

Annotation validation guide

A. INTRODUCTION

The goal of this tool is the fine-tuning and validation of the annotations produced by the chemical literature annotation tool.

Validate the **Reactants** in the description

10.1021/ja00133a032-4

conversion of **1a** back to **2a** was monitored by ¹H NMR by observing the decay of the signal at 6.3.62 or the increase of the signal at 6.9.57 for the cyclobutenyl hydrogen of **2a**, with approximate rate constants of 7 x s-l at 22 °C for both processes. The decrease in UV absorption due to **1a** or the increase of the absorption due to **2a** gave good first-order kinetics, with the same rate constant for either process (Table 2). Photolysis of diphenylcyclobutenedione (**2b**) in pentane at -195 °C gave a change in the UV spectrum with a decrease in the A₂₆₀ of **2b** at 260 and 320 nm and formation of **bisketene 1b** with strong absorption at low wavelength and a shoulder at 220 nm, which re-formed **2b** with good first-order kinetics (Table 2). The UV spectrum of diphenylacetylene was also observed. At 33.5 °C the rate of ring closure of the 2,3-diphenyl **bisketene 1b** exceeded that of the monophenyl analogue **1a** by factors of 216 (isooctane) and 186 (CDC13). The greater reactivity of **1b** is consistent with the lower stabilizing influence of phenyl as a ketene substituent relative to hydrogen, as shown by the calculated (HF/6-31G**/HF/6-31G*) $\Delta H^\ddagger = -2.6$ kcal/mol for the isodesmic reaction of eq 2.6h $\text{PhCH-C=O} + \text{CH}_2 = \text{CH}_2$.

Undo Reset

Reactants
Products
Yield
Reaction type
Workup reagents
Catalyst / Reagents
Solvent
Temperature
Time

Paper DOI: <https://pubs.acs.org/doi/10.1021/ja00133a032>

Copy

Warning: Chemical entity names may be either (i) incorrectly spelled and / or (ii) split into several parts. In case (i) annotate regardless. In case (ii) make sure to annotate the entity as a single span.

Reactants

2a

☐ There is no Reactants

Products

1a

☐ There is no Products

Yield

☒ There is no Yield

Reaction type

☒ There is no Reaction type

Workup reagents

☒ There is no Workup reagents

Catalyst / Reagents

☒ There is no Catalyst / Reagents

Solvent

☒ There is no Solvent

Temperature

☒ There is no Temperature

Time

☒ There is no Time

Validate annotation

Validate annotation and add another reaction

☐ There is no reaction ☐ Paragraph discarded due to:

B. VALIDATION PROCESS

1. The text paragraph to be validated will be shown in the text window on the left side of the screen.
 - The paragraph shown may include from none to multiple chemical reactions.
 - The validation tool will automatically go through each and every reaction annotated in the paragraph, one at a time.
 - The annotated entities are automatically highlighted in order to facilitate the validation.

Validate the **Products** in the description

(14) For the reaction of N,-acylated indoles with dimethyldioxirane , see : (a) Zhang,X. ; Foote , C. S. J. Am. Chem. SOC. 1993 , 115 , 8867. (b) Adam , W. ; Ahrweiler , M. ; Peters , K. ; **Schmiedeskamp** , B. J. Org. Chem. 1994 , 59 , 2733 and references therein. (15) Diketopiperazine 12 can be prepared directly , albeit only in 35 % yield , by heating tryptophan methyl ester (9) at 140 'C for 3 h , thus saving four steps in the synthetic sequence described above. (16) There are relatively few direct methods for the preparation of 2,3-disubstituted indoles. For some current methods , see : (a) Saulnier , M. G. ; Gribble , G. W. J. Org. Chem. 1982 , 47 , 2810. (b) Fukuyama , T. F. ; Chen , X. ; Peng , G. J. Am. Chem. SOC. 1994 , 126 , 3127 and references therein .

FOR EACH PARAGRAPH REPEAT SETPS 2 – 6 BELOW:

2. If a change is required, select (highlight in green) in the window on the right the entity class to be modified.

Reactants
Products
Yield
Reaction type
Workup reagents
Catalyst / Reagents
Solvent
Temperature
Time

3. Proceed as per one of the following three options depending on the required type of modification:
 1. If there should be no annotation at all, reset it by clicking the reset button and check the “There is no XXX” box next to the entity class:

 Reset

☒ There is no Catalyst

- If the entity class contains no annotation but one or more entities should be included, add them by selecting the relevant word(s) or span(s) in the paragraph.

Validate the **Products** in the description

(14) For the reaction of N,-acylated indoles with dimethyldioxirane , see : (a) Zhang,X. ; Foote , C. S. J. Am. Chem. SOC. 1993 , 115 , 8867. (b) Adam , W. ; Ahrweiler , M. ; Peters , K. ; Schmiedeskamp , B. J. Org. Chem. 1994 , 59 , 2733 and references therein. (15) **Diketopiperazine 12 can** be prepared directly , albeit only in 35 % yield , by heating tryptophan methyl ester (9) at 140 °C for 3 h , thus saving four steps in the synthetic sequence described above. (16) There are relatively few direct methods for the preparation of 2,3-disubstituted indoles. For some current methods , see : (a) Saulnier , M. G. ; Gribble , G. W. J. Org. Chem. 1982 , 47 , 2810. (b) Fukuyama , T. F. ; Chen , X. ; Peng , G. J. Am. Chem. SOC. 1994 , 126 , 3127 and references therein .

Undo

Reset

Reactants
Products
Yield
Reaction
Catalyst
Solvent
Temperature
Time

Reactants

tryptophan methyl ester (9)

☐ There is no Reactants

Products

Diketopiperazine 12 can

☐ There is no Products

- If the entity class contains an incorrect annotation that should be substituted, reset the field and annotate the entity class as described above.
- In case that, after the review, no entity should be annotated, the **‘There is no reaction’** box must be checked in order to proceed to the next annotation.

Validate annotation

☒ There is no reaction

- In case that the paragraph should be discarded, the **‘Paragraph discarded due to’** box must be checked and a reason chosen from the dropdown list in order to proceed to the next annotation.

Validate annotation and add another reaction

☒ Paragraph discarded due to:

- Once the current reaction has been validated, and no additional reactions must be added, click on **‘Validate annotation’** in order to review the next annotation.

Validate annotation

- In case additional reactions must be added, click on **‘Validate annotation and add another reaction’**

Validate annotation and add another reaction

D. CORRECTIONS

The 'Undo' and 'Reset' buttons allow to make corrections during the validation process:

- Undo: Undoes the last action
- Reset: Clears the active entity field



E. GENERAL ANNOTATION RULES

This section describes the general annotation rules for the different types of entities.

Legend:

- 'Annotate'
- '~~Do not annotate~~'

1. General

- In case a paragraph is describing more than one reaction:
 - Discard multi-step reactions.
 - If a paragraph describes multiple reactions, label them as separate reactions (e.g. 4a and 4b were reacted to form 5a and 5b, it should be two reactions: 4a → 5a and 4b → 5b). If it describes a reaction with multiple products, it should be annotated as a single reaction.
 - Annotate all entities explicitly linked to the reaction being annotated
 - Annotate as well those entities implicitly linked to the reaction being annotated, which are mentioned in other reactions within the paragraph.

Example:

"On the basis of conventional Knoevenagel reactions, we initially investigated reaction conditions using benzaldehyde (1a) and dimethyl malonate (2a) as a model substrate (Table 1). When a reaction was performed with 10 mol % of InBr₃ in toluene at 60 °C for 8 h, only 3% of Knoevenagel product 3aa was detected (entry 1) [Reaction 1]. Thus, to promote the initial abstraction of the activated proton, the addition of 1 equiv of several bases to the reaction mixture was examined. Consequently, when the primary amine 2-aminoethanol was added, the yield was remarkably increased to 61% (entry 2) [Reaction 2]."

Annotate [Reaction 2] as follows:

- **Reactants:** benzaldehyde, (1a), dimethyl malonate, (2a) [Reaction 1]

- **Products:** Knoevenagel, 3aa [Reaction 1]
 - **Yield:** 61% [Reaction 2]
 - **Reaction:** Knoevenagel [Reaction 1]
 - **Catalyst:** InBr₃ [Reaction 1], primary amine 2-aminoethanol [Reaction 2]
 - **Solvent:** toluene [Reaction 1]
 - **Temperature:** 60 [Reaction 1]
 - **Time:** 8h [Reaction 1]
- For reversible reactions, annotate as two reaction if the reverse reaction is explicitly described (e.g. different conditions are used to reverse the reaction)
 - Do not annotate expected results but actual results. Example:
 - 'Since CuCl(PPh₃) is a widely studied and common copper salt, the active catalytic species was expected to be ~~CuCN-(PPh₃)~~ in our optimized reaction condition'
 - Annotate not only the reactions obtained in the actual experiments but also past reactions described. Example:
 - 'Both the Ullmann and Buchwald-Hartwig aminations are well-known copper-catalyzed crosscoupling reactions between an aryl halide and an amine'

2. Conditions

- Do annotate compound expressions when they form a single word. Examples:
 - 'Copper-catalyzed crosscoupling reactions'
 - 'Phosphine-catalyzed [3 + 2] annulation'
- Do not annotate references to reaction conditions. Examples:
 - '~~condition A~~ shows the highest reactivity'
- Do annotate generic reaction conditions. Example:
 - 'Elevated temperature'
- Do annotate physical units. Example:
 - '32 C', '32 °C', '25 F'
 - '25 min', '8 h', '10 hours'

3. Chemical entities (reactants, products, catalysts, reagentes, and solvents)

- ALL ENTITIES
 - Annotate both the entity and its corresponding reference when they are shown together. Example:

- 'We started our investigation by examining the Bu₃P catalyzed reaction of 2-hydroxyisoindoline-1,3-dione (1a) and ethyl propiolate (2a)'
 - Annotate references (to Schemes, Tables, Figures, etc.) to entities. Example:
 - 'The reaction of 1a with 2a in the presence of Bu₃P in DMF...'
 - Annotate all references to an entity when shown together. Example:
 - pivalonitrile (2,2,-dimethylpropanenitrile, bp 105 °C)
 - Only label the chemicals, without additional details about concentration, state, etc. E.g. "1% aqueous FeCl₃", only label "FeCl₃"
 - If the text mentions a range of chemicals, only annotate those explicit text (e.g. 4g – 4i were used to form 5a – 5c: only annotate two reactions 4g->5a and 4i->5c). If the range is not separable, e.g., 4a-c or 4a-4c (without space around the "-"), discard the reaction
 - Default to reactant if unsure between reactant and catalyst/reagent. Default to catalyst/reagent if unsure between catalyst/reagent and solvent
- PRODUCTS AND REACTANTS
 - Do not annotate references to entity types but to specific entities. Examples:
 - 'the initial ~~hexameric PPh₃-bounded copper-cyanide~~ species'
 - 'the expected ~~alcohols~~'
 - 'the corresponding ~~alkene 3aa~~'
 - 'however, only ~~colorless-crystals~~ were obtained'
 - Do not annotate generic references to entities. Examples:
 - '~~the-product~~', '~~final-product~~', '~~the-reactant~~'
 - '~~the-corresponding-product~~'
 - '~~same-starting-materials~~'
 - Do not annotate entity classes but only specific entities. Examples:
 - 'While the ~~C-2-arylated-product~~ (4aa) was the major product'
 - '~~Benzoxazoles bearing substituents with diverse electronic properties such as methyl-(1b-1d), phenyl-(1e), and chloro-(1f) groups~~'
 - 'effectively promotes the Knoevenagel condensation of ~~aromatic-/aliphatic-/heteroaromatic-aldehydes~~ with a ~~variety-of-activated-methylene-compounds~~'
- REAGENTS, CATALYSTS AND SOLVENTS
 - Annotate even if the text only describes the type of chemical (e.g. "Pd catalyst": annotate "Pd"; "in-situ generated catalyst": annotate "in-situ generated").

4. Yields

- Annotate generic yield expressions. Examples:
 - 'similar yield', 'lower yield', 'higher yield', 'diminished yield', 'improved reaction yield'
- Annotate all yield measures in case more than one is provided. Examples:
 - 'Higher yield (62%)'
- Alternative expressions of yield: **TBD – Chemistry**
 - **'increased catalytic efficiency'**
 - **'improved reactivity'**
 - **'perfect selectivity'**
 - **'significant effect'**
 - **'highest conversion'**
 - **'no reactivity'**
 - **'no further reaction observed'**

5. Reaction type

- Annotate if the description is a verb (e.g. A is oxidized to B: annotate "oxidized" as the reaction type).