Synthesis, Molecular Modeling Studies, and Selective Inhibitory Activity against Monoamine Oxidase of 1-Thiocarbamoyl-3,5-diaryl-4,5-dihydro-(1 H)- pyrazole Derivatives

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ACS Publications

Journal of Medicinal Chemistry

Guidelines for Authors

Revised May 2015

Major Changes for 2015

- Section 2.1.9 Interference Compounds added.
- Section 2.3.2 Purity of Tested Compounds addition of qHNMR protocol as evidence of purity.

Contents (click on the topic)

1 Scope and Editorial Policy

1.1 Scope of the Journal

The *Journal of Medicinal Chemistry* (Journal) invites original research contributions dealing with chemical-biological relationships. The primary objective of the Journal is to publish studies that contribute to an understanding of the relationship between molecular structure and biological activity or mode of action.

Some specific areas that are appropriate include the following.

- Design, synthesis, and biological evaluation of novel biologically active compounds, diagnostic agents, or labeled ligands employed as pharmacological tools.
- Molecular modifications of reported series that lead to a significantly improved understanding of their structure-activity relationships (SAR). Routine extensions of existing series that do not utilize novel chemical or biological approaches or do not add significantly to a basic understanding of the SAR of the series will normally not be considered for publication.
- Structural biological studies (X-ray, NMR, etc.) of relevant ligands and targets with the aim of investigating molecular recognition processes in the action of biologically active compounds.
- Molecular biological studies (e.g., site-directed mutagenesis) of macromolecular targets that lead to an improved understanding of molecular recognition.
- Computational studies that analyze the SAR of compound series of general interest and lead to experimental studies or analysis of other available chemical and/or biological data that substantially advance medicinal chemistry knowledge.
- Substantially novel computational chemistry methods with demonstrated utility for the identification, optimization, or target interaction analysis of bioactive molecules.
- Effect of molecular structure on the distribution, pharmacokinetics, and metabolic transformation of biologically active compounds. This may include design, synthesis, and evaluation of novel types of prodrugs.
- Novel methodology with *broad* application to medicinal chemistry, but only if the methods have been tested on relevant molecules.

1.2 Manuscript Categories

Manuscripts can be submitted as *Articles*, *Brief Articles*, *Perspectives*, or *Drug Annotations*.

1.2.1 *Articles* are definitive, full accounts of significant studies.

1.2.2 *Brief Articles* are definitive reports whose scope is more limited than the scope of *Articles*, but whose format is identical except for length. They are subject to the same editorial appraisal as *Articles* and should be of similar scientific quality.

1.2.3 *Perspectives* are interpretive accounts on subjects of current interest to medicinal chemists. This series is intended to be a forum for experts to present their perspectives on emerging or active areas of research that affect the practice of medicinal chemistry. Manuscripts are usually submitted at the invitation of the Perspectives Editor. However, experts are welcome to contact the Perspective Editor to ensure that a topic is suitable. Approval is recommended prior to submission.

1.2.4 *Drug Annotations* are reports of drug candidates in phase I, II, and III clinical trials, as well as new drugs in the market. *Drug Annotations* manuscripts focus on a single drug and should provide a description of a candidate molecule (including structure), target(s), mechanism of action, and rationale for bringing the candidate to clincial trial (for example, first in class or improvement over previous compounds). Reports on original research are also acceptable. Manuscripts are usually submitted after an invitation from the *Drug Annotations* Editors. However, authors are welcome to contact the *Drug Annotations* Editors to ensure that a topic is suitable. Approval is recommended prior to submission.

1.2.5 *Viewpoint* manuscripts are invited by the Editors. *Viewpoint* manuscripts are typically accompanied commentaries to *Featured Article*s.

1.2.6 *Featured Articles* are selected by the Editors from accepted *Articles*, *Brief Articles*, and *Drug Annotations.*

1.3 Prior Publication

Authors should submit only original work that has not been previously published and is not under consideration for publication elsewhere.

Academic theses, including those on the Web or at a college Web site, are not considered to be prior publication.

1.4 Patents and Intellectual Property

Authors need to resolve all patent and intellectual property issues. Acceptance and publication will not be delayed for pending or unresolved issues of this type. Note that *Just Accepted* manuscripts (section 3.11) and ASAP manuscripts (section 3.12) are published documents.

1.5 Professional Ethics

Editors, reviewers, and authors are expected to adhere to the American Chemical Society's Ethical Guidelines to Publication of Chemical Research. The guidelines are available at http://pubs.acs.org/page/jmcmar/submission/index.html.

1.5.1 ***Author Consent.*** Submitting authors are reminded that consent of all coauthors must be obtained prior to submission of manuscripts. If an author is removed after submission, the submitting author must have the removed author consent to the change by e-mail or faxed letter to the assigned Editor.

1.5.2. ***Plagiarism.*** Manuscripts must be original with respect to concept, content, and writing. It is not appropriate for an author to reuse wording from other publications, including one's own previous publications, whether or not that publication is cited. Suspected plagiarism should be reported immediately to the editorial office. Report should *specifically* indicate the plagiarized material within the manuscripts.

1.5.3. ***Use of Human or Animal Subjects.*** Manuscripts must comply with the ACS Ethical Guidelines to Publication of Chemical Research: *Research involving animals must be performed in accordance with institutional guidelines as defined by Institutional Animal Care and Use Committee for U.S. institutions or an equivalent regulatory committee in other countries. Research studies involving humans must have institutional review board approval. Authors are requested to identify the institutional or licensing committee that has approved the experiments. For research involving animals or humans, Editors reserve the right to request additional information from authors.*

1.6 Issue Frequency

The Journal publishes 24 issues per year on the second and fourth Thursdays of each month.

2 Preparing the Manuscript

2.1 General Considerations

Manuscripts should be kept to a minimum length. Authors should write in clear, concise English, employing an editing service if necessary. For convenience, ACS has compiled a list of language-editing companies (http://pubs.acs.org/page/4authors/tools/language_editing.html). The responsibility for all aspects of manuscript preparation rests with the authors. Extensive changes or rewriting of the manuscript will not be undertaken by the Editors. Information on a standard list of abbreviations for ACS Journals is in *The ACS Style Guide* (2006), available from Oxford University Press, Order Department, 2001 Evans Road, Cary, NC 27513.

Authors are strongly encouraged to use the templates available on the Journal Web site.

It is best to use the fonts "Times" and "Symbol." Other fonts, particularly those that do not come bundled with the system software, may not translate properly. Ensure that all special characters (e.g., Greek characters, math symbols) are present in the body of the text as characters and not as graphic representations. Be sure that all characters are correctly represented throughout the manuscript—e.g., 1 (one) and l (letter l), 0 (zero) and O (letter o).

All text (including the title page, abstract, all sections of the body of the paper, figure captions, scheme or chart titles, and footnotes and references) and tables should be in *one* file. Graphics may be included with the text or uploaded as separate files.

Manuscripts that do not adhere to the guidelines may be returned to authors for correction.

2.1.1 ***Articles***. *Articles* must be double-spaced including text, references, tables, and legends. Vertically orient all pages. Use page size 8.5 x 11 inches. This applies to figures, schemes, and tables as well as text. Manuscripts do not have page limitations but should be kept to a minimum length. The experimental procedures for all of the steps in the synthesis of target compounds must be included in the experimental section of the manuscript.

2.1.2 ***Brief Articles.*** Manuscripts must not exceed 7 pages of the double-column template including title page, abstract, text with experimental section, references, tables, illustrations, and table of contents graphic. The abstract is limited to 75 words. If manuscripts exceed 7 journal pages at the galley stage, authors will be asked to reduce the length of their manuscripts. To remain within the page limit, some material may be included in supporting information. However, the experimental procedures for all of the steps in the synthesis of target compounds must be included in the experimental section of the manuscript.

2.1.3 ***Perspectives.*** *Perspectives* manuscripts do not have the same headings as other manuscript types. Author(s) biographies of less than 125 words each should be placed immediately before the references. Generally, *Perspectives* are no more than 25 journal pages (100 double-spaced manuscript pages) and should not contain more than 180 references. *Miniperspectives* are no more than 8 journal pages (32 double-spaced manuscript pages) and should not contain more than 70 references. Page limits for Award Perspectives are flexible, but they should conform to other requirements stated for *Perspectives* or *Miniperspectvies*.

2.1.4 ***Drug Annotations.*** Manuscripts should be double-spaced including text, references, tables and legends. Vertically orient all pages. Use page size 8.5 x 11 inches. This applies to figures, schemes, and tables as well as text. Limit manuscripts to approximately 40 double-spaced pages

(10 journal pages), including title page, abstract of 150 words or less, up to 50 references, and tables, charts, schemes, and figures. In general, manuscripts should include design and chemistry, known biological targets, in vitro and in vivo biological activity, pharmacological properties, available toxicity information, and clinical data.

2.1.5 ***Viewpoint.*** Manuscripts are limited to 8 double-spaced pages (2 journal pages), including title page, abstract, references, tables, and illustrations.

2.1.6 Nomenclature. It is the responsibility of the authors to provide correct nomenclature. Nomenclature should conform to current American usage. It is acceptable to use semisynthetic or generic names for certain specialized classes of compounds, such as steroids, peptides, carbohydrates, etc. In such a case, the name should conform to the generally accepted nomenclature conventions for the compound class. Chemical names for drugs are preferred. If these are not practical, generic names, or names approved by the U.S. Adopted Names Council or by the World Health Organization, may be used. Authors may find the following sources useful for recommended nomenclature:

- *The ACS Style Guide*; Coghill, A. M., Garson, L. R., Eds.; American Chemical Society: Washington DC, 2006.
- *Enzyme Nomenclature*; Webb, E. C., Ed.; Academic Press: Orlando, 1992.
- IUPHAR database of receptors and ion channels (http://www.iuphar-db.org/index.jsp).

2.1.7 Compound Code Numbers. Code numbers assigned to a compound may be used as follows:

- Once in the manuscript title, when placed in parentheses AFTER the chemical or descriptive name.
- Once in the abstract.
- Once in the text (includes legends) and once to label a structure. Code numbers in the text must correspond to structures or, if used only once, the chemical name must be provided before the parenthesized code number, e.g., "chemical name (JEM-398)." If appearing a second time in the text, a bold Arabic number must be assigned on *first* usage, followed by the parenthesized code number, e.g., "**1** (JEM-398)." Subsequently, only the bold Arabic number may be used. All code numbers in the text must have a citation to a publication or a patent on first appearance.

Compounds *widely* employed as research tools and recognized primarily by code numbers may be designated in the manuscript by code numbers without the above restrictions. Their chemical name or structure should be provided as above. Editors have the discretion of determining which code numbers are considered widely employed.

2.1.8 Trademark Names. Trademark names for reagents or drugs must be used only in the experimental section. *Perspectives* may use trademark names once in the manuscript. Do not use trademark or service mark symbols.

2.1.9. Interference Compounds. Active compounds from any source must be examined for known classes of assay interference compounds and this analysis must be provided in the General Experimental section. Compounds shown to display misleading assay readouts by a variety of mechanisms include, but are not limited to, aggregation, redox activity, fluorescence, protein reactivity, singlet-oxygen quenching, the presence of impurities, membrane disruption, and their decomposition in assay buffer to form reactive compounds. Many of these compounds

have been classified as Pan Assay Interference Compounds (PAINS; see Baell & Holloway, *J. Med. Chem.* **2010**, *53*, 2719-2740). Provide firm experimental evidence in at least two different assays that reported compounds with potential PAINS liability are specifically active and their apparent activity is not an artifact.

2.2 Manuscript Organization

2.2.1 Title Page. *Title*: The title of the manuscript should reflect the purposes and findings of the work in order to provide maximum information in a computerized title search. Minimal use of nonfunctional words is encouraged. Only commonly employed abbreviations (e.g., DNA, RNA, ATP) are acceptable. Code numbers for compounds may be used in a manuscript title when placed in parentheses AFTER the chemical or descriptive name.

Authors' Names and Affiliations: The authors' full first names, middle initials, last names, and affiliations with addresses at time of work completion should be listed below the title. The name of the corresponding author should be marked with an asterisk (*).

2.2.2 Abstract. *Articles*, *Brief Articles*, *Perspectives*, and *Viewpoints* must have an abstract following the title page. *Brief Articles* have a strict 75 word limit; for *Articles* and *Perspectives*, 150 words are usually adequate; for *Viewpoints*, 1–3 sentences are adequate. Abstracts should be presented in a findings-oriented format in which the most important results and conclusions are summarized. Code numbers may be used once in the abstract.

2.2.3 Introduction. The rationale and objectives of the research should be discussed in this section. The background material should be brief and relevant to the research described.

2.2.4 Results. This section could include synthetic schemes and tables of biological data. The discussion of the chemistry and biology should be descriptive.

2.2.5 Discussion and Conclusions. Authors should discuss the analysis of the data together with the significance of results and conclusions, if an optional conclusions section is not employed.

2.2.6 Experimental Section. Authors should be as concise as possible in experimental descriptions. General reaction conditions should be given only once. The title of an experiment should include the chemical name and a bold Arabic identifier number; subsequently, only the bold Arabic number should be used. Experiments should be listed in numerical order. Molar equivalents of all reactants and percentage yields of products should be included.

A general introductory section should include general procedures, standard techniques, and instruments employed (e.g., determination of purity, chromatography, NMR spectra, mass spectra, names of equipment) in the synthesis and characterization of compounds described subsequently in this section. Special attention should be called to hazardous reactions or toxic compounds. Provide analysis for known classes of assay interference compounds.

Abbreviations. Standard abbreviations should be used throughout the experimental section (see 4. Standard Abbreviations and Acronyms). Please note that these are used in ACS Journals without periods. The preferred forms for some of the more commonly used abbrevations are mp, bp, ºC, K, min, h, mL, μL, g, mg, μg, cm, mm, nm, mol, mmol, μmol, ppm, TLC, GC, NMR, UV, and IR. Units are abbreviated in table column heads and when used with numbers, not otherwise. For further information, refer to *The ACS Style Guide* (see 2.1 General Considerations).

2.2.7 Ancillary Information. Include pertinent information in the order listed immediately before the references.

Supporting Information Availability. If supporting information has been submitted, include a statement of the availability using the following format:

> **Supporting Information.** Brief statement in nonsentence format listing the contents of the material supplied as Supporting Information.

PDB ID Codes: Include the PDB ID codes.

Corresponding Author Information: Provide telephone numbers and email addresses for each of the designated corresponding authors.

Present/Current Author Addresses: Provide information for authors whose affiliations or addresses have changed.

Author Contributions: Include statement such as "These authors contributed equally."

*Acknowledgment***:** Authors may acknowledge people, organizations, and financial supporters in this section.

Abbreviations Used: Provide a list of nonstandard abbreviations and acronyms used in the paper, e.g., YFP, yellow fluorescent protein. Do not include compound code numbers in this footnote. It is not necessary to include abbreviations and acronyms from the Standard Abbreviations and Acronyms list (http://pubs.acs.org/page/jmcmar/submission/authors.html).

2.2.8 References and Notes. Number literature references and notes in one *consecutive* series by order of mention in the text. Numbers in the text are non-parenthesized superscripts. The accuracy of the references is the responsibility of the author. List all authors; do not use et al. Provide inclusive page numbers. Titles may have capitalization of first word only (excluding, for example, acronyms and trade names) or standard capitalization as shown below. The chosen style should be used consistently throughout the references. Double-space the references using the following format.

- For journals: Rich, D. H.; Green, J.; Toth, M. V.; Marshall, G. R.; Kent, S. B. H. Hydroxyethylamine Analogues of the p17/p24 Substrate Cleavage Site Are Tight-Binding Inhibitors of HIV Protease. *J. Med. Chem.* **1990**, *33*, 1285-1288.
- For online early access: Rubner, G.; Bensdorf, K.; Wellner, A.; Kircher, B.; Bergemann, S.; Ott, I.; Gust, R. Synthesis and Biological Activities of Transition Metal Complexes Based on Acetylsalicylic Acid as Neo-Anticancer Agents. *J. Med. Chem.* [Online early access]. DOI: 10.1021/jm101019j. Published Online: September 21, 2010.
- For periodicals published in electronic format only: Author 1; Author 2; Author 3; etc. Title of Article. *Journal Abbreviation* [Online] **Year**, *Volume*, Article Number or other identifying information.
- For monographs: Casy, A. F.; Parfitt, R. T. *Opioid Analgesics*; Plenum: New York, 1986.
- For edited books: Rall, T. W.; Schleifer, L. S. Drugs Effective in the Therapy of the Epilepsies. In *The Pharmacological Basis of Therapeutics*, 7th ed.; Gilman, A. G., Goodman, L. S., Rall, T. W., Murad, F., Eds.; Macmillan: New York, 1985; pp 446-472.

List submitted manuscripts as “in press” only if formally accepted for publication. Manuscripts available on the Web with a DOI number are considered published. For manuscripts not accepted, use “unpublished results” after the names of authors. Incorporate notes in the correct numerical sequence with the references. Footnotes are not used.

2.2.9 Tables. Tabulation of experimental results is encouraged when this leads to more effective presentation or to more economical use of space. Tables should be numbered consecutively in order of citation in the text with Arabic numerals. Footnotes in tables should be given italic lowercase letter designations and cited in the tables as superscripts. The sequence of letters should proceed by row rather than by column. If a reference is cited in both table and text, insert a lettered footnote in the table to refer to the numbered reference in the text. Each table must be provided with a descriptive title that, together with column headings, should make the table self-explanatory.

Titles and footnotes should be on the same page as the table. Tables may be created using a word processor's text mode or table format feature. The table format feature is preferred. Ensure each data entry is in its own table cell. If the text mode is used, separate columns with a single tab and use a return at the end of each row. Tables may be inserted in the text where first mentioned or may be grouped after the references.

2.2.10 Figures, Schemes/Structures, and Charts. The use of illustrations to convey or clarify information is encouraged. Structures should be produced with the use of a drawing program such as ChemDraw. Authors using other drawing packages should, in as far as possible, modify their program's parameters so that they conform to ChemDraw preferences. Remove all color from illustrations, except for those you would like published in color. Illustrations may be inserted into the text where mentioned or may be consolidated at the end of the manuscript. If consolidated, legends should be grouped on a separate page(s). Include as part of the manuscript file.

To facilitate the publication process, please submit manuscript graphics using the following guidelines:

1. The preferred submission procedure is to embed graphic files in a Word document. It may help to print the manuscript on a laser printer to ensure all artwork is clear and legible.
2. Additional acceptable file formats are: TIFF, PDF, EPS (vector artwork) or CDX (ChemDraw file). If submitting individual graphic files in addition to them being embedded in a Word document, ensure the files are named based on graphic function (i.e. Scheme 1, Figure 2, Chart 3), not the scientific name. Labeling of all figure parts should be present and the parts should be assembled into a single graphic.

   EPS files: Ensure that all fonts are converted to outlines or embedded in the graphic file. The document settings should be in RGB mode. **NOTE:** *While EPS files are accepted, the vector-based graphics will be rasterized for production.* Please see below for TIFF file production resolutions.
3. TIFF files (either embedded in a Word doc or submitted as individual files) should have the following resolution requirements:
   - Black & White line art: 1200 dpi
   - Grayscale art (a monochromatic image containing shades of gray): 600 dpi
   - Color art (RGB color mode): 300 dpi
   - The RGB and resolution requirements are essential for producing high-quality graphics within the published manuscript. Graphics submitted in CMYK or at lower resolutions may be used; however, the colors may not be consistent and graphics of poor quality may not be able to be improved.

- Most graphic programs provide an option for changing the resolution when you are saving the image. Best practice is to save the graphic file at the final resolution and size using the program used to create the graphic.

4. Graphics should be sized at the final production size when possible. Single column graphics are preferred and can be sized up to 240 points wide (3.33 in.). Double column graphics must be sized between 300 and 504 points (4.167 in. and 7 in.). All graphics have a maximum depth of 660 points (9.167 in.) including the caption (please allow 12 points for each line of caption text).

   Consistently sizing letters and labels in graphics throughout your manuscript will help ensure consistent graphic presentation for publication.

For more information, please visit http://pubs.acs.org/page/jmcmar/submission/authors.html and http://pubs.acs.org/page/4authors/submission/index.html.

2.2.11 Image Manipulation. According to *ACS Ethical Guidelines*, images should be free from misleading manipulation. Images included in an account of research performed or in the data collection as part of the research require an accurate description of how the images were generated and produced. Apply digital processing uniformly to images, with both samples and controls. Cropping must be reported in the figure legend. For gels and blots, use of positive and negative controls is highly recommended. Avoid high contrast settings to avoid overexposure of gels and blots. For microscopy, apply color adjustment to entire image and note in the legend. When necessary, authors should include a section on equipment and settings in supporting information to describe all image acquisition tools, techniques and settings, and software used. All final images must have resolutions of 300 dpi or higher. Authors should retain unprocessed data in the event that the Editors request them. Unprocessed data can also be part of the supporting information.

2.2.12 Table of Contents Graphic. A graphic entry for the table of contents (TOC) must be supplied as the last page of the manuscript and labeled "Table of Contents graphic." This *small* graphic should capture the reader's attention and, in conjunction with the manuscript title, should give the reader an idea of the key target compounds or series discussed in the paper. The TOC graphic will also appear in the abstract of the published PDF file.

• A chemical structure should be clearly depicted.

• The TOC graphic should be entirely original work created by one of the coauthors and should not be a duplicate of a graphic appearing elsewhere in the manuscript.

• The TOC graphic should be no wider than 21 cm and no taller than 5.5 cm.

• Code numbers should not be used in the TOC graphic.

For additional information see the *ACS Publications Guidelines for Table of Contents/Abstract Graphics*. For resolution/quality requirements see *Figures, Schemes/Structures, and Charts.*

2.2.13 Supporting Information. Authors are encouraged to make use of this resource when manuscripts contain extensive tabulations of data that are of interest only to those readers who may need more complete data.

The first page of the supporting information file should contain the title of the manuscript, the names of all authors, and a table of contents; label this page "Supporting Information". The pages must be consecutively numbered S1 (the title page), S2, etc. Figure captions, titles to tables, and other identifying captions should appear on the same page as the figures or tables. Supporting information may be single-spaced. Generally, if one has difficulty reading the

material as submitted, it is unacceptable. Refer to *The ACS Style Guide* (see 2.1 General Considerations) for more specific information.

Supporting information must be submitted at the same time as the manuscript and uploaded separately to the ACS Paragon Plus Environment. A list of acceptable file types is available on the Web. All supporting information files of the same type should be prepared as a single file (rather than submitting a series of files containing individual images or structures). For example, all supporting information available as PDF files should be contained in one PDF file. Author-created file names will be automatically replaced with standardized file names generated at the time of publication.

DO NOT UPLOAD FIGURES AND TABLES THAT ARE TO BE PUBLISHED IN THE MANUSCRIPT INTO THE SUPPORTING INFORMATION FILE.

2.2.14 Molecular Formula Strings. Authors are encouraged to submit SMILES string computer-readable identifiers of molecules discussed in the manuscript along with the associated biochemical and biological data. Submission of molecular formula strings and associated data enables enhanced quality control at review and can increase an article's discoverability and citability. Complete submission instructions are available at http://pubs.acs.org/page/jmcmar/submission/jmcmar_mfstrings.html.

2.3 Specialized Data

2.3.1 Biological Data. Quantitative biological data are required for all tested compounds. Biological test methods must be referenced or described in sufficient detail to permit the experiments to be repeated by others. Detailed descriptions of biological methods should be placed in the experimental section. Standard compounds or established drugs should be tested in the same system for comparison. Data may be presented as numerical expressions or in graphical form; biological data for extensive series of compounds should be presented in tabular form. Tables consisting primarily of negative data will not usually be accepted; however, for purposes of documentation they may be submitted as supporting information.

Active compounds obtained from combinatorial syntheses should be resynthesized and retested to verify that the biology conforms to the initial observation.

Statistical limits (statistical significance) for the biological data are usually required. If statistical limits cannot be provided, the number of determinations and some indication of the variability and reliability of the results should be given. References to statistical methods of calculation should be included. Doses and concentrations should be expressed as molar quantities (e.g., mol/kg, μmol/kg, M, mM). The routes of administration of test compounds and vehicles used should be indicated, and any salt forms used (hydrochlorides, sulfates, etc.) should be noted. The physical state of the compound dosed (crystalline, amorphous; solution, suspension) and the formulation for dosing (micronized, jet-milled, nanoparticles) should be indicated. For those compounds found to be inactive, the highest concentration (in vitro) or dose level (in vivo) tested should be indicated. See section on *Statistical Criteria* for more detailed requirements.

Cytotoxicity mean graphs from the National Cancer Institute (NCI) should appear in Supporting Information and not in the main body of the manuscript. Numerical data derived from a limited number of cell lines may be tabulated in the text of the manuscript.

2.3.2 Purity of Tested Compounds.

Methods: All scientifically established methods (e.g., HPLC, combustion analysis, absolute quantitative ^{1}H NMR (qHNMR) following the established Journal protocol or equivalent

qHNMR methods) of establishing purity are acceptable. If the target compounds are solvated, the quantity of solvent should be included in the compound formulas. No documentation is required with the exception of qHNMR (see Purity by Absolute qNMR instructions).

Purity Percentage: All tested compounds, whether synthesized or purchased, should possess a purity of at least 95%. Target compounds must have a purity of at least 95%. In exceptional cases, authors can request a waiver when compounds are less than 95% pure. For solids, the melting point or melting point range should be reported as an indicator of purity.

Statements: Include the specific analytical method used to determine purity in the general part of the experimental section together with a statement confirming ≥95% purity. If the purity of a particular compound is less than 95%, specify the percentage of purity at the end of the description of its synthesis in the experimental section. For qHNMR experiments, additional documentation is required.

Cover Letter: Specify the method employed for establishing purity and percentage of purity in the cover letter. Waivers for compounds of less than 95% purity should be requested in the cover letter.

2.3.3 Confirmation of Structure. Adequate evidence to establish structural identity must accompany all new compounds that appear in the experimental section of *Articles* and *Brief Articles*. Sufficient spectral data should be presented in the experimental section to allow for the identification of the same compound by comparison. Generally, a listing of ^{1}H or ^{13}C NMR peaks is sufficient. However, when the NMR data are used as a basis of structural identification, the peaks must be assigned. See *NMR Guidelines for ACS Journals*.

List only infrared absorptions that are diagnostic for key functional groups. If a series contains very closely related compounds, it may be appropriate merely to list the spectral data for a single representative member when they share a common major structural component that has identical or very similar spectral features. HRMS data may be supplied as an additional criterion of compound identity. For the first member of a new class of oligomers containing up to 10 residues, ^{1}H NMR (300-500 MHz) and HRMS are a requirement.

Specific optical rotations should be reported for isolated natural products, enantiopure compounds, and enantioenriched isomer mixtures when sufficient sample is available. Specific rotations based on the equation $[\alpha] = (100\alpha)/(lc)$ should be reported as unitless numbers as in the following example: $[\alpha]^{20}_{D}$ 25 (*c* 1.9, $CHCl_3$), where the concentration *c* is in g/l00 mL and the path length *l* is in decimeters. The units of the specific rotation, (deg*mL)/(g*dm), are implicit and are not included with the reported value.

2.3.4 Combinatorial Chemistry. When combinatorial chemistry has been employed to generate molecules which become prototypes for a subsequent focused SAR investigation, the lead compounds and any other compounds that are key to the analysis and interpretation of the SAR of the focused series must conform to the appropriate criteria for purity and structural identity required by this Journal. However, the combinatorial chemistry methodology, screening data, and *preliminary* SAR which led to the generation of the lead molecule(s) may be reported as supporting information without confirmation of structure or demonstration of purity. These data may be briefly summarized in the main manuscript when they clarify the SAR discussion of the focused series.

2.3.5 Computational Chemistry.

2.3.5.1 Manuscript Categories. When computational chemistry is a major component of a study, manuscripts must fall into one or more of the following categories:

(A) Practical applications of existing computational methods combined with original experimental data. Manuscripts that report prospective computational design, synthesis, and experimental evaluation of new chemical entities are highly encouraged.

Applications of existing computational methods are not considered without original experimental data that assess the computational predictions. QSAR modeling is acceptable only if a significant number of new compounds is predicted, prepared, and tested. Avoid overinterpretation of computational predictions and conclusions drawn from molecular models as if they represent experimental data.

(B) Substantially novel methods along with evidence for utility in medicinal chemistry with significant potential for advancing the field.

Clearly describe computational methods manuscripts to be accessible to a general medicinal chemistry audience and clarify the relevance of the new method to medicinal chemistry. Present sufficient information to allow the method to be reproduced and tested in other laboratories.

(C) Statistical analysis or data mining of publicly available databases or data sets that provide unexpected or provocative insights into the advancement of topical medicinal chemistry problems.

Such investigations must be based upon large data sets. Small series of compounds whose properties are reinvestigated using computational methods do not qualify for this category.

2.3.5.2 Proprietary Data. Normally, the use of proprietary data for computational modeling or analysis is not acceptable because it is inconsistent with the ACS Ethical Guidelines. All experimental data and molecular structures used to generate and/or validate computational models must be reported in the paper, reported as supporting information, or readily available without infringements or restrictions. The Editors may choose to waive the data deposition requirement for proprietary data in a rare case where studies based on very large corporate data sets provide compelling insight unobtainable otherwise.

2.3.5.3 Virtual Screening Studies. In order to validate virtual screening hits obtained from any source, provide proof of dose-response behavior, confirmation of IC_{50} or K_i values, and controls for nonspecific or artificial inhibition (i.e., proof of reversibility, detergent controls). Submit structure confirmation (^{1}H NMR and MS; see section 2.3.3) for active compounds.

For virtual screens that produce compound rankings, provide as supporting information the total number of compounds that were screened and the ranks of identified hits before application of any further manual or other subjective selection steps.

Complex virtual screening protocols are not validated per se by identifying a few active compounds. Evidence must be provided that much simpler approaches would not have yielded comparable results (e.g., 2D similarity or substructure searching). Experimental findings must be significant. For example, identifying weakly potent ATP-site directed protein kinase inhibitors through virtual screening is no longer considered a significant advance due to the availability of many known potent inhibitors acting by this mechanism.

2.3.5.4 Retrospective Use of Computational Methods. Manuscripts that contain experimental studies with a retrospective computational component will be considered only under the following conditions:

(a) Computational work must lead to a clearly stated message, either an improved understanding of the experimental work or a well-defined experimentally testable hypothesis.

(b) Clearly distinguish models and hypothetical statements from experimental observations both

in the text and in figure captions.

(c) Describe computational methods in sufficient detail for the reader to reproduce the results.

(d) Computational methods must be thoughtfully selected. Explain why the applied method is an appropriate choice and was chosen over similar existing methods. Calculation results, in particular those of automated modeling software, must be critically examined.

(e) Draw conclusions from modeling with an appropriate amount of caution in light of assumptions made and within the accuracy limitations of the applied computational methods. The overall amount of space (text and figures) devoted to retrospective computational work must be proportionate to its significance.

2.3.5.5 Predicted Compound Binding Modes. The prediction of compound binding modes by docking is a frequent computational application submitted to the Journal in combination with experimental data. Models derived by minor modifications of known X-ray structures are often reliable, whereas binding modes suggested on the basis of a protein homology model are usually speculative. To be considered for publication in the Journal, all binding mode predictions must be well founded. In the absence of supporting structural information, demonstrate that putative binding modes are consistent with structure–activity relationships for a series of analogues.

QSAR, pseudo-receptor, or machine learning models that are occasionally applied retrospectively to analyze biological activities observed in the context of experimental SAR studies are acceptable only when used in a predictive fashion or used to illustrate a point of central relevance for a manuscript.

2.3.5.6 Computational Data Analysis. The Journal encourages the submission of manuscripts presenting analyses of publicly available databases or data sets that provide unexpected or provocative insights into topical problems and advance medicinal chemistry knowledge. Investigations must be based upon large data sets rather than small series of compounds. Benchmark investigations, such as comparisons of virtual screening algorithms, are considered only if they provide particularly clear and generally relevant conclusions that set new standards in the field. General relevance must be clearly stated and put into scientific context.

2.3.6 QSAR/QSPR and Proprietary Data. The following are general requirements for manuscripts reporting work done in this area:

(1) Authors should explicitly state in the abstract, introduction, and/or results sections of the paper what is novel about the quantitative structure–activity relationships/quantitative structure–property relationships (QSAR/QSPR) study being reported. In this respect, "novel" must be presented with respect to methodology/theory and/or the findings from the system(s) studied.

(2) If a new method/theory is being reported, it should be compared and “validated” against at least one other common data set of reasonable size for which a published study exists using at least one other method/approach and preferably a method/approach that has been widely used in the field.

(3) All data and molecular structures used to carry out a QSAR/QSPR study are to be reported in the paper and/or in its supporting information or should be readily available without infringements or restrictions. The use of proprietary data is generally not acceptable.

(4) Standard QSAR/QSPR studies are considered only if the predictions are experimentally tested and if the experimental data are novel and significant. Only QSAR/QSPR analyses that provide new insights into the activity are encouraged.

Some guidelines to assist prospective Journal authors of manuscripts in the field of QSAR/QSPR that report novel methods are as follows:

(i) 3D-QSAR studies that overlap with, and enhance, structure-based design (SBD) methods are encouraged. QSAR models that lead to subsequently validated experimental findings are encouraged.

(ii) Papers reporting new QSAR/QSPR methods and approaches for facilitating a mechanistic understanding of ADMET properties, and/or for reliable ADMET screening, are welcomed.

(iii) New QSAR/ QSPR methods that interface with chem- and bio-informatics methods and/or with data-mining techniques are encouraged.

(iv) QSAR/QSPR approaches for virtual screening must demonstrate distinct advantages or advances over current virtual screening schemes. For methods falling into categories (1)-(3), the same acceptance criteria apply as for any manuscript describing new computational methods according to 2.3.5.

Specifically discouraged are (a) QSAR and QSPR modeling for data sets that have already been extensively modeled, (b) model development featuring high ratios of descriptors to data points, and (c) reports of new descriptors without clear evidence for their superiority in QSAR/QSPR modeling to existing, commonly used alternatives.

2.3.7 Statistical Criteria. Appropriate statistical assessment is equally important for experimental and computational studies in medicinal chemistry. Reported results generally require statistical validation. Statistical analyses of compound data are also frequently presented, which must adhere to acceptable statistical and scientific standards. Specifically:

(1) A clear and comprehensive description of experimental data or computed data underlying the analysis is required.

(2) Statistical methods used must be clearly identified. Non-standard statistical methods should be described in sufficient detail or precisely referenced.

(3) Underlying assumptions of statistical methods should be specified. For example, many statistical tests assume the presence of normal data distributions, which is often an approximation in practice.

(4) Depending on the type of experiments reported, either confidence limits must be provided or a statistical significance analysis performed. For example, assay curves must contain errors bars derived from multiple measurements.

(5) For regression curves, their uncertainty must be assessed by plotting the original data along the curve or by establishing experimental or calculation confidence limits.

(6) If average values are reported from computational analysis, their variance must be documented. This can be accomplished by providing the number of times calculations have been repeated, mean values, and standard deviations (or standard errors). Alternatively, median values and percentile ranges can be provided. Data might also be summarized in scatter plots or box plots.

(7) Reporting averages of data assigned to pre-defined value ranges and ‘averages of average values’ must be avoided.

2.3.8 Software. Software used as a part of computer-aided drug design (e.g., molecular modeling or QSAR) should be readily available from reliable sources, and the authors should specify where the software can be obtained. When conformational calculations are included in such

papers, the parameters employed for the relevant potential functions should be given. All details needed to reproduce the numbers in the manuscript should be indicated in the paper or as supporting information. This includes coordinates of hypothetical computer-generated receptor models. Authors should refer to *J. Med. Chem.* **1988**, *31*, 2230–2234 for publication guidelines.

2.3.9 Structural Data. For papers describing structures of biological macromolecules, the atomic coordinates and the related experimental data (structure factor amplitudes/intensities and/or NMR restraints) must be deposited at a member site of the Worldwide Protein Data Bank (http://www.wwpdb.org): RCSB PDB (http://www.pdb.org), Protein Databank in Europe (PDBe) (http://www.ebi.ac.uk/pdbe/docs/References.html), PDBj (http://www.pdbj.org), or BMRB (http://www.bmrb.wisc.edu). The PDB ID must appear before the references (see section 2.2.7). Authors must agree to release the atomic coordinates and experimental data when the associated article is published. Questions related to deposits should be sent to info@wwpdb.org. Papers that utilize coordinates of molecules already in the database should specify the PDB ID as a reference.

For X-ray diffraction of structures of small molecules with anisotropically refined atoms, a figure displaying the thermal ellipsoids should ordinarily be presented; a spherical-atom representation may be substituted if necessary for clarity. If a spherical atom view is chosen for the manuscript, a thermal ellipsoid figure should be included in the supporting information. In cases where intermolecular interactions are relevant to the discussion, a view of the unit cell may be included. Articles should list for each structure the formula, formula weight, crystal system, space group, unit cell parameters, temperature of data collection, and values of *Z*, *R*, and GOF in the experimental section. Tables of atom coordinates and thermal parameters will not be printed. CIF files must be deposited with Cambridge Crystallographic Data Centre (CCDC).

2.3.10 Compound Characterization Checklist. When manuscripts report the synthesis of compounds, submission of a completed Compound Characterization Checklist (CCC) is recommended *but not required*. The CCC form (accessed via http://pubs.acs.org/page/jmcmar/submission/authors.html) can be completed on-screen and saved for uploading with the submission of the manuscript (Supporting Information for Review Only). The CCC will be provided to reviewers to help them assess the overall thoroughness of the characterization of synthesized compounds.

3 Submitting the Manuscript

3.1 Paragon Plus Web Site

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3.2 Cover Letter

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3.3 Conflict of Interest Disclosure

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4. Standard Abbreviations and Acronyms

α	observed optical rotation in degrees
[α]	specific rotation [expressed without units; the units, (deg·mL)/(g·dm), are understood]
δ	chemical shift in parts per million downfield from tetramethylsilane
μ	micro
Å	angstrom(s)
°C	degrees Celsius
2-D	two-dimensional (also 2D)
3-D	three-dimensional (also 3D)
5HT	5-hydroxytryptamine (serotonin)
9-BBN	9-borabicyclo[3.3.1]nonyl
9-BBN–H	9-borabicyclo[3.3.1]nonane
Aβ	amyloid β-protein
aa	amino acid
AA	arachidonic acid
Ac	acetyl
Acac	acetylacetonate
AcCh; ACh	acetylcholine
AcChE; AChE	acetylcholine esterase
ACE	angiotensin-converting enzyme
ACP	acyl carrier protein
ACTH	adrenocorticotropic hormone
AD	Alzheimer's disease
ADH	antidiuretic hormone
ADME	absorption, distribution, metabolism and excretion
ADMET	absorption, distribution, metabolism, excretion, and toxicity
ADP	adenosine 5'-diphosphate
ADR	adverse drug reaction
AE	adverse event
AIBN	2,2'-azobisisobutyronitrile
AIDS	acquired immune deficiency syndrome
ALK	anaplastic lymphoma kinase
ALS	amyotrophic lateral sclerosis
AM1	Austin model 1
AMI	acute myocardial infarction
AML	acute myelogenous leukemia
AMP	adenosine 5'-monophosphate; adenosine 5'-phosphate
AMPA	2-amino-3-(3-hydroxy-5-methyl-4-isoxazolyl)propionic acid
Anal.	combustion elemental analysis
anhyd; anh	anhydrous
ANP	atrial natriuretic peptide
antilog	antilogarithm
AO	atomic orbital
API	active pharmaceutical ingredient
ApoB	Apolipoprotein B
ApoE	Apolipoprotein E
APP	amyloid-β precursor protein
aq	aqueous
Ar	aryl
ARB	angiotensin receptor blocker
ARDS	adult respiratory distress syndrome
atm	atmosphere(s)
ASO	antisense oligonucleotide
ATP	adenosine 5'-triphosphate
ATPase	adenosine triphosphatase
AUC	area under the curve

b.i.d.	twice a day
B3LYP	3-parameter hybrid Becke exchange/ Lee–Yang–Parr correlation functional
BACE	beta-site amyloid precursor protein cleaving enzyme
BACE-1	beta-secretase
BBB	blood-brain barrier
BChE; BuChE	butyrylcholinesterase
Bcl-xL	B-cell lymphoma-extra large
BMI	body mass index
Bn	benzyl
BOC, boc	*tert*-butoxycarbonyl
bp	boiling point; base pair
BPH	Benign Prostatic Hypertrophy
BRCA1	breast cancer gene 1
BSA	bovine serum albumin
Bu, *n*-Bu	normal (primary) butyl
BUN	blood urea nitrogen
Bz	benzoyl (not benzyl)
ca.	circa, about [used before an approximate date or figure (ca. 1960)]
CADD	computer-assisted drug design
calcd	calculated
cAMP	3',5'-cyclic adenosine monophosphate
CAN	ceric ammonium nitrate
CASPT2	complete active space with second-order perturbation theory
CASSCF	complete active space self-consistent field
cat	catalytic
CB	cannabinoid
CBC	complete blood count
CBZ, Cbz	benzyloxycarbonyl (preferred over the abbreviation Z)
CC	coupled cluster
CCK	cholecystokinin
CD	circular dichroism
CDC	center for disease control
CDER	Center for Drug Evaluation and Research, FDA
CDK	cyclin-dependent kinase
cDNA	complementary deoxyribonucleic acid
CETP	cholesteryl ester transfer protein
cGLP	current good laboratory practices
cGMP	current good manufacturing practice; 3,5'-cyclic guanosine monophosphate
CGRP	calcitonin gene-related peptide
CHF	congestive heart failure
CHK1	checkpoint kinase 1
CHK2	checkpoint kinase 2
CHMP	Committee for Medicinal Products for Human Use
Ci	curie
CI	chemical ionization; configuration interaction
CIDNP	chemically induced dynamic nuclear polarization
CIF	crystallographic information file
CKD	chronic kidney disease
cLopP	calculated logP
cm	centimeter(s)
cm^{-1}	wavenumber(s)
CML	chronic myelogenous leukemia
CMV	cytomegalovirus
CNS	central nervous system
CoA	coenzyme A
cod	1,5-cyclooctadiene
CoMFA	comparative molecular field analysis
compd	compound
CoMSIA	computational molecular similarity index analysis
concd	concentrated
conc; concn	concentration
COPD	chronic obstructive pulmonary disease
CoQ	coenzyme Q10
COSY	correlation spectroscopy
COX	cyclooxygenase
Cp	cyclopentadienyl
CRH	corticotrophin-releasing hormone
CRP	C-reactive protein
CSF	cerebrospinal fluid
CV	cyclic voltammetry
Cy	cyclohexyl
CYP	cytochrome P
d	day(s); doublet (spectral); deci
d	density
DA	dopamine
DABCO	1,4-diazabicyclo[2.2.2]octane
DART	developmental and reproductive toxicology
DAT	dopamine transporter
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
DBP	diastolic blood pressure
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	*N*,*N'*-dicyclohexylcarbodiimide
DCE	1,2-dichloroethane
DCM	dichloromethane
DDI	drug-drug interaction
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DDT	1,1,1-trichloro-2,2-bis(p-chlorophenyl)ethane
de	diastereomeric excess
DEAD	diethyl azodicarboxylate
dec	decomposition
DEPT	distortionless enhancement by polarization transfer

DFT	density functional theory
DIBALH	diisobutylaluminum hydride
DIO	diet induced obesity
DLT	dose limiting toxicity
DMA	dimethylacetamide
DMAP	4-(*N*,*N*-dimethylamino)pyridine
DMDO	dimethyldioxirane
DME	1,2-dimethoxyethane
DMF	dimethylformamide
DMPK	drug metabolism and pharmacokinetics
DMPU	1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone
DMSO	dimethyl sulfoxide
DMT	4,4'-dimethoxytrityl (4,4'-dimethoxyltriphenylmethyl)
DNA	deoxyribonucleic acid
Dopa	3-(3,4-dihydroxyphenyl)alanine (also DOPA)
DTT	dithiothreitol
e.g.	for example (exempli gratia)
E1	unimolecular elimination
E2	bimolecular elimination
EC_{50}	half maximal effective concentration
ECG	electrocardiogram
ED_{50}	dose effective in 50% of test subjects
EDTA	ethylenediaminetetraacetic acid
ee	enantiomeric excess
EEG	electroencephalogram
EGF	epidermal growth factor
EGFR	epidermal growth factor receptor
EI	electron impact
EKG	electrocardiogram
ELISA	enzyme-linked immunosorbent assay
EPR	electron paramagnetic resonance
eq	equation
equiv	equivalent
er	enantiomer ratio
ERK	extracellular regulated kinase
ESI	electrospray ionization
ESR	electron spin resonance
Et	ethyl
et al.	and others
etc.	and so forth
F%	% oral bioavailability
FAAH	fatty acid amide hydrolase
FAB	fast atom bombardment
FAD	flavin adenine dinuleotide
FaSSIF	fasted state simulated intestinal fluid
FBDD	fragment-based drug discovery
FD	field desorption
FDA	Food and Drug Administration
FeSSIF	fed state simulated intestinal fluid
FGF	fibroblast growth factor
FID	flame ionization detector; free induction decay
Fmoc	9-fluorenylmethoxycarbonyl
FRET	Förster resonance energy transfer
FSH	follicle-stimulating hormone
FT	Fourier transform
g	gram(s); prefix to NMR abbreviation denoting gradient-selected (e.g. gCOSY, gHMQC)
GABA	γ-aminobutyric acid
GC	gas chromatography
GDP	guanosine 5'-diphosphate
GERD	gastroesophogeal reflux disease
GFP	green fluorescent protein
GFR	glomerular filtration rate
GI	gastrointestinal
GLP-1	glucagon like peptide-1
GlyR	glycine receptor
GMP	guanosine 5'-monophosphate; guanosine 5'-phosphate
GnRH	gonadotropin-releasing hormone
GPCR	G-protein coupled receptor
GFR	growth factor receptor
GST	glutathione S-transferase
GTP	guanosine 5'-triphosphate
h	hour(s); human
HBA	hydrogen bond acceptors
HBD	hydrogen bond donors
HBV	hepatitis B virus
HCS	high-content screening
HCV	hepatitis C virus
HDAC	histone deacetylase
hERG	human Ether-a-go-go-Related Gene
HDL-C	high-density lipoprotein cholesterol
HEK	human embryonic kidney
HF	Hartree–Fock
HGH	human growth hormone
HIV	human immunodeficiency virus
HMBC	heteronuclear multiple bond correlation
HMPA	hexamethylphosphoric triamide (hexamethylphosphoramide)
HMQC	heteronuclear multiple quantum correlation
HOMO	highest occupied molecular orbital
HPLC	high-performance liquid chromatography; high-pressure liquid chromatography
HPV	human papilloma virus
HR	heart rate
HRMS	high-resolution mass spectrometry
HRT	hormone replacement therapy
HSA	human serum albumin
HSP	heat shock protein
HSQC	heteronuclear single quantum correlation

HSV	herpes simplex virus
HTS	high throughput screening
Hz	hertz
i-NOS	inducible nitric oxide synthase
i-Pr	isopropyl
IC_{50}	half-maximum inhibitory concentration
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
ICR	ion cyclotron resonance
icv	intracerebroventricular (dosing)
Ig	immunoglobulin
iGluR	ionotropic glutamate receptor
IHC	immunohistochemistry
IM	intramuscularly
INDO	intermediate neglect of differential overlap
ip	intraperitoneally
IP	ionization potential
IR	infrared
it	intrathecal
iv	intravenous
IVUS	intravascular ultrasound
J	coupling constant (in NMR spectrometry)
K	kelvin(s) (absolute temperature)
k	kilo
K_i	inhibition constant
Km	Michaelis constant
L	liter(s)
LAH	lithium aluminum hydride
LBD	ligand binding domain
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LCAO	linear combination of atomic orbitals
LD_{50}	dose that is lethal in 50% of test subjects
LDA	lithium diisopropylamide; local density approximation
LDL-C	low-density lipoprotein cholesterol
LE	ligand efficiency
LFER	linear free energy relationship
LFT	liver function test
LH	luteinizing hormone
LHMDS	lithium hexamethyldisilazane; lithium bis(trimethylsilyl)amide
LHRH	luteinizing hormone releasing hormone
lit.	literature value (abbreviation used with period)
LogP	logarithm of partition coefficient
LPS	lipopolysaccharide
LTMP	lithium 2,2,6,6-tetramethylpiperidide
LTP	long-term potentiation
LUMO	lowest unoccupied molecular orbital
M	molar (moles per liter); mega
m	multiplet (spectral); meter(s); milli; isotopic mass; magnetic quantum number (ESR and NMR spectroscopy); meta; molal (mol kg-1)
m-CPBA	*meta*-chloroperoxybenzoic acid
m/z	mass-to-charge ratio (not *m/e*)
M^+	parent molecular ion
mAcChR	muscarinic ACh receptor
MALDI	matrix-assisted laser desorption ionization
MAP	mean arterial pressure
MAPK	mitogen-activated protein kinase
max	maximum
MCD	magnetic circular dichroism
MCR	multicomponent reaction
MCSCF	multi-configuration self-consistent field
MD	molecular dynamics
MDR	multidrug resistance
Me	methyl
MED	medium effective dose/minimum efficacious dose
MEM	(2-methoxyethoxy)methyl
Mes	2,4,6-trimethylphenyl (mesityl) [not methylsulfonyl (mesyl)]
mGluR	metabotropic glutamate receptor
MHC	major histocompatibility complex
MHz	megahertz
MIC	minimal inhibitory concentration
min	minute(s); minimum
mL	milliliter
mM	millimolar (millimoles per liter)
MMP	matrix metalloproteinase
MO	molecular orbital
MOA	mechanism of action
mol	mole(s); molecular (as in mol wt)
MOM	methoxymethyl
mp	melting point
MP	Møller–Plesset perturbation theory
MRCI	multi-reference configuration interaction
MRSA	methicillin-resistant Staphylococcus aureus
MRI	magnetic resonance imaging
mRNA	messenger RNA
mRNA	messenger ribonucleic acid
MRSA	methicillin-resistant Staphylococcus aureus
MS	mass spectrometry
Ms	methylsulfonyl (mesyl)

MTBE	methyl *tert*-butyl ether
MTD	maximum tolerated dose
MW, mol wt	molecular weight
nAcChR	nicotinic ACh receptor
NAD^+	nicotinamide adenine dinucleotide
NADH	reduced nicotinamide adenine dinucleotide
NADP	nicotinamide adenine dinucleotide phosphate
NADPH	reduced nicotinamide adenine dinucleotide phosphate
NAM	negative allosteric modulator
NBO	natural bond orbital
NBS	*N*-bromosuccinimide
NCE	new chemical entity
NCI	National Cancer Institute
NCS	*N*-chlorosuccinimide
NDA	new drug application
NE	norepinephrine
NF-kB	nuclear factor k B
NICS	nucleus-independent chemical shift
NIH	National Institutes of Health
nm	nanometer(s)
NMDA	*N*-methyl-D-aspartic acid
NME	new molecular entity
NMO	*N*-methylmorpholine-*N*-oxide
NMP	*N*-methylpyrrolidone
NMR	nuclear magnetic resonance
NNRTI	non-nucleoside reverse transcriptase inhibitor
NO	nitric oxide
NOAEL	no adverse effect level
NOE	nuclear Overhauser effect
NOEL	no-effect level
NOESY	nuclear Overhauser effect spectroscopy
NOS	nitric oxide synthase
NPY	neuropeptide Y
NRT	natural resonance theory
NRTI	nucleoside reverse transcriptase inhibitor
NSAID	non-steroidal anti-inflammatory drug
NSCLC	non-small cell lung cancer
Nu	nucleophile
o	ortho
obsd	observed
OCT	organic cation transporter
OD	optical density
ORD	optical rotary dispersion
p	para
PAF	platelet activating factor
PAGE	polyacrylamide gel electrophoresis
PAM	positive allosteric modulator
PAMPA	parallel artificial membrane permeability assay
PAS	peripheral anionic site
PBO	placebo
PBS	phosphate buffered saline
PCA	principle component analysis
PCC	pyridinium chlorochromate
PCR	polymerase chain reaction
PD	pharmacodynamics; Parkinson's disease
PDB	Protein Data Bank
PDC	pyridinium dichromate
PDE	phosphodiesterase
PEG	polyethylene glycol
PES	photoelectron spectroscopy
PET	positron emission tomography
P-gp	P-glycoprotein
Ph	phenyl
PI3K	phosphoinositide 3-kinase
PIPES	1,4-piperazinediethanesulfonic acid; piperazine-N,N'-bis(2-ethanesulfonic acid)
PK	pharmacokinetics
PKA	protein kinase A
PKB	protein kinase B
PKC	protein kinase C
PLS	partial least squares
pm	picometer(s)
PM3	parametric method 3
PMB	*p*-methoxybenzyl
PNS	peripheral nervous system
po	oral administration
PPA	poly(phosphoric acid)
PPAR	peroxisome proliferator-activated receptor
PPB	plasma protein binding
ppm	part(s) per million
PPTS	pyridinium *para*-toluenesulfonate
Pr	propyl
PRH	prolactin releasing hormone
PSA	polar surface area
psi	pounds per square inch
PT	perturbation theory; prothrombin time
PTT	partial thromboplastin time
PTC	phase-transfer catalysis
PTH	parathyroid hormone
PXR	pregnane X receptor
py	pyridine
q	quartet (spectral)
q.d.	once daily ("quaque die")
q.i.d.	four times a day (dosing) ("quater in die")
QSAR	quantitative structure–activity relationship
QSPR	quantitative structure-property relationship

QW	once a week (dosing)
RAS	renin-angiotensin system
RBC	red blood cell
RCM	ring-closure metathesis
redox	reduction–oxidation
R_f	retention factor (in chromatography)
RHF	restricted Hartree–Fock
RIA	radioimmunoassay
rmsd	root mean square deviation
RNA	ribonucleic acid
RO5	rule of five (Lipinski)
ROESY	rotating frame Overhauser effect spectroscopy
ROMP	ring-opening metathesis polymerization
ROS	reactive oxygen species
rpm	revolutions per minute
rRNA	ribosomal ribonucleic acid
rt	room temperature
s	singlet (spectral); second(s)
s-Bu	*sec*-butyl
SAHA	suberoylanilide hydroxamic acid
SAR	structure–activity relationship
SARM	selective androgen receptor modulator
SBDD	structure-based drug discovery
SBP	systolic blood pressure
sc	subcutaneous
SCF	self-consistent field
SDS	sodium dodecyl sulfate
SEM	scanning electron microscopy
SERM	selective estrogen-receptor modulator
SERT	serotonin transporter
SET	single electron transfer
SFC	supercritical fluid chromatography
SIRT1	silent mating type information regulation 2 homolog 1
S_N'	nucleophilic substitution with allylic rearrangement
S_N1	unimolecular nucleophilic substitution
S_N2	bimolecular nucleophilic substitution
SNP	single nucleotide polymorphism
SOMO	single-occupied molecular orbital
SPECT	single-photon emission computed tomography
PR	surface plasmon resonance; stroboscopic pulse radiolysis
SSRI	selective serotonin reuptake inhibitor
T	absolute temperature in units of kelvins (K)
t	time; temperature in units of degrees Celsius (°C)
t	triplet (spectral)
t-Bu	*tert*-butyl
$t_{1/2}$	half-time
t.i.d.	three times daily ("ter in die")
T2DM	type 2 diabetes mellitus
TAE	tris-acetate-EDTA
TB	tuberculosis
TBAB	tetrabutylammonium bromide
TBAC	tetrabutylammonium chloride
TBAF	tetrabutylammonium fluoride
TBHP	*tert*-butyl hydroperoxide
TBS	*tert*-butyldimethylsilyl
TCA	trichloroacetic acid
TCA	tricyclic antidepressant
TCNE	tetracyanoethylene
TDDFT	time-dependent density functional theory
TEAB	tetraethylammonium bromide
temp	temperature
Tf	trifluoromethanesulfonyl (triflyl)
TFA	trifluoroacetic acid
TFAA	trifluoroacetic anhydride
THF	tetrahydrofuran
THP	tetrahydropyran-2-yl
TIPS	triisopropylsilyl
TK	toxicokinetics
TLC	thin-layer chromatography
TLR	toll-like receptor
TMAI	tetramethylammonium iodide
TMEDA	*N*,*N*,*N*′,*N*′-tetramethyl-1,2-ethylenediamine
TMS	trimethylsilyl; tetramethylsilane
TNF	tumor necrosis factor
TNF-alpha	tumor necrosis factor-alpha
TOF	time of flight
TON	turn over number (in catalysis)
^tR	retention time (in chromatography)
Tr	triphenylmethyl (trityl)
Tris	tris(hydroxymethyl)aminomethane
tRNA	transfer ribonucleic acid
Ts	para-toluenesulfonyl (tosyl)
TS	transition state
TSH	thyroid stimulating hormone
TT	thrombin time
UDP	uridine 5'-diphosphate
UHF	unrestricted Hartree–Fock
UHPLC	ultra-high pressure liquid chromatography
UV	ultraviolet
v.i.	see below (vide infra)
v.s.	see above (vide supra)
v/v	volume per unit volume (volume-to-volume ratio)
VCD	vibrational circular dichroism

VEGFR	vascular endothelial growth factor receptor	WT	wild type
		wt	weight
vis	visible		
viz.	namely	XAFS	X-ray absorption fine structure spectroscopy
VLDL	very low density lipoprotein		
vol	volume		
VRE	vancomycin resistant enterococci	ZINDO	Zerner parameterization of intermediate neglect of differential overlap
WBA	whole body autoradiography		
w/w	weight per unit weight (weight-to-weight ratio)		

STANDARD AMINO ACID ABBREVIATIONS:

•The three-letter code or name may be used in the text.

•With a single amino acid, use the three-letter code (e.g., Met246).

•If more than one amino acid is specified, as in mutants or substitutions, use one-letter code (S238H).

•When two or more amino acids are used in a string, use either the three-letter code or single letter (e.g., His-Ile-Thr-Ser or HITS).

•For use of D amino acids, use the 3 letter abbreviation only (e.g., DAla)

alanine	Ala	A	leucine	Leu	L
arginine	Arg	R	lysine	Lys	K
asparagine	Asn	N	methionine	Met	M
aspartic acid	Asp	D	phenylalanine	Phe	F
cysteine	Cys	C	proline	Pro	P
glutamic acid	Glu	E	serine	Ser	S
glutamine	Gln	Q	threonine	Thr	T
glycine	Gly	G	tryptophan	Trp	W
histidine	His	H	tyrosine	Tyr	Y
isoleucine	Ile	I	valine	Val	V

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