“For Its Size, the Most Complex Natural Product Known.” Who Deserves Credit for Determining the Structure of Strychnine?

Jeffrey I. Seeman* and Mark C. House

Scientists expect to receive appropriate credit for their achievements. Credit for the determination of the structure of strychnine, the most complex natural product for its size, has been given to both Sir Robert Robinson and R. B. Woodward for their independent discoveries in the late 1940s. In this paper, the following question is explored: Who should be given credit for a discovery of a scientific phenomenon: the individual who first published the correct solution but subsequently published another (wrong) explanation and later reverted to the correct structure or several analogues (Robinson)? Or the individual who was second to publish the correct solution (along with additional supporting data) and did not reverse him/herself (Woodward)? A survey of chemists, mathematicians, life scientists, and social scientists at Ph.D.-granting universities in the U.S. was conducted in which credit allocation and “being first but later recanting versus being second and steadfast” were probed. In addition, ombudspersons, members of institutional review boards, and individuals who have conducted research in the responsible conduct of research were surveyed. The survey revealed a predominant amount of variability among the survey’s respondents, and it supports the conclusion that there is great diversity in scientists’ behavioral judgments and decisions, even when dealing with such seemingly simple yet important credit issues.

1. PREFACE

Strychnine! The fearsome poisonous properties of this notorious substance... Over a period of 40 years, one of the great classics of structural organic chemistry was constructed. In that effort, described in more than two hundred and fifty separate communications, Robert Robinson played a brilliant and commanding role, and the extensive beautiful experimental contributions of Hermann Leuchs were of definitive importance. In 1947, the task was finished,[Woodward’s reference 4 was cited here] and strychnine stood revealed as 1... It was now possible to contemplate the synthesis of the substance of which it has been said: “For its molecular size it is the most complex substance known.”

—Woodward, R. B. et al. The Total Synthesis of Strychnine. 
Tetrahedron 1963, 19, 247–288.
rather inclusive; it contained eight citations to Robert Robinson’s research publications on the structure of strychnine plus Robinson’s 1947 Nobel Prize lecture, three citations to Vladimir Prelog’s publications, and the last two to Woodward’s publications on this topic.

Woodward et al. reported the total synthesis of strychnine in 1954,1−3 further confirming its structure. It would be nearly 40 years before the next total synthesis of strychnine was recorded.4,5 Since this four decade hiatus, many total syntheses of strychnine have been reported.6 Thus, the structure of strychnine is secure beyond any doubt. But what remains unsettled is, who should get the credit for determining the structure of strychnine, Robinson or Woodward?

2. INTRODUCTION

Natural product chemistry is based entirely on structure determination. Not much makes sense without a knowledge of structure. And the stories that we chemists tell ourselves and others are clouded in chemical mystery and flights of fantasy—until the structures of our compounds have been rigorously determined. It is not too hard to imagine how confused and foggy chemists were in the 19th century before modern structure theory was discovered. Many chemists experience that shadowy feeling when we study compounds whose structures are as yet undetermined. Thus, structure determination is the seminal accomplishment in chemical research with a history that goes back to the first days of the discipline.

In keeping with the extraordinary structure of strychnine, there is an equally extraordinary story dealing with its structure determination. As would be expected, in the absence of UV, NMR, mass spectrometry, IR, and X-ray analyses, the determination of strychnine’s structure took many decades. And when the structure was finally determined in 1946−19477−9 using the classical method of structure determination,10,11 with the entire natural products community paying careful attention, there was nonetheless ambiguity as to who deserved credit for one of the most compelling chemistry achievements of the first half of the 20th century. This ambiguity was caused by Robinson’s inconsistencies in his structure assignments for strychnine. After he published the correct structure in 1946,7 Robinson changed his mind twice in 1947.12,13 And then Woodward stepped in. Prelog, on the other hand, made a singular contribution,14−17 and then seemingly disappeared from this story.

The stories that we chemists tell ourselves and others are clouded in chemical mystery and flights of fantasy—until the structures of our compounds have been rigorously determined.

Within the scientific community, credit is one of most powerful motivators.18−23 There are at least two motifs of credit for scientific achievement. The obvious form is that of authorship and acknowledgment in scientific publications, patents, books, and lectures. This mode is not without its controversies and ambiguities, notwithstanding the numerous codes of publication conduct that are currently available. There are many shades of gray, and principal investigators and their collaborators do not always agree on the criteria and their application. The most obvious is the order of authors in a paper. The second credit motif is the opinion of the relevant community regarding an achievement. This latter form of credit is rather amorphous and integrates over the wide diversity of community members and their knowledge, their biases, and their experiences. In this paper, we focus on both forms of credit and how they influence and inform each other.

Our initial understanding of the chemistry community’s allocation of credit for this achievement comes directly from what has been reported in the literature: some cite Robinson as the sole discoverer;24−26 others cite Woodward;27,28 and yet others cite both29,30 or are ambivalent.31−33 While the patent laws in various countries have their own idiosyncratic rules regarding inventorship, often with policies that have changed over time, there are no such standards for discoverers of scientific phenomena. In contrast, various professional societies have codes dealing with authorship criteria for scientific publications.34,35

Intentional misrepresentations in the assignment of authorship, inventorship, or discovery are a form of misconduct of science, as these are falsifications of the literature. We have some guidance from the Office of Science Technology Policy in the Executive Office of the President of the United States, which adopted a Federal Policy on Research Misconduct in 2000.36 One of this Policy’s criteria for research misconduct is that the questionable action must represent a “significant departure from accepted practices...[but] not honest error or differences of opinion.”36 Knowledge of the accepted “tribution of credit” practices within a relevant community should be helpful and enlightening for unique discovery events in the practice of science. And there ought to be many such events, given that multiple simultaneous independent discoveries are likely to be the norm, not the exception, in science.20,37−41 This guidance suggests the need to interrogate the relevant scientific community regarding any specific case under examination in which there is ambiguity, at best, and conflict, at worst.

Our primary goal is to understand better the adjudication of credit for chemical achievements.

Our primary goal is to understand better the adjudication of credit for chemical achievements within the chemistry community, in particular, and within the academy, in general. Our strategy was to perform a survey of academics (chemists, biologists, and mathematicians) in Ph.D.-granting institutions in the United States regarding this specific issue of scientific discovery, the structure of strychnine. Ph.D.-granting institutions were used because the topic is about receiving and judging the appropriateness of credit for major scientific discoveries, which is the domain of research scientists. These researchers typically are found at institutions that grant research-based advanced degrees. Respondents also included individuals in those same schools who are or were members of their Institutional Review Boards (IRBs) or members of their departments of research integrity or individuals who had conducted research in responsible conduct of research (RCR). A related analysis dealing with “Whom Should We Credit for the Discovery of Isotopes?” was recently published by Eaton.42

The first step of this research was to develop a survey tool, then distribute, collect, and analyze the survey results.
The survey was constructed to examine a very specific theme, namely:

Who deserves credit for a scientific discovery (or an explanation for a natural phenomenon), the first person who made the discovery (or explanation) but who subsequently abandons that discovery (or explanation) in favor of an alternative, or another individual who, after the above abandonment, proposed the same discovery (or explanation) and never recanted this proposal?

The second step of this research was to determine if academics’ research disciplines are related to the ways judgments are made about credit. The third step was to assess whether individuals who have professional experience in RCR activities at their universities have judgements that differ from those of their academic colleagues. An editorial by one of the authors of this paper (JIS) was recently published.43

3. BACKGROUND: THE REAL-LIFE CASE

This case derives directly from real-life events of an important discovery in natural products chemistry, namely, the determination of the structure of strychnine (Figure 1). For the purposes of this paper, descriptions of this real-life event will be presented before the related survey questions and results.
By 1947, when the structure of strychnine was established, more than 270 publications had appeared in the chemical literature on the topic. The leader in this effort, certainly in terms of the number of publications (47) and cumulative scientific advances, was Sir Robert Robinson. Robinson began this research with his graduate school professor William Henry Perkin, Jr. at the University of Manchester in 1910. Between then and 1947, Robinson published 47 papers on and proposed many structures for strychnine (Figure 1), including the correct structure in 1946.7,44

Even the nonchemist can appreciate from a graphical perspective the range of structures Robinson proposed for the structure of strychnine (Figure 1). A full discussion of the sequence of numerous structural proposals by Robinson recently was published.44 A recent book39 and earlier papers on the search for the structure of strychnine are also available.45,46 Even in the 21st century, research continues on various structural and historical details of strychnine’s structure.47−50

By the late 1940s, there was tremendous competition to solve this long-lasting, major problem in natural products chemistry. Besides Robinson, the competition included one Nobel laureate (Heinrich Wieland51 with his then graduate student Rolf Huisgen45,52−54) and two future Nobel Prize laureates (Prelog14 and Woodward8,9,55).

We now provide the most critical chronologically relevant issues regarding the final steps of the strychnine structure story. In the January 14, 1946, issue of Experientia, Robinson proposed the correct structure of strychnine.7 However, Robinson was committed to the quite reasonable idea that the structures of natural products are related to their biosynthetic pathways (as was Woodward,35 though wrongly56). In the February 22, 1947, issue of Nature, Robinson discarded his previous and correct assignment as suggested 2 (Figure 2).12 Robinson’s structure revision was based on the idea that there ought to be a biosynthetic relationship between the biosynthesis of the cinchona alkaloids, e.g., cinchonine, which is a natural product desmethoxy analogue of quinine, and strychnine. Robinson provided the graphic in Figure 2 to illustrate his biosynthetic thinking.

Robinson then changed his ideas again.13 In the July 5, 1947, issue of Nature, Robinson wrote,

The discovery of unexpected and somewhat remarkable molecular rearrangements [that is, new experimental results just obtained] disposes of this natural explanation. It does not disprove the quinuclidine formula [2] recently proposed,12 but it removes the necessity for its postulation and, in these circumstances, we revert, as the best hypothesis to guide future work, to an earlier suggestion [1].7,58

The relation of this structure to that of cinchonine has already been indicated.59 Several slight modifications of this expression are feasible, and these have special advantages and disadvantages which must be discussed at a later date, especially since it is probable that crucial experimental tests can be devised.13

It is critical to note that Robinson’s reversion to the correct structure 1 was not definitive. To emphasize this point, we repeat Robinson’s words,

Several slight modifications of this expression are feasible, and these have special advantages and disadvantages which must be discussed at a later date, especially since it is probable that crucial experimental tests can be devised.13

In the September 1, 1947, issue of the Journal of the American Chemical Society (JACS), submitted on July 28, 1947, Woodward assigned the correct structure to strychnine, giving credit to Robinson as follows:

Taken with the recent observations of Robinson...the new evidence completes the inferential proof for a particular expression for strychnine...The way is now open to build up an unequivocal degradative proof of structure for strychnine.8

Woodward6 also cited Robinson’s paper13 in the July 5, 1947, issue of Nature.

On January 28, 1948, Woodward submitted a nine-page full paper that was published in JACS in June 1948.9 The last sentence of that paper is a finality,

We conclude that the structure [1] for strychnine is established.9

We rush to point out: neither Robinson nor Woodward discussed the finer details of the stereochemistry of strychnine nor its absolute configuration in their 1940s papers.

There are more details to this story, including a single in-person meeting between Woodward and Robinson in 1947 and several letters exchanged between them in this time period.60 At that meeting, actually a dinner hosted by Robinson, Woodward shared his (correct) structure of strychnine. According to Derek Barton, the competitive Robinson

looked at it for a while and cried in great excitement, “That’s rubbish, absolutely rubbish!” So ever after, Woodward called it the rubbish formula.60

But the essence of matter before us now is, Who should receive credit for determining the correct structure of strychnine? Clearly, this was an important chemical conundrum in the first half of the 20th century and is a classic in the history of chemistry. Should the credit go to the person who first proposed the correct structure, even if that person later retracted his suggestion in favor of another structure? Or should the credit go to the person who unambiguously and

Figure 2. An excerpt from Robinson’s 1947 paper proposing 2 (the top structure) for the structure of strychnine (1).13 At a lecture at Columbia University in early 1947, Woodward was asked what he thought of Robinson’s proposal of 2. According to Jerome Berson who was present at the event,7 Woodward’s response was, "I regret to say that this must be a figment of his imagination."66
steadfastly proposed one structure, the correct structure, even though he was second to propose the structure!

Apparently, Robinson intended for his structural suggestions to be just that—suggestions, rather than firm, definitive assignments.

As illustrated in Figure 1, Robinson employed a substantial degree of spontaneity and hypothesis-proposing in his publication strategy. Apparently, Robinson intended for his structural suggestions to be just that—suggestions, rather than firm, definitive assignments. And apparently, the natural products community of that era operated in that manner as there was no onslaught of criticism against Robinson’s continuous series of structure revisions.

We can even go one step further in this analysis: Robinson began his career as a chemistry undergraduate in 1909, not many years after the first steps in understanding of structure and chemical bonds had been achieved. In the early decades of the 20th century, guesses were much more tolerated in the chemical literature than they were by the 1950s; certainly, such speculations are not tolerated in today’s literature. Today, bold conjectures are the norm only in settings much more informal than in chemistry journals, such as in lectures at research group meetings and perhaps at departmental lectures or professional society meetings, especially meetings like the Gordon Research Conferences and the Bürgenstock Conferences.

With this background, we now move to examine the views of today’s scientific community in Ph.D.-granting institutions in the U.S. regarding the allocation of credit for important discoveries when ambiguous or even self-contradictory behaviors occurred.

4. MATERIALS AND METHODS. THE SURVEY

The survey was performed following the policies of and after receiving approval from the Institutional Review Boards (IRBs) of the University of Richmond and of Santa Fe College. The survey respondents were all faculty members in Ph.D.-granting institutions in the United States. Only Ph.D.-granting institutions were included in the survey because we were interested in examining the opinions of academics who had been and likely were researchers. The survey was programmed on the Qualtrics.com site and administered online. The data were recorded in a simple tab delimited file that was downloaded periodically. In accord with the IRB guidelines of the University of Richmond and Santa Fe College and our representation to the respondents and those two IRBs, all identifying information was deleted from the data set.

The survey consisted of 27 questions (referred to herein as Q1, Q2, etc.). The survey was conducted by email to 2400 faculty or emeritus faculty members of chemistry, biology, and mathematics departments as well as individuals associated with either the IRBs or research integrity departments of Ph.D.-granting degrees institutions in the United States. Ombuds-persons, also referred to herein as “ombuds,” were also included in the survey. Two hundred and eighty-seven complete responses were obtained (a 16% response rate, taking into consideration undeliverable emails), after cleaning the data for short survey times and incomplete survey responses. A 16% response rate raises the issue of nonresponse bias, an important concern that was evaluated and discounted, as discussed previously. Analyzes were performed using Statistical Package for the Social Sciences (SPSS). Where possible, a Pearson’s Chi Square test of Independence was used to determine the relationship between variables. There are several instances where individual cell counts were below the recommended level for this test. In its stead, the Fisher’s exact test was used to calculate the likelihood of the independence of the variables.

The question regarding the independence of groups is met with the design of the survey. If a participant indicated that they were a chemist, they were not asked if they were from another discipline as well. The within-group independence for who received credit is also addressed with the survey language because participants could only select one answer when asked who should receive credit.

In this research, the term validity is used to ask whether we have accurately represented the thoughts of academic research chemists. Bias can tilt the results of an experiment away from the actual population values in a variety of ways. If only men were surveyed or if surveys were only returned by people with lots of time on their hands or by people who really like doing surveys, then the results may not represent the population.

Well-researched survey practices were used to reduce bias as much as possible. Notices and reminders were sent to prompt reluctant respondents. The sample was drawn from publicly available data with no regard for gender, race, or other variable, and the data were tested for demographic differences. None were found. Data were not collected on whether someone likes surveys or had availability in their schedules. This does not rule out biases, but there do not seem to be any obvious issues.

5. RESULTS

The accumulated survey responses are shown in Table 1. The question used in the survey was exactly as follows.

Professor A published the correct structure for a natural product.

Six months later, Professor A characterized his correct structure as “inadequate” and “questionable” and stated “feasible alternatives of a more complicated character have been devised.” He then published an alternative (and wrong) structure which he characterized as “the best working hypothesis at present available.”

Shortly thereafter, Professor A changed his mind again, writing “we revert, as the best hypothesis to guide future work, to an earlier [and correct] structure... Several slight modifications of this structure are feasible, and these have special advantages and disadvantages, which must be discussed at a later date, especially since it is probable that crucial experimental tests can be devised.”

Two months later, Professor B published the correct structure. Professor B was unambiguous in his conclusion, saying “The new evidence completes the inferential proof for what is the correct structure. Following Professor B’s suggestion, the relevant scientific community, including Professor A, considered the structure determination solved.

Who should be recognized as the discoverer of the correct structure?
Table 1. Survey Responses to the Question “Who Should Be Recognized As the Discoverer of the Correct Structure?”

| Question | All Respondents | Prof. A | Prof. B | Both |
|----------|-----------------|---------|---------|------|
| How are chemists different from nonchemists? | 253 | 27.9 | 13.6 | 58.5 |
| Chemists | 85 | 14.1 | 21.2 | 64.7 |
| All nonchemists | 168 | 33.9 | 10.1 | 56.0 |
| How are chemists different from specific disciplines? | 253 | 27.9 | 13.6 | 58.5 |
| Life sciences | 81 | 32.1 | 11.1 | 56.8 |
| Mathematics | 46 | 34.8 | 8.7 | 56.5 |
| Medicine and health | 16 | 16.7 | 0 | 83.3 |
| Social sciences including law | 19 | 36.8 | 10.5 | 52.6 |
| Humanities | 3 | 66.7 | 0 | 33.3 |

If chemists are removed from the data set, do other professional experiences create a difference in who gets credit?

| Professional Experience | All Respondents | Prof. A | Prof. B | Both |
|-------------------------|-----------------|---------|---------|------|
| IRB membership (nonchemists) | 32 | 43.8 | 9.4 | 46.9 |
| Conducted RCR research (nonchemists) | 17 | 35.3 | 5.9 | 58.8 |
| Taught classes in RCR (nonchemists) | 38 | 44.7 | 10.5 | 44.7 |

“See text for more details.”

6. BEING FIRST OR BEING STEADFAST: WHO DESERVES THE CREDIT?

The respondents were presented a case that is as close as possible (while still being comprehensible to the respondents) to the actual events of the strychnine structure record, as described in the above sections. Differences in who was given credit for the discovery were tested using either a Pearson’s chi square test for independence or Fisher’s exact test, depending on whether the cell counts were sufficient for the chi square test. Table 1 provides the question as presented to the respondents and lists the results of the survey and the statistical analyses of the data.

The major conclusions from the survey are as follows.

- Within each discipline and for all the disciplines combined, there was no consensus as to who should receive the credit for determining the structure of the natural product, Professor A, or Professor B, or both.
- The majority (58.5%) of all respondents felt that Professor A and Professor B should jointly receive the credit.
- Among those who chose either Professor A or Professor B, chemists were significantly more likely to choose Professor B, and nonchemists were much more likely to choose Professor A (Person’s chi square value = 13.845; p value = 0.000985). One might conclude that many chemists have higher standards in credit allocation, feeling that once an individual changes their mind, that fact counters the earlier proposal, and that only the fixed, definitive exposition counts.
- There is also a significant difference between chemists and life scientists (Pearson’s chi square value = 8.86; p-value = 0.011863); and chemists and mathematicians (Fisher’s exact test, p-value = 0.012813). The reason for the difference is not obvious but may be connected to publishing traditions within those disciplines.
- Individuals who are or were ombuds or members of IRBs and/or had conducted research in the field of responsible conduct of research (RCR) mostly favored giving credit to both, but among those who chose only one, they very highly favored Professor A. In this regard, ombuds and IRB members differed from chemists.
- A reader of an advanced draft of this paper asked, “Could the ‘both’ answer actually be an insightful synthesis by the community of the difficulty of giving credit? Or it could be that ‘both’ is the sum of (a) a true belief that getting to a structure is complicated, with several competitors contributing, and (b) just being conflicted on how to give an answer, they chose the least decisive.” This is an interesting possibility. The survey data were insufficient for us to make a distinction between those two possibilities and a third possibility, that Robinson and Woodward do jointly deserve the credit for their own individual contributions. Unfortunately, individual interviews would be required to determine the reasoning underlying the respondents’ choices.
- There was not a single instance in which >70% of the respondents (when n > 6 respondents) shared the same opinion. Also of note: A portion of the chemists seems to be more negative in assigning credit to an individual who displayed ambiguity and more willing to credit a person who was second but definitive. This distinction may be influenced by the fact that the situation dealt with chemistry, and the chemists are more familiar with the peculiarities within their own discipline.
- The data revealed few demographic differences. No demographic variables were significantly related to the relevant questions in this paper.

7. STUDY LIMITATIONS

A 16% response rate raises the issue of response bias, a concern that is reasonable and must be acknowledged. This study may include a bias toward respondents who are willing and able to complete the survey in a timely manner. However, we cannot imagine how being a willing participant in a survey might bias responses dealing with credit allocation. We note that the most recent (2021) large-scale survey in responsible conduct of research by Gopalakrishna et al.64 received immediate media attention.65 These researchers sent out 63,778 email solicitations and 6,813 completed surveys (10.7%) were received. We cite this response rate of 10.7%, not because our higher response rate implies that we have addressed the response bias but rather to give an indication as to the response rates obtained for other RCR surveys. Our results are in the same range.

Within each discipline and for all the disciplines combined, there was no consensus as to who should receive the credit for determining the structure of the natural product, Professor A, or Professor B, or both.

Another limitation in our research is that the survey was limited to academics in Ph.D.-granting institutions in the United States. We randomly chose the various institutions from which email addresses were then obtained for all members of the chosen departments. Thus, the survey addresses reflected whatever racial and cultural distributions were present within those departments and the individual propensities to complete
the surveys. One question asked the location of the respondents’ birth by continent. No statistically significant relationship was found between credit assignment questions and this demographic-based question. Very little research has been published on cross-cultural differences in the attribution of authorship. Ren et al. found that cultural collectivism is related to the willingness to give unmerited authorship; however, this effect was mediated when participants worked in an institution that was situated in a culture that leaned toward individualism—like the universities in the U.S. Fetters and Elwyn reported, in a study of a limited sample, that the number of authors in Japanese medical journals in the 1990s was significantly greater than in non-Japanese medical journals. The authors attributed that observation to “the Japanese penchant for “groupism” and limited individual funding.” Since our survey was only sent to participants in U.S. universities in which individualism is pronounced, we do not believe that culture was a primary factor in these results, especially in the decision by some respondents to prefer crediting both scientists. However, we believe that cultural factors in credit attributions, in particular, and in RCR issues, in general, is an area ripe for additional research.

8. CONCLUSIONS

The following conclusions stem from this research:

There is great diversity among the respondents regarding their judgments about credit issues. The diversity of the survey responses has significant implications regarding range in personal viewpoints on social, professional, and ethical situations. Perhaps this suggests a need for clearer guidance and the development of experiential precedents, just as in the law. Leiv K. Sydnes, former president of IUPAC, has suggested that IUPAC take a lead in hosting conferences and continuing its traditional role in scrutinizing statements and definitions to develop clear terminology that enables fruitful discussions.

The survey revealed a tendency for chemists to have somewhat different judgments from those of individuals in the other disciplines. There appears to be an experiential bias involved; i.e., for an issue involving chemistry, chemists are better to understand and weigh specific disciplinary nuances in their decision-making processes. This reasonable conclusion likely spreads to other discipline-specific issues that occur.

For the situation in which the initial discoverer of the correct explanation for a phenomenon changes his/her mind and proposes another explanation, the majority of respondents judged that that individual should share the credit for the discovery with another individual who subsequently proposes and maintains the correct explanation. Making the extrapolation from Professor A and Professor B of our survey to real life, the majority of the chemist respondents—indeed, the majority of the respondents—felt that Robinson and Woodward should share the credit for the structure determination of strychnine.

A reader of an advanced draft of this paper commented, “There are many places in the world around us when the wrong people get credit in the mind of the public.” Our response to that valid observation is that very thorough, impartial historical analyses are likely necessary to uncover the information necessary to make such judgments, especially given the norm of multiple simultaneous discoveries. For example, a 2007 historical analysis by Seeman contradicted Gilbert Stork’s 2001 claim that the Woodward—Doering total synthesis of quinine was a “myth”. That historical analysis prompted Williams and Smith to conduct an experimental study that further confirmed the viability of Woodward and Doering’s reliance on Rabe and Kindler’s 1918 partial synthesis of quinine from quinotoxine. Beyond historical studies, it is interesting to note that the performing arts have witnessed a number of creative works that address credit determination (e.g., the play Oxygen by noted chemists Carl Djerassi and Roald Hoffmann and the books Cantor’s Dilemma and How I Beat Coca-Cola and Other Tales of One-Upmanship by Djerassi) and other ethical and RCR issues (e.g., the play Copenhagen by Michael Frayn).

Surveys continue to be an excellent source of insight and information about a topic that is often judged by the RCR criterion “accepted practices of the relevant community.”

9. CODA

A reviewer wrote,

“This is a difficult question and several answers emerged that provided insight into how different communities assign credit... I understand that the authors do not want to appear biased, but it would be good to have some statements about what their thoughts are on who deserves credit or whether the “both” option is indeed the correct one.

JIS’s Response. Today, I am a chemist-historian. I come from a background of more than 30 years as a natural products chemist with a bent toward mechanism and theory. I am not surprised by this reviewer’s request. When I have presented this or related RCR issues in my lectures, I am often asked for my own opinion. As a historian of chemistry, I am extremely careful to avoid any biases in my research, deep thinking, and writing. But, yes, I have examined this question from my own perspective and using my own values and sensibilities. I must also say, I have no bias toward Robinson or Woodward. I enjoyed a sabbatical year in the Dyson Perrins Laboratory that was once Robinson’s; I enjoyed morning tea in the lounge underneath a huge portrait of Robinson. I am a fan of his and, of course, of Woodward (warts and all). I am also a purist. For me, Robinson’s changing his mind and proposing an incorrect structure, then reverting to the correct structure along with the caveat “Several slight modifications of this expression are feasible, and these have special advantages and disadvantages which must be discussed at a later date...” means he’s lost his place in the line. It is Woodward who is now alone in first place. As for sharing the credit, well, the ambiguity in the community is enough credit for Robinson, in my view.
MCH’s Response. My degrees are in business and anthropology, and I have many years of commercial experience focusing on the identification and measurement of consumer behavior and the translation of that data into impactful decisions. However, I am an outsider to both chemistry and history of chemistry. Most areas of academia have had some controversy involving authorship, and I have spent the past decade researching and discussing the topic in various forums. I dislike the idea of splitting the credit, although I do not have a worthwhile justification for my displeasure. Ideally, a researcher emerges from the lab with definitive results and proudly claims their reward. However, my academic research is built with considerable help from colleagues, friends, spouses, and even competitors. The question becomes, where we draw the line for receiving credit. In this instance, we have one researcher who had the idea, but did not stake his claim unambiguously, while the second researcher was able to plant the flag, so to speak. At the risk of rewarding boldness over insight, I would give my gold star to Woodward, but if asked to argue my point, I’ll retreat to the old standby of “it depends.”

■ AUTHOR INFORMATION

Corresponding Author

Jeffrey I. Seeman – Department of Chemistry, University of Richmond, Richmond, Virginia 23173, United States; orcid.org/0000-0003-0395-2536; Email: jseeman@richmond.edu

Author

Mark C. House – Business Programs, Santa Fe College, Gainesville, Florida 32606, United States

Complete contact information is available at: https://pubs.acs.org/10.1021/acssciencet.1c01348

■ ACKNOWLEDGMENTS

We especially thank and acknowledge the participants in our survey. We thank Caitlin Livesey, then an undergraduate researcher at the University of Richmond, for technical assistance in the early stages of this research and Christopher L. Stevenson for his support of this research. We thank Anthony G. M. Barrett, Kelling J. Donald, Roald Hoffmann, Klaus Roth, Dean Tantillo, several anonymous readers of an advanced version of this paper, and several reviewers for helpful suggestions and commentary. J.I.S. thanks the staff of the Boatwright Memorial Library of the University of Richmond for continuing technical information support. There were no sources of funding for this project.

■ REFERENCES

(1) Woodward, R. B.; Cava, M. P.; Ollis, W. D.; Hunger, A.; Daeniker, H. U.; Schenker, K. The Total Synthesis of Strychnine. Tetrahedron 1963, 19, 247–288.
(2) Woodward, R. B.; Cava, M. P.; Ollis, W. D.; Hunger, A.; Daeniker, H. U.; Schenker, K. The Total Synthesis of Strychnine. J. Am. Chem. Soc. 1954, 76, 4749–4751.
(3) Woodward, R. B. The Total Synthesis of Strychnine. Experientia 1955, 12 (Supplementum II), 213–238.
(4) Knight, S. D.; Overman, L. E.; Pairaudreau, G. Synthesis Applications of Cationic Aza-Cope Rearrangements. 26. Enantioselective Total Synthesis of (−)-Strychnine. J. Am. Chem. Soc. 1993, 115, 9293–9294.
(5) Knight, S. D.; Overman, L. E.; Pairaudreau, G. Asymmetric Total Syntheses of (−)- and (+)-Strychnine and the Wieland-Gumlich Aldehyde. J. Am. Chem. Soc. 1995, 117, 5776–5788.
(6) Cannon, J. S.; Overman, L. E. Is There No End to the Total Syntheses of Strychnine? Lessons Learned in Strategy and Tactics in Total Synthesis. Angew. Chem., Int. Ed. 2012, 51, 4288–4311.
(7) Robinson, R. The Constitution of Strychnine. Experientia 1946, 2, 28–29.
(8) Woodward, R. B.; Brehm, W. J.; Nelson, A. L. The Structure of Strychnine. J. Am. Chem. Soc. 1947, 69, 2250.
(9) Woodward, R. B.; Brehm, W. J. The Structure of Strychnine. Formulation of the Neo Bases. J. Am. Chem. Soc. 1948, 70, 2107–2115.
(10) Hoffmann, R. W. Classical Methods in Structure Elucidation of Natural Products; Wiley-VHCA: Zürich, Switzerland, 2018.
(11) Seeman, J. I. On the Relationship between Classical Structure Determination and Retrosynthetic Analysis/Total Synthesis. Isr. J. Chem. 2018, 58, 28–44.
(12) Robinson, R. Constitution of Strychnine and Its Relation to Cinchonine. Nature (London) 1947, 159, 263.
(13) Chakravarti, R. N.; Robinson, R. Oxidation of Neostrychnine. Nature (London) 1947, 160, 18.
(14) Prelog, V.; Szpilfogel, S. Die Konstitution Des Strychnins. Experientia 1945, 1, 197–198.
(15) Prelog, V.; Kocór, M. Strychnos-Alkaloide. (4. Mitteilung). Über Die Lage Der Oxy-Gruppe in Pseudostrychnin. Helv. Chim. Acta 1947, 30, 359–366.
(16) Prelog, V.; Szpilfogel, S.; Battagay, J. Strychnos-Alkaloide. (5. Mitteilung). Über Die Dihydro-Derivate Der Isomeren Strychninone Und Brucinolone. Helv. Chim. Acta 1947, 30, 366–374.
(17) Prelog, V. (translated by O. T. Benfley and D. Ginsburg) My 132 Semesters of Chemistry Studies. In The Series of Autobiographies Profiles, Pathways and Dreams; Seeman, J. I., Ed.; American Chemical Society: Washington, D.C., 1991.
(18) Merton, R. K. On the Shoulders of Giants. A Shandean Postscript; Harcourt Brace & World: New York, 1965.
(19) Merton, R. K. Social Theory and Social Structure; Free Press: New York, 1968.
(20) Merton, R. K. Behavior Patterns of Scientists. Am. Scholar 1969, 57 (Spring), 1–23.
(21) Merton, R. K. The Sociology of Science. Theoretical and Empirical Investigations; University of Chicago Press: Chicago and London, 1973.
(22) Merton, R. K.; Zuckerman, H. The Matthew Effect in Science; 2nd ed.; Chicago University Press: Chicago, IL, 1973.
(23) Merton, R. K. Scientists’ Competitive Behavior Is Not Peculiar To Our Competitive Age. Scientist 1994, 9 (July25), 12. 14.
(24) Zhang, H.; Boonsombat, J.; Padwa, A. Total Synthesis of (±)-Strychnine Via a [4 + 2]-CycloadDITION/Rearrangement Cascade. Org. Lett. 2007, 9, 279–282.
(25) Shibasaki, M.; Oshihama, T. Recent Studies on the Synthesis of Strychnine. In The Alkaloids: Chemistry and Biology; Elsevier: Amsterdam, The Netherlands, 2007.
(26) Curtis, R.; Leith, C.; Nall, J.; Jones, J. The Dyson Perrins Laboratory and Oxford Organic Chemistry, 1916–2004; John Jones, Balliol College, Oxford, England, 2008.
(27) Prelog, V. Discussion. In Further Perspectives in Organic Chemistry; Tod, L., Ed.; Elsevier: Amsterdam, 1978; p 83.
(28) Stork, G. Obituary: R. B. Woodward, 1917–1979. Nature 1980, 284, 383–384.
(29) Todd, A.; Cornforth, J. W. Robert Robinson. 13 September 1886–8 February 1975. Biographical Memoirs of Fellows of the Royal Society 1976, 22, 414–527.
(30) Beemelmanns, C.; Reîffig, H.-U. Strychnine as Target, Samarium Diiodide as Tool: A Personal Story. Chem. Rec. 2015, 15, 872–885.
(31) Roth, K.; Russey, W. E.(translator), 2015, Strychnine: From Isolation to Total Synthesis – Part 2, https://www.chemistryviews.org/details/ezine/7978151/Strychnine_From_Isolation_to_Total_Synthesis_Part_2.html (accessed on March 19, 2019).
(32) Roth, K. Die Tödliche Brechhuss. Strophanthin – Von Der Isolierung Zur Totsynthese. Chem. unserer Zeit 2011, 45, 202–218.
(33) Huisgen, R. The Wieland Memorial Lecture. Proc. Chem. Soc. 1958, 210–219.
(34) Ethical Guidelines to Publication of Chemical Research; American Chemical Society: Washington, DC, 2020.
(35) Anonymous, 2021, Author Responsibilities. Ethical Guidelines and Code of Conduct for Authors, https://www.rsc.org/journals-books-databases/author-and-reviewer-hub/authors-information/responsibilities/ (accessed on October 6, 2021).
(36) Office of Science and Technology Policy, Executive Office of the President, 2000, Federal Policy on Research Misconduct Preamble for Research Misconduct Policy, https://ori.hhs.gov/federal-research-misconduct-policy and https://www.govinfo.gov/content/pkg/FR-2000-12-06/pdf/FR-2000-12-06.pdf, pp 76260–76264 (accessed on May 3, 2022).
(37) Merton, R. K. Priorities in Scientific Discovery: A Chapter in the Sociology of Science. American Sociological Review 1957, 22, 635–659.
(38) Merton, R. K. Singletons and Multiples in Scientific Discovery: A Chapter in the Sociology of Science. Proc. Am. Philos. Soc. 1961, 105, 470–486.
(39) Merton, R. K. The Thomas Theorem and the Matthew Effect. Social Forces 1995, 74, 379–424.
(40) Tambolo, L.; Cevolani, G. Multiple Discoveries, Inevitability, and Scientific Realism. Studies in History and Philosophy of Science Part A 2021, 90, 30–38.
(41) Seeman, J. I. From "Multiple Simultaneous Independent Discoveries" to the Theory of "Multiple Simultaneous Independent Errors": A Conduit in Science. Found. Chem. 2018, 20, 219–249.
(42) Eaton, G. R. Whom Should We Credit for the Discovery of Isotopes? Found. Chem. 2020, 22, 87–98.
(43) Seeman, J. I. Diverse Views in the Assignment of Credit for Research Discoveries. ACS Omega 2022, 7, 1–4.
(44) Seeman, J. I.; Tantillo, D. J. From Decades to Minutes. Steps toward the Structure of Strophanthine, 1910 – 1948, and the Application of Today’s Technology. Angew. Chem. Inter. Ed. 2020, 59, 10702–10721.
(45) Huisgen, R. Die Strochynos-Alkaloiode Ein Überblick Über Ein Halbes Jahrhundert Alkaloidforschung [the Strochynose Alkaloids. A Review of One-half Century of Alkaloid Research]. Angew. Chem. 1950, 62, 527–534.
(46) Huisgen, R. Zur Arbeit: Die Strochynos-Alkaloiode [to Work: The Strochynose Alkaloids]. Angew. Chem. 1951, 63, 124.
(47) Koos, M. R. M.; Navarro-Vazquez, A.; Anklin, C.; Gil, R. R. Computer-Assisted 3d Structure Elucidation (Case-3d): The Strychnose Alkaloids]. Angew. Chem. Internat. Ed. 2020, 59, 3938–3941.
(48) Burvich, A. V.; Elyashberg, M. E. Enhancing Computer-Assisted Structure Elucidation with Dft Analysis of J-Couplings. Magn. Reson. Chem. 2020, 58, 594.
(49) Hehre, W.; Klunzinger, P.; Deppeimeier, B.; Driessen, A.; Uchida, N.; Hashimoto, M.; Fukushima, E.; Takata, Y. Efficient Protocol for Accurately Calculating 13C Chemical Shifts of Conformationally Flexible Natural Products: Scope, Assessment, and Limitations. J. Nat. Prod. 2019, 82, 2299–2306.
(50) Tamba, G.; Camilloni, C.; Vendruscolo, M. Determination of the Conformational States of Strophanthine in Solution Using Nmr Residual Dipolar Couplings in a Tensor-Free Approach. Methods 2018, 148, 4–8.
(51) Witkop, B. Remembering Heinrich Wieland (1877–1957). Portrait of an Organic Chemist and Founder of Modern Biochemistry. Med. Res. Rev. 1992, 12, 195–274.
(52) Huisgen, R. On Strochynine Alkaloid and Vomiconia; University of Munich: Munich, Germany, 1943.
(53) Huisgen, R. Die Konstitution Der Strochynosalkaloiode. Pharmaz. 1944, 11, 383–388.
(54) Huisgen, R. Über Strochynos-Alkaloiode, XXXI. Weitere Synthesen in Der Reihe Des 5,6(N)-Pyrocholinins. Liebigs Ann. Chem. 1948, 559, 174–190.
(55) Woodward, R. B. Biogenesis of Strochynos Alkaloids. Nature (London) 1948, 162, 155–156.
(56) Berson, J. A. Chemical Discovery and the Logicians’ Program; Wiley-VCH: Weinheim, Germany, 2003.
(57) Berson, J. A. Chemical Discovery and the Logicians’ Program; Wiley-VCH: Weinheim, Germany, 2003.
(58) Briggs, L. H.; Openshaw, H. T.; Robinson, R. Strochynine and Brucine. Part XII. Constitution of the Neo-Series of Bases and Their Oxidation Products. J. Chem. Soc. 1946, 903–908.
(59) Openshaw, H. T.; Robinson, R. Constitution of Strochynine and the Biogenetic Relationship of Strochynine and Quinine. Nature 1946, 157, 438.
(60) Barton, D. H. R. Ingold, Robinson, Weinstein and Woodward’s Synthesis of Quinine. J. Am. Chem. Soc. 1946, 681, 42.
(61) House, M. C.; Seeman, J. I. Credit and Authorship Practices. Educational and Environmental Influences. Account. Res. 2010, 17, 223–256.
(62) Pearson, K. On the Criterion That a Given System of Deviations from the Probable in the Case of a Correlated System of Variables Is Such That It Can Be Reasonably Supposed to Have Arisen from Random Sampling. Philos. Mag. 1900, 50 (Series 5), 157–175.
(63) Fisher, R. A. Statistical Methods for Research Workers; Oliver & Boyd: Edinburgh, 1934.
(64) Gopalakrishna, G.; Wicherts, J. M.; Vink, G.; Stoop, I.; van den Akker, O. R.; ter Riet, G.; Bouter, L. M. Prevalence of Responsible Research Practices among Academics in the Netherlands. MetarXiv Preprints 2021, DOI: 10.31222/osfo/3vm94.
(65) de Vrieze, J. Large Survey Finds Questionable Research Practices Are Common. Science 2021, 373, 265–265.
(66) Ren, X.; Su, H.; Lu, K.; Dong, X.; Ouyang, Z.; Talhelm, T. Culture and Unmerited Authorship Credit: Who Wants It and Why? Front. Psych. 2016, 7, 1–12.
(67) Fetters, M. D.; Elwyn, T. S. Authorship. Assessment of Authorship Depends on Culture. BMJ 1997, 315, 747–747, https://pubmed.ncbi.nlm.nih.gov/9314774, https://pmc/articles/PMMC2172482/.
(68) Sydnes, L. K. The Hedulick Case—a Reflection on the Current State of Affairs. Chem. Internat. 2021, 43, 42–44.
(69) Seeman, J. I. The Woodward-Doering/Rabe-Kindler Total Synthesis of Quinine. Angew. Chem. Internat. Ed. 2007, 46, 1378–1413.
(70) Stork, G. Quinine Synquany. Chem. Eng. News 2000, 78 (September 25), 8.
(71) Stork, G. Quinine Synthesis. Chem. Eng. News 2001, 79 (October 22), 8.
(72) Stork, G.; Niu, D.; Fujimoto, A.; Koft, E. R.; Balkovec, J. M.; Tata, J. R.; Dake, G. R. The First Stereoselective Total Synthesis of Quinine. J. Am. Chem. Soc. 2001, 123, 3239–3242.
(73) Woodward, R. B.; Doering, W. E. The Total Synthesis of Quinine. J. Am. Chem. Soc. 1944, 66, 849.
(74) Woodward, R. B.; Doering, W. E. The Total Synthesis of Quinine. J. Am. Chem. Soc. 1945, 67, 860–874.
(75) Smith, A. C.; Williams, R. M. "Rabe Rest in Peace": Confirmation of the Rabe-Kindler Conversion of D-Quinotoxine to Quinine. Experimental Affirmation of the Woodward-Doering Formal Total Synthesis of Quinine. Angew. Chem., Int. Ed. 2008, 47, 1736–1740.
(76) Rabe, P.; Kindler, K. Cinchona Alkaloids. XIX. Partial Synthesis of Quinine. Ber. deutsch. Chem. Ges. 1918, 51, 466–467.
(77) Djerassi, C. Cantor’s Dilemma; Doubleday: New York, NY, 1991.
(78) Djerassi, C. How I Beat Coca-Cola and Other Tales of One-Upmanship; Terrace Books (an imprint of the University of Wisconsin Press): Madison, 2013.
(79) Office of Science and Technology Policy, Executive Office of the President, 2000, Federal Policy on Research Misconduct Preamble for
Research Misconduct Policy, https://ori.hhs.gov/federal-research-misconduct-policy and https://www.govinfo.gov/content/pkg/FR-2000-12-06/pdf/FR-2000-12-06.pdf, pp 76260–76264 (accessed on May 3, 2022).

(80) Woodward, J.; Goodstein, D. Conduct, Misconduct and the Structure of Science. Am. Sci. 1996, 84, 479–490.

(81) Office of Science and Technology Policy, Executive Office of the President, 2000, Federal Policy on Research Misconduct; Preamble for Research Misconduct Policy, http://www.ostp.gov/cs/federal_policy_on_research_misconduct (accessed on 14 January 2010).

(82) Department of Health and Human Services Public Health Service Policies on Research Misconduct. 42 Cfr Parts 50 and 93, Rin 0940-Aa04, Final Rule. Federal Register 2005, 70 (94), 28370–28400.

(83) Fostering Integrity in Research; National Academies of Sciences, Engineering, and Medicine, The National Academies Press: Washington, D.C., 2017.

(84) De Winter, J.; Kosolosky, L. The Epistemic Integrity of Scientific Research. Sci. Eng. Ethics 2013, 19, 757–774.

(85) On Being a Scientist: A Guide to Responsible Conduct in Research; National Academies of Sciences, Engineering, and Medicine, The National Academies Press: Washington, D.C., 2009.

(86) On Being a Scientist. A Guide to Responsible Conduct of Research; 3rd ed.; Committee on Science, Engineering, and Public Policy, The National Academies Press: Washington, D.C., 2009.

(87) Stoneck, N. H. Introduction to the Responsible Conduct of Research; U.S. Department of Health and Human Services: Washington, D.C., 2007.