring containing 6 carbon atoms, labeled A1–A6 consecutively. At A1, attach a carbonyl group so that the carbonyl carbon (one carbon atom) is directly bonded to A1, is double-bonded to one oxygen atom, and is single-bonded to an amide nitrogen N2.
2. Hydrazide linkage: connect N2 by a single bond to a second nitrogen N1 (so the sequence is carbonyl carbon–N2–N1). N2 bears no hydrogen because it is substituted by the carbonyl carbon, by N1, and by a sulfonyl group (next step).
3. Sulfonamide substituent on N1: bond N1 to a sulfonyl sulfur atom S.sulf. This sulfur is double-bonded to two oxygen atoms and single-bonded to Ring B (a phenyl ring). Define Ring B as a benzene ring of 6 carbon atoms labeled B1–B6, with B1 bonded to S.sulf. Place a nitro group (--NO_2 , i.e., one nitrogen atom and two oxygen atoms) on B3, which is the meta position relative to B1.
4. Substituent on N1: bond N1 to a stereogenic carbon X2. Build a straight six-carbon chain X1–X2–X3–X4–X5–X6 (six carbon atoms total), where X2 is the chiral center. The segment X3–X4–X5–X6 consists of four consecutive methylene carbons, and X6 carries a terminal primary amino group (one nitrogen atom, --NH_2).
5. Thioether at X1: X1 is a methylene carbon attached to X2 and also to a thioether sulfur atom S.thio. Bond S.thio to Ring C, an unsubstituted phenyl ring containing 6 carbon atoms.
6. Absolute configuration: X2 has the R configuration. Using CIP priorities at X2 (N1 has highest priority; X1 next because it leads to sulfur; X3 next; hydrogen lowest), orient the X2–H bond away from the viewer; the order N1 \rightarrow X1 \rightarrow X3 then traces a clockwise path.
7. Para quinoline substituent on Ring A: at A4 (para to A1), attach a quinoline group through a single bond from A4 to atom Q8 of the quinoline. Construct the quinoline as an aromatic fused bicyclic system with 10 ring atoms total (9 carbons and 1 ring nitrogen). Label the pyridine-like ring as Q1 (the ring nitrogen), then Q2–Q3–Q4–Q4a–Q8a returning to Q1. Fuse to it a benzene ring that shares the Q4a–Q8a bond and follows Q4a–Q5–Q6–Q7–Q8–Q8a–Q4a. Place a fluorine atom on Q5.

(d) Medium category example 2 (complex structure): *N'*-[(2*R*)-6-azanyl-1-phenylsulfanyl-hexan-2-yl]-4-(5-fluoranylquinolin-8-yl)-*N*-(3-nitrophenoxy)sulfonyl-benzohydrazide

**Generated Description:**

Build a fully conjugated, all-aromatic molecule that contains two substituted benzothiadiazole units connected by a thiophene–difluorophenyl–thiophene linker, and with the “inner” benzothiadiazole additionally attached to a tricyclic sulfur-containing fused core that bears two identical fluoro/hexyl thiophene substituents.

1. Terminal benzothiadiazole unit (Unit A)

- Make an aromatic “benzothiadiazole” fused bicyclic system by fusing:
 - a benzene ring (6 carbons) and
 - a 1,2,5-thiadiazole ring (a 5-member aromatic ring whose atom sequence around the ring is N–S–N–C–C), with the fusion occurring through the two carbon atoms of the thiadiazole (so the fused system contains 6 ring carbons, 2 ring nitrogens, and 1 ring sulfur; 9 non-hydrogen atoms in the fused core).
- On the benzene portion of this fused system, there are four consecutive carbons that are not part of the fusion. Label these four benzene carbons A1–A4 in order around that benzene ring.
 - A1 is bonded to a thiophene ring (thiophene T α , described below).
 - A2 and A3 each bear a 2-ethylhexyloxy substituent (an ether: ring–O–(2-ethylhexyl), where the 2-ethylhexyl group is the 8-carbon chain O–CH₂–CH(–CH₂CH₃)–CH₂–CH₂–CH₂–CH₃).
 - A4 bears a methyl group (–CH₃).

2. Linker from Unit A to the second benzothiadiazole

- Thiophene T α : an aromatic thiophene ring (5-member ring with 1 sulfur and 4 carbons). Use the usual thiophene positions where the two “ α ” carbons are the two carbons adjacent to sulfur. Connect T α through its two α carbons: one α carbon is bonded to A1 of Unit A, and the opposite α carbon is bonded to a difluorophenyl ring (Unit P) described next.
- Unit P (difluorophenyl): a benzene ring (6 carbons). Label the ring carbons P1–P6 consecutively around the ring.
 - Bond P1 to thiophene T α .
 - Bond the para carbon P4 to a second thiophene ring (T β , next bullet).
 - Put fluorine atoms on P2 and P5 (so each fluorine sits on a carbon adjacent to one of the two para substituent positions).
- Thiophene T β : another aromatic thiophene ring (again 5 atoms: 1 sulfur, 4 carbons), substituted at its two α carbons. Bond one α carbon of T β to P4 of Unit P, and bond the opposite α carbon of T β to the second benzothiadiazole unit (Unit B) described below.

3. Second benzothiadiazole unit (Unit B)

- Create a second benzothiadiazole fused system with the same ring composition as Unit A (again 6 ring carbons, 2 ring nitrogens, 1 ring sulfur).
- On the benzene portion of Unit B, label the four non-fusion benzene carbons B1–B4 in order around that benzene ring.
 - B1 is bonded to the tricyclic fused core (Core X, defined next) by a direct C–C bond.
 - B2 and B3 each bear a 2-ethylhexyloxy group of the same structure defined above (ring–O–CH₂–CH(–CH₂CH₃)–CH₂–CH₂–CH₂–CH₃).
 - B4 is bonded by a C–C bond to thiophene T β (from step 2).

4. Tricyclic fused sulfur-containing core (Core X) attached to Unit B

Define Core X explicitly as a 12-atom fused aromatic system with atom labels 1, 2, 3, 3a, 4, 4a, 5, 6, 7, 7a, 8, 8a:

- Atoms 1 and 5 are sulfur; all other labeled atoms in Core X are aromatic carbons.
- Ring L (a thiophene): 1–2–3–3a–8a–1.
- Ring M (a benzene): 7a–8–8a–3a–4–4a–7a.
- Ring R (a thiophene): 5–6–7–7a–4a–5.

(So Ring L and Ring M share the 3a–8a edge, and Ring R and Ring M share the 4a–7a edge.)
Substitution on Core X:

- Bond B1 of Unit B to atom 2 of Core X (single C–C bond).
- Put a methyl group (–CH₃) on atom 6 of Core X.
- Attach two identical substituted thiophene rings (step 5) to Core X by single C–C bonds at atoms 4 and 8.

5. The two identical peripheral thiophene substituents on Core X (one on atom 4, one on atom 8)

- Each substituent is an aromatic thiophene ring (5-member ring with 1 sulfur and 4 carbons). Number within each such substituent thiophene as: position 1 = sulfur; position 2 = the carbon bonded to Core X; positions 3 and 4 = the two β carbons; position 5 = the other α carbon.
- Place a fluorine atom on position 4 of this thiophene.
- Place an n-hexyl substituent (a straight six-carbon chain, –CH₂–CH₂–CH₂–CH₂–CH₂–CH₃) on position 5 of this thiophene, attached via the chain’s first carbon to the thiophene.

No stereochemical configuration is specified for the chiral center at the 2-position of each 2-ethylhexyl group.

(e) Hard category example 1 (complex structure): 4-[5-[4-[5-[4-[4,8-bis(4-fluoranyl-5-hexyl-thiophen-2-yl)-6-methyl-thieno[2,3-f][1]benzothiol-2-yl]-5,6-bis(2-ethylhexoxy)-2,1,3-benzothiadiazol-7-yl]thiophen-2-yl]-2,5-bis(fluoranyl)phenyl]thiophen-2-yl]-5,6-bis(2-ethylhexoxy)-7-methyl-2,1,3-benzothiadiazole

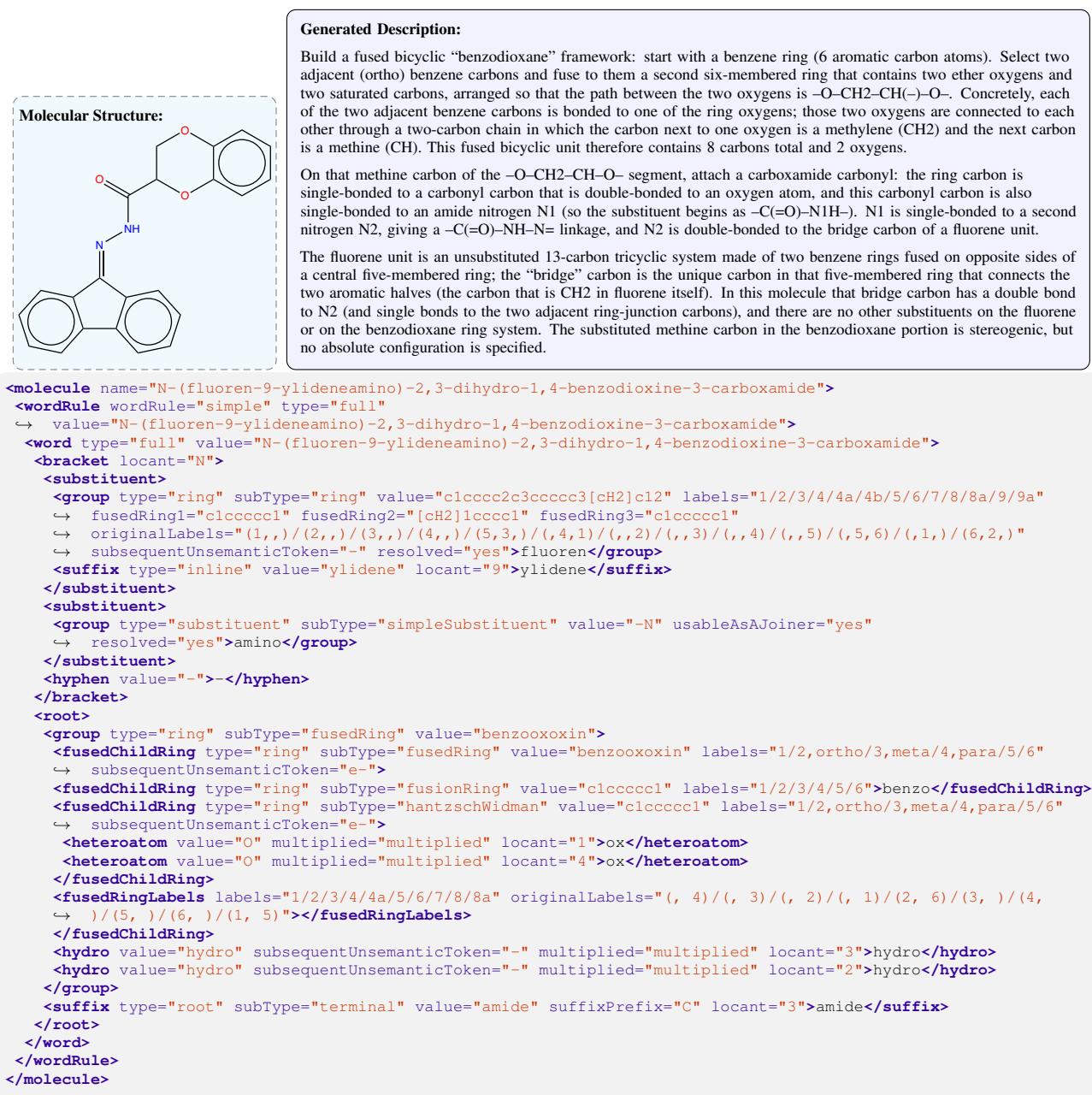
(f) Hard category example 2 (simple structure): *N*-(fluoren-9-ylideneamino)-2,3-dihydro-1,4-benzodioxine-3-carboxamide

Figure S4. Representative examples for the generated dataset.