

Chemical Guidelines

These guidelines have been developed to provide assistance to authors, with the goal of ensuring that compounds reported in the Journal, including both compounds that were previously known and compounds new to science, have been rigorously and unequivocally identified. The editors recognize that in some circumstances, because of the small amounts of material available from natural sources, it will not be possible to provide all the information suggested in the guidelines below. It is also impossible for the editors to anticipate all possible scenarios, given the variety of different types of structures, and the relative ease or difficulty of unambiguous identification of different types of compounds. In such cases, the editors will use their best judgment in determining whether:

1. authors are justified in claiming full identification of a compound,
2. the identification should be reported as tentative only, or
3. there is insufficient evidence to support the identification of a compound at all. In such cases, the editor may request that a compound be designated as an unknown.

The editors stress that these guidelines are not intended as barriers to publication. Rather, the intent is to help authors determine the information that is required to identify compounds properly, and to the extent possible, to prevent publication of information or structures that are incorrect. Publication of incorrect information is detrimental to the reputations of both the authors and the Journal. If authors are in doubt with regard to the data required to claim identification of new compounds, please contact the editors for guidance.

The editors also encourage authors to submit reasonable tentative identifications (clearly designated as such) for compounds for which they have partial but not necessarily conclusive identification information. As an example, such compounds might include analogs or homologs of a compound that is completely identified in a manuscript, where the spectral, chromatographic, or other data strongly suggest structural similarities. In short, the editors encourage the careful and responsible publication of results in a way that maximizes new information available to the research community while minimizing errors.

Please note the following:

1. It *will not be acceptable under any circumstances* to claim conclusive identification of a compound based only on a "match" with a computerized mass spectral data base spectrum. Any such claims will be rejected by the editors.
2. Normally, it will not be acceptable to claim *conclusive* identification of a compound when it is possible or even likely that the compound could be, for example, a different isomer or even a different compound than claimed. As an example, it may be difficult or impossible to claim conclusive identification of a monounsaturated alkenyl acetate by close matches of mass spectra and retention times alone because of uncertainty about the position and stereochemistry of the double bond. In cases such as this, wherever possible, the retention index and mass spectral data should be supported by, for example, microscale derivatizations that unambiguously demonstrate the double-bond position and geometry. This is used as an example: Different types of compounds will require different methods and pieces of information for proper identification.

I. Identification of Compounds

A. Conclusive Identification of Compounds New to Science

For the types of data listed below, authors are asked to use their *best judgment* as to the information required to identify a compound unequivocally. This will vary with the types and complexity of the molecules involved. Authors should use as many of the methods listed below (and additional methods as appropriate) as are required to completely and unequivocally identify a compound.

In cases where authors have data that strongly suggest, but do not conclusively prove, a particular structure, they are requested to list identifications as tentative. As mentioned above, a match with a database mass spectrum, *in the absence of other supporting data*, will not be sufficient to claim even a tentative identification.

Acceptable Methods

1. Mass spectral data or other confirmation of molecular weight/molecular formula. Determination of the molecular weight by chemical ionization mass spectrometry (CI-MS) or exact mass determination is encouraged. Elemental composition by combustion or elemental analysis is an acceptable alternative.
2. NMR data:
 - (a) Basic proton spectral data, fully analyzed.
 - (b) Basic carbon spectral data.
 - (c) Other NMR data required to prove unequivocally the structure (e.g., results of NOE, COSY, HMBC, HSQC, other NMR experiments).
3. Matches with a standard synthesized to prove the structure.

4. Optical rotation for chiral compounds is desirable but not mandatory. Chromatographic analysis on a chiral stationary phase, or other more reliable and accurate methods of demonstrating enantiomeric purity, are preferred.
5. Optional: other supporting information such as results of microchemical tests, UV and IR data, chromatographic characteristics/retention indices, boiling or melting points, etc.
6. If applicable, unequivocal X-ray crystal structure data would be an asset.

For Very Small Amounts

1. Mass spectral data.
2. Results of microchemical tests to confirm the presence and positions of functional groups, or other methods that can provide structural information on very small quantities, are recommended.
3. Confirmation of structure with a standard synthesized to prove the structure, including exact matches of chromatographic and mass spectral data, taken under equivalent concentration and other operating conditions.
4. Any other information that helps to prove the structure unequivocally.

B. Previously Known Compounds for Which Data are Available in the Literature

It is not necessary to provide full and detailed structural information on compounds that are well known in the literature. Nevertheless, authors are strongly encouraged to confirm identification with an authentic standard whenever possible to minimize the possibility of errors.

In general terms, authors are requested to provide as many of the following types of information as necessary to support the identification of known compounds:

1. One or more literature references in which the compound has been properly identified from a particular source.
2. Matching mass spectrum with a known standard.
3. Matching chromatographic properties with a known standard. Corroborating analyses by using two or more chromatography columns with different stationary phases.
4. If necessary, matching NMR or other spectral data with a known standard.
5. Any other data required to prove the structure unequivocally. For example, microchemical tests to prove the presence or positions of functional groups, retention index matches, IR or UV spectral matches, etc.
6. If a compound is chiral, determination of its absolute configuration by comparison with known standards by using enantioselective gas chromatography. Chromatographic methods that provide unequivocal information on both absolute configuration and enantiomeric composition are preferred over measurements of optical rotation and comparison with rotations of known standards or literature values, which are affected by impurities, traces of solvent, etc.

II. Synthetic Routes and Synthesized Compounds

A. Synthesis of Compounds New to Science

1. Sufficient information should be provided to enable complete replication of the work by someone with a reasonable knowledge of synthetic chemistry.
2. Any novel or special sets of conditions, *particularly with regard to safety*, should be described in detail.
3. Sufficient spectral data, particularly NMR and MS data, should be provided for purified key intermediates that, in combination with the synthetic route and reagents used, will allow unequivocal identification of those intermediates.
4. For intermediates that were previously known, and which were made according to previously published syntheses, the conditions used should be summarized briefly, with a reference to the previous synthesis. Full spectral data for such intermediates are not required so long as the spectral data matched those previously reported; authors should provide an explicit statement to that effect, along with the relevant citation(s). Any changes of conditions from the published route should be described.
5. For intermediates that were not previously known, and for the final product, full details of the reaction conditions should be provided. In cases of common and well-known reactions (e.g., acetylation, tosylation, LiAlH₄ reduction), abbreviated descriptions of conditions are sufficient (reagents, temperature, solvent, time, other relevant conditions).
6. For intermediates that were not previously known, and for the final product, sufficient spectral data should be provided to prove the structures unequivocally. This typically should include proton and carbon NMR data, mass spectral data, and optical rotation data if applicable. Other requisite data might include IR and UV, ORD, etc. For chiral compounds, determinations of enantiomeric excess are recommended. However, if the enantiomeric excess has been determined for an intermediate that is then carried through several subsequent steps, in which there is no chance of epimerization of the chiral center(s), it is not necessary to determine the enantiomeric excess for each intermediate.
7. It is not necessary to provide full spectral data on intermediates that were carried through a series of *straightforward* steps without isolation and purification. However, it is expected that authors will provide corroborative spectral data on, at a minimum, every third or fourth intermediate.
8. Yields, chemical purities, and isomeric purities should be provided for all steps in which compounds are isolated and purified, and particularly for the final product.

B. Synthesis of Previously Known Compounds

a. *By a Previously Published Route*

1. Authors need only provide a reference, a statement that the compound was made as previously described, and sufficient spectral data to prove that they do indeed have the correct compound. Alternatively, an explicit statement that the spectral and physical properties of their product matched literature values, with the citation(s) given, will be sufficient.
2. Any deviations from the published route should be described.
3. Yield, chemical purity, and isomeric purity (including enantiomeric excess if applicable) should be provided for the final product.

b. *By a New Route*

1. Requirements are the same as for synthesis of previously unknown compounds, see above.