JOC The Journal of Organic Chemistry
Editorial
pubs.acs.org/joc

Beauty in Simplicity: Celebrating 50 Years of the Woodward–Hoffmann Rules

The first definition of "science" in the *Merriam-Webster Dictionary* is "knowledge about or study of the natural world based on facts learned through experiments and observation". One might find that definition to be somewhat deficient because it says nothing about theories or models, the construction, testing, and development of which many would consider to be vital components of the scientific enterprise. They certainly constitute central features of the science described in this special issue of *The Journal of Organic Chemistry*.

Science is, on this planet at least, a scheme invented by human beings and, as such, is constrained by human limitations. But those limitations are not identical for all individuals—some may have greater ability to generate and manipulate three-dimensional mental images than others; some may be better able to deal with abstract mathematical concepts than others. The differences in limitations (or, if one prefers, differences in skills) of people learning chemistry may tend to shepherd them to one or other of its subdisciplines. If one sees truth only in equations, one might be more attracted to physical chemistry, whereas organic chemistry may be more attractive if pictures provide the best understanding for you. Such a segregation of scientists according to their differing abilities can tend to reinforce disciplinary boundaries, as the cohorts within each discipline develop languages and conceptual models that are understood locally, but may not be so well understood globally. However, "...the natural world..." neither knows nor cares about our boundaries and limitations. And so it can sometimes occur that phenomena are discovered, notionally within the walls of one discipline, for which the best understanding comes from a different discipline. Events of this kind are often important in the development of science because they force its practitioners to learn concepts and languages that are new to them and thereby to begin to break down the artificial barriers between disciplines. An outstanding example of this interdisciplinary crosstalk can be found in the development of the Woodward–Hoffmann rules for classifying and understanding what some organic chemists used to call "no-mechanism" reactions, but which subsequently became known as pericylic reactions. Jeffrey Seeman describes this development beautifully in his historical perspective, found in the present special issue.

Doering and Roth said, when they coined the phrase "no mechanism" to characterize reactions such as the Diels–Alder cycloaddition and the Cope and Claisen rearrangements, that they had done so "...half in jest, half in desperation⋯".[1] In order to understand the problem that they and others studying these reactions faced, one needs to enquire what a mechanism meant in the organic chemistry of the time. Arguably, the whole concept of a mechanism in the discipline can be traced back to the work of Robert Robinson in the early 1920s, who pioneered what is now known as the curved (or, in Britain, "curly") arrow formalism for organic reactions.[2] That formalism need hardly be explained to readers of this Journal, but it will be important for the present purposes to recall that the idea is intimately linked to G. N. Lewis' earlier concept of the electron-pair covalent bond. Each of these bonds consists of a pair of electrons conceptually localized to a region of space between a pair of atoms. Robinson's arrows were a book-keeping device that tracked the Lewis electron pairs during bond-making and bond-breaking events. The Lewis model can, in turn, be related to a primitive version of valence-bond (VB) theory, and so one could reasonably argue that what Robinson and Lewis had done between them was to turn the equations of VB theory into pictures that organic chemists could understand and use productively. Of special note is the fact that application of the curved-arrow prescription, when combined with ideas about electronegativity and bond strength, can lead to the identification of plausible intermediates in multistep reactions. In the first half of the 20th century it is probably fair to say that writing a mechanism for an organic reaction meant using curved arrows to show how intermediates might plausibly be formed from the reactants and how they might then go on to give the observed products. The problem presented by the "no-mechanism" reactions was that they provided no experimental evidence for involvement of any intermediates. Application of the curved arrow formalism to these reactions constituted nothing more than a restatement of the observed facts about how bonds of the reactants must be rearranged to give the known products. Furthermore, one could draw fully consistent curved-arrow schemes for any number of hypothetical "no-mechanism" reactions, but not all of them actually occurred. Although not particularly highlighted at the time, one can identify now perhaps the greatest of these deficiencies in the curved-arrow explanation for organic chemistry in the contrasting chemistry of carbocations and carbanions. The Wagner–Meerwein rearrangement led to a carbocation chemistry of baroque complexity, whereas the analogous 1,2 migration in carbanions, despite looking equally plausible in the curved-arrow representation, was all but unknown.

It is an interesting fact that the shortcomings of the curved-arrow formalism in dealing with "no-mechanism" reactions—really the shortcomings of the approximate VB theory on which it was based—were identified by Robinson just three years after he published the first paper using his version of curved arrows. In 1925, he and J. W. Armit recommended a representation of benzene in which the bonding was designated by a hexagon for the C–C σ bonding but an inscribed circle for the π bonding.[3] This is fundamentally a molecular orbital (MO) rather than a VB picture of the π bonding because it implies that the six π electrons are free to roam over all six carbons, rather than being localized to pairs of carbons as a Lewis model would require. At increasing levels of sophistication, VB and MO theory, of course, converge on identical, exact solutions to the

Special Issue: 50 Years and Counting: The Woodward-Hoffmann Rules in the 21st Century

Published: December 4, 2015

DOI: 10.1021/acs.joc.5b02469
J. Org. Chem. 2015, 80, 11630–11631

Schrödinger equation, but at their most approximate levels they are different. Approximate VB theory is arguably better than approximate MO theory at describing how simple σ bonds in diatomic molecules are broken, but approximate MO theory is superior when it comes to describing situations where electrons are delocalized over more than two atoms. Of course, VB theory can invoke resonance to fix up its deficiencies in describing delocalization, but even that addition to the model requires additional refinement to get the energetic consequences of cyclic delocalization right. Simple counting of resonance structures does not explain why delocalization stabilizes D_{6h} benzene but fails to stabilize D_{4h} cyclobutadiene. By contrast, as Erich Hückel had pointed out, even the simplest version of MO theory does explain that difference.

The relevance of all this to the development of the Woodward−Hoffmann rules is that the transition states of the "no-mechanism" reactions all involve cyclic delocalization of electrons, as several bonds are made and broken in concert. What one needs to analyze the problem is a theory suited to the situation, viz. MO theory, and that is what Roald Hoffmann could bring to the table. But he could bring much more than that. Once the explanation was at hand, he could translate it into pictorial representations that organic chemists could understand and then use themselves. This is a vital component for success of any boundary-crossing efforts in science—if the questions arise in one discipline and the answers arise in another, those answers must be couched in the local language of the scientists who raised the questions. More or less contemporaneous with Hoffmann's developing analysis, Kenichi Fukui was publishing his analysis of reactions based on the frontier orbital theory—again a simplified version of MO theory—which he had first described in 1952. He, too, was adept at presenting the results in ways that organic chemists of the time could easily understand and then use themselves.

Since these early appearances of MO theory in the organic chemistry literature, the increasing power of digital computers and the increasing usability of programs for calculating electronic structures have made application of MO methods, and more recently density functional theory, a common part of organic chemistry research, even in groups whose focus is primarily experimental. The models employed today are much more sophisticated than those used by Hoffmann and Fukui, but it is interesting to ponder whether their greater sophistication and consequent quantitative accuracy necessarily leads to greater understanding. Because the methods available in the 1960s were not capable of giving quantitative matches to experiment, it became necessary for the practitioners to think hard about what the calculations could reveal that would be useful and more or less correct. Hoffmann and Fukui were masters at this art, and it was from their deep insights that, among other things, the rules celebrated in this special issue of JOC were developed. Had it been possible at the time for any organic chemist to run a calculation on individual "no-mechanism reactions" and obtain a near quantitative match of activation parameters to those seen experimentally, one wonders whether there would have been the impetus to look for the more global understanding that the Woodward−Hoffmann rules provide.

It is not surprising, perhaps, that in the first few decades following the publication of the Woodward−Hoffmann rules there was an enormous burst of experimental research aimed at testing their validity. In addition, experimentalists of the time found that they could use the rules to predict new reactions that might be of synthetic value. What may be more surprising is that, 50 years later, the rules continue to provide inspiration for new research, even in the face of the more sophisticated computational methods alluded to above. The breadth of contemporary research based on the rules is an impressive testament to their universality. In this issue, one sees application of the rules to new hydrocarbon reactions in the papers of Castro and Karney, Hoye, Johnson, Slipchenko and McMahon, and Tantillo and Brummond. The rules themselves are extended and refined in the articles by Bao and Borden, Birney, Herges, Hsung and Houk, and Mikami and Houk, while the development of new synthetic methods from Woodward−Hoffmann analyses are illustrated in the papers from Cossío, Danheiser, Denmark, Feldman, Tantillo, and White. The new field of mechanochemistry is shown to borrow from and contribute to the rules in two papers by the Craig group, one in collaboration with Martínez, and analyses intimately linked to those of Woodward and Hoffmann are found in the organotin chemistry reported by Alabugin, in carbene chemistry described by Brinker, in a study of Möbius aromaticity by Kim and Osuka, and even in enzyme-catalyzed reactions reported by Williams.

Surely this cornucopia of new research stimulated by the half-century-old Woodward−Hoffmann Rules is a cause for celebration, and I hope that our readers feel that sense of joy in reading the papers in this special of issue of *The Journal of Organic Chemistry*.

Barry K. Carpenter

AUTHOR INFORMATION

Notes

Views expressed in this editorial are those of the author and not necessarily the views of the ACS.

REFERENCES

(1) Doering, W. v. E.; Roth, W. R. *Tetrahedron* **1962**, *18*, 67−74.
(2) Kermack, W. O.; Robinson, R. *J. Chem. Soc., Trans.* **1922**, *121*, 427−440.
(3) Armit, J. W.; Robinson, R. *J. Chem. Soc., Trans.* **1925**, *127*, 1604−1618.

DOI: 10.1021/acs.joc.5b02469
J. Org. Chem. 2015, 80, 11630−11631