ORGANOMETALLICS

Volume 21, Number 25, December 9, 2002

Reviews

Henry Gilman: American Pioneer in the Rise of Organometallic Chemistry in Modern Science and Technology[†]

John J. Eisch[‡]

Department of Chemistry, The State University of New York at Binghamton,
Binghamton, New York 13902-6016

Received October 29, 2001

The growth and development of organometallic chemistry from an esoteric, well-nigh alchemical art into a completely integrated and essential part of both current organic chemistry and inorganic chemistry have occurred with escalating rapidity over the last 150 years. The sesquicentennial history of organometallic chemistry falls rather naturally into three 50-year periods, each of which began with far-reaching discoveries: (1) the discovery of zinc alkyls by Frankland in 1849 and the use of such alkyls to prepare alkyls of other metals; (2) the discovery of organomagnesium halides by Grignard in 1900 and their many reactions with organic compounds; and (3) the dual discoveries of the existence and structure of ferrocene by Pauson and Miller in 1951 and of the polymerization of olefins by Ziegler and Natta in 1952−1953. The marked burgeoning of organometallic chemistry after World War I is traced to an international group of young pioneers launching their careers with high hope and vigor: Gilman, Kharasch, Ziegler, Wittig, Kipping, Pope, Grignard and his school, Nesmeyanov, and Razuvaev. The thesis of this historical review is that Henry Gilman, through the breadth and depth of his numerous, original contributions on covalent, σ-bonded organometallics, is the one pioneer of this group who has integrated and systematized the great lode of empirical observations on organometallics into correlations with the metal's position in a Mendeleevian periodic table. He has thereby transformed this field from alchemical art into chemical science. In support of this thesis of Henry Gilman as the prototypical pioneer of modern organometallic chemistry, this account traces his academic career at Iowa State and points out his scientific contributions made at successive stages: (1) his studies of the Grignard reagents, which did much to make their preparation convenient and reliable and their reactions of broad and useful scope; (2) his investigations of organolithium reagents and his discovery and key development of the lithium−hydrogen and lithium−halogen exchange processes, which reactions were studied independently by Karl Ziegler and by Georg Wittig but merit being termed the Gilman lithium−hydrogen exchange and the Gilman−Wittig lithium−halogen exchange reactions, respectively; (3) the preparation and reactions of many other organometallics, obtained by the transmetalation reaction of the appropriate metal salts with a magnesium or lithium organometallic; and (4) finally the preparation, structure, and chemical reactivity of diverse organometallics of group 14, especially those with metal−metal and metal−alkali metal bonds. It can be argued with great cogency that such a lifetime of research set the stage and drew the curtail for the dawn of the third era of organometallic chemistry: the discovery and utility of π-bonded organometallics. Because of Gilman's towering role in uncovering, developing, and systematizing the chemistry of σ-bonded organometallics, many of Gilman's colleagues and former students had thought him deserving of chemistry's highest honor.

Prologue: Symbiosis of Henry Gilman and Organometallic Chemistry

At the start of this new millennium the principles of organometallic chemistry have become an indispensable part of such diverse and broad chemical subdisciplines as organic synthesis, molecular structure and bonding, materials science, polymerization catalysis, and bioinorganic chemistry. The current integration of compounds containing carbon−metal bonds into pure and applied chemistry has occurred in just over the 150 years since the discovery of zinc alkyls by Edward

---

[†] Dedicated to the memory of Henry Gilman, my former mentor in chemistry and lasting exemplar in living.

[‡] Fax: 607-777-4865. E-mail: jjeisch@binghamton.edu.

10.1021/om0109408 CCC: $22.00 © 2002 American Chemical Society
Publication on Web 11/06/2002

Frankland in 1849.[1] But the science of organometallic chemistry really took on stature and wider acceptance among chemists in the latter half of that period, namely, the years after World War I. For it was then that a handful of young, enthusiastic chemists in Europe and the United States launched their academic careers with investigations devoted to organometallic compounds. The principal figures in this period, as judged by their subsequent publications, were Henry Gilman and Morris Kharasch in the United States, Karl Ziegler and Georg Wittig in Germany, F. Stanley Kipping and William Pope in Great Britain, Victor Grignard and his followers in France, and A. N. Nesmeyanov and G. A. Razuvaev in Russia. These pioneers evinced both great imagination and hope in undertaking research with such seemingly impractical laboratory oddities. Not only were such organometallic compounds of little apparent utility but many were unusually dangerous to handle. They were often spontaneously flammable in air and explosively decomposed by water, and the majority were toxic to inhale and corrosive to the skin. Indeed, in the early years of organometallic chemistry, 1849−1900, preparations and reactions frequently involved the use of mercury, thallium, bismuth, arsenic, and lead or their compounds, clearly reminiscent of the venturesome work of early alchemists.

Now that the efforts of these pioneering chemists have come to fruition in modern organometallic chemistry, it is instructive to attempt an analysis of how these impressive developments came about. In such a treatment of the history of organometallic chemistry there is much truth in Emerson's dictum, "There is properly no history, only biography". If we undertake such a treatment of developments in this field after 1920, whose professional biography would serve as a worthy vehicle for this task? From my doctoral studies begun in 1953 at Iowa State University and from my lifelong involvement with organometallic chemistry and its literature, my unhesitating choice would be my former mentor, Henry Gilman.[2] Long heralded as the Father of Organometallic Chemistry in the United States, Henry Gilman may fairly be considered as the prototypical pioneer in the growth of organometallic chemistry worldwide during the 20th century. This judgment is not meant to overlook the superb contributions of the other pioneers mentioned earlier nor to diminish the importance of many key discoveries by a host of other outstanding chemists over the last 75 years. Rather the choice of Henry Gilman is favored by the extraordinary number and variety of his research publications on the organometallic chemistry of both main-group and transition metals: over 1000 papers published during the 55 years from 1920 to 1975 covering compounds of over 35 different metals and often demonstrating for the first time whether a particular carbon−metal bond could be formed. The growth and blossoming of Gilman's research career thus has run parallel with the similar contemporaneous burgeoning developments in organometallic chemistry as a whole. Therefore, Gilman's research career bears close scrutiny for what it can tell us about the history of organometallic chemistry.

In any history, political or scientific, it is important to recall that "History is lived forward but is written in retrospect. We know the end before we consider the beginning and we can never wholly recapture what it was to know the beginning only".[3] As applied to chemical progress in the early 20th century, it is difficult to realize, now 75 years later, that chemical research then had little of the conceptual and instrumental infrastructure we now take for granted: the present, widely accepted electronic theory of molecular structure and reaction mechanisms and the modern panoply of electronic instrumentation with which to probe and to give credence to detailed molecular structures and reactive intermediates.

In actuality, the present electronic theory of chemical bonding had evolved and gained widespread acceptance only in the some 50 years following the discovery of the electron by J. J. Thomson in 1897.[4] The relevance of the electron to atomic structure was elucidated by the nuclear model of the atom proposed by Ernest Rutherford in 1911[5a] and was further specified in 1913 by Niels Bohr in his planetary and energy level-quantized model of the hydrogen atom.[5b] Although this theory was expanded and refined especially by G. N. Lewis in his celebrated publication in 1916,[6] extensions and amplifications of the theory to molecules and covalent bonding continued to be made in succeeding years in numerous articles and in several influential books, such as by Lewis himself in *Valence and the Structure of Atoms and Molecules* in 1923;[7] by Sidgwick in 1927; by Pauling in 1938;[8] and by Coulson in 1952.[9] The efforts of organic chemists, such as Robinson, Ingold, Lapworth, Hammett, Whitmore, Kharasch, and Bartlett during this period, were directed toward understanding reacting organic systems in terms of such electronic theory.[8] Accordingly, prior to World War II the electronic theory of molecular structure and reactivity was still under development and by no means widely appreciated by Gilman and many of his contemporaries.

Gilman understood that the electrolytic decomposition of certain compounds is consistent with the presence of positive and negative chemical fragments, an idea stemming from Berzelius and his dualistic theory of bonding proposed already in 1811. But he was more

---

(1) Frankland, E. *Ann. Chem. Pharm.* **1849**, *71*, 177.

(2) After receiving a B.S. degree in chemistry, *summa cum laude*, from Marquette University in 1952, the author joined Henry Gilman's research group at the then Iowa State College for his doctoral studies. After being awarded a Ph.D. degree in organic chemistry in 1956, he was privileged through the recommendation of Henry Gilman to be awarded a one-year postdoctoral fellowship, sponsored by Union Carbide, which he was able to spend in Karl Ziegler's research laboratories at the Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr, West Germany, focused on the study of group 13 organometallic compounds. The author maintains an enduring gratitude for the steady guidance and unfailing support that Henry Gilman provided during both his doctoral studies and his professional career. An appreciation of the impact of Henry Gilman on modern organic chemistry has been published by the present author: Eisch, J. J. *J. Organomet. Chem.* **1988**, *338*, 281.

(3) Wedgwood, C. V. *William the Silent*; W.W. Norton: New York, 1960; p 35.

(4) Thomson, J. J. *Philos. Mag.* **1897**, *44* (5), 293.

(5) (a) Rutherford, E. *Philos. Mag.* **1911**, *21* (6), 669. (b) Bohr, N. *Philos. Mag.* **1913**, *26* (6), 476, 857.

(6) Lewis, G. N. *J. Am. Chem. Soc.* **1916**, *38*, 762.

(7) Lewis, G. N. *Valence and the Structure of Atoms and Molecules*; The Chemical Catalog Co.: New York, 1923.

(8) Full bibliographic data on the monographs by Sidgwick and by Pauling, as well as on many leading references on the applications of such electronic theory to the structure and reactions of organic compounds, are admirably presented in the following reference: Johnson, J. R. In *Organic Chemistry: An Advanced Treatise*, 2nd ed.; Gilman, H., Ed.; Wiley: New York, 1943; p 1821.

(9) Coulson, C. A. *Valence*; Clarendon Press: Oxford, 1952.

impressed by the generation, detection, and characterization of the triphenylmethyl radical by Gomberg[10] in 1900 and by the electronic interpretation of Lewis in 1923 of the covalent bond as the result of the coupling of such radicals. Thus, in the course of his researches Gilman was more inclined to view covalent bond rupture, even of a polar carbon−metal bond, as occurring in a homolytic rather than a heterolytic manner.

With the electronic theory of structure and reaction mechanism in its incipient stage in the 1920s Gilman and his colleagues launched their researches in organometallic chemistry guided principally by the purely empirical relations uncovered by Mendeleev in the course of developing his periodic table of the elements.[11] In carrying out their investigations of the structure and properties of a given organometallic compound, they continually strove to make comparisons with the organometallic derivatives of neighboring metals in a family or period. Without any theoretical preconception, they sought to learn directly from nature, by experiment, how the position of the metal in the periodic table would affect its properties. In keeping with this approach to research, monographs on organometallic chemistry generally have been organized into chapters and subsections based on such a periodic table. The classic volume by Krause and von Grosse in 1937 is typical of this format.[12] Henry Gilman was to demonstrate his mastery in such empirical organometallic research and thereby was to become one of the pioneers of modern organometallic chemistry. The great store of experimental findings that Gilman and co-workers amassed over his career have permitted younger chemists to develop a unifying electronic understanding of carbon−metal bonding and of the complex pathways by which such bonds are made and broken.[13]

Aside from such retarding deficiencies in existing theory, early 20th century organometallic chemists had substantial experimental difficulties as well. Provisions had to be made for manipulating these reactive and toxic “unnatural” organic compounds at a time when appropriate laboratory glassware, equipment, inert atmospheres, and solvents were not readily available at any cost. Inert atmosphere chambers and apparatus for the purification of gases and solvents were not to be commercially available for decades, and such equipment therefore had to be devised and fashioned in individual research laboratories. These seminal laboratory experiments have made the manipulation of organometallic reagents for current chemists into routine laboratory operations, but still requiring appropriate care.

The sesquicentennial history of organometallic chemistry falls rather naturally into three 50-year periods, the start of each period being signaled by a far-reaching discovery in preparative chemistry. The first period was ushered in by the synthesis of zinc alkyls by Edward Frankland in 1849[1] and the subsequent extension of the preparative methodology by Frankland and others to alkyls of mercury, lead, antimony, bismuth, aluminum, silicon, and gemanium.[12] Frankland himself, Butlerov and his students, Zaitsev and Reformatskii, and others realized the potential value of such compounds in organic synthesis and applied them to organic substrates for the preparation of carbon−carbon bonds. The second period began in 1900 with the discovery by Victor Grignard of the formation of organomagnesium halides directly from the organic halide and the metal. In this instance, Grignard himself saw the significance of such reagents and in remarkably short time demonstrated their great versatility in organic synthesis. Motivated by such pronounced success, Ziegler, Gilman, and Wittig, all organic chemists by training and by research interests, discovered and developed novel and convenient routes to the more reactive organolithium reagents, thereby opening up access to almost every conceivable σ-bonded metal alkyl by the general alkylation process and, in addition, uncovering many transformations of organic substrates not even possible with Grignard reagents.

Finally, the third period of development, the most dramatic and remarkable of all, can be dated as beginning in the early 1950s with the dual discoveries of the synthesis of ferrocenes by Kealy and Pauson and by Miller, Tebboth, and Tremaine, on one hand, and the facile polymerization of olefins by Karl Ziegler in 1952 and their stereoselective polymerization by Giulio Natta in 1953 on the other. Within the three-year span of 1951−1954 these revolutionary disclosures opened up the entire field of transition-metal π-complexes and demonstrated the unforeseen, revolutionary utility of organometallics in industrial science and technology. Compounds containing carbon−metal bonding were transformed from laboratory curiosities having only academic interest into sought-after reagents and catalysts for a host of hydrocarbon reactions in the flourishing petrochemical industry.[14]

In recounting the interplay of Henry Gilman’s career and the growth of organometallic chemistry, we shall be chiefly concerned with the period after 1900, since Gilman was born in Boston in 1893 and completed his doctoral studies in 1918. Before we begin this analysis, it is useful to examine the status and scope of both organic and organometallic chemistry in 1899, that is, the year before Victor Grignard’s discovery, to perceive how organometallic chemistry has come to shed its vestiges of the esoteric and alchemical and has become a mainstay of modern organic and inorganic chemistry.

---

(10) Gomberg, M. *J. Am. Chem. Soc.* **1900**, *22*, 757.

(11) An engaging account of Mendeleev’s conception of his periodic arrangement of the elements based upon their properties and those of their principal compounds has appeared recently: Strathern, P. *Mendeleyev’s Dream: The Quest for the Elements*; St. Martin’s Press: New York, 2000.

(12) An authoritative treatment of the original literature of organometallic chemistry can be found in: Krause, E.; von Grosse, A. *Die Chemie der Metall-organischen Verbindungen*; Verlag Gebrüder Borntraeger: Berlin, 1937. The edition published in the United States by Edwards Brothers, Inc. in 1943 has had the greater influence upon American chemists. Incidentally, there is a 10-page summary written by von Grosse of the Bohr-Lewis-Kossel valence-bond theory and of the Heitler-London-Mulliken molecular orbital theory generally applied to organometallic compounds. However, the presentation is too concise and sketchy to be comprehensible or even convincing for a contemporary organometallic chemist.

(13) The pervasive influence of such modern electronic theory on organometallic structure is manifest in all of the chapters presented in *Comprehensive Organometallic Chemistry*, first published in 1982, with the addendum, *Comprehensive Organometallic Chemistry II*, published in 1995, under the editorship of G. Wilkinson, F. G. A. Stone, and E. W. Abel by Pergamon Press.

(14) A landmark monograph that summarizes the research achievements of Ziegler−Natta polymerization catalysis as of 1979 is an instructive source of information: Boor, J., Jr. *Ziegler−Natta Catalysts and Polymerizations*; Academic Press: New York, 1979; 670 pp.

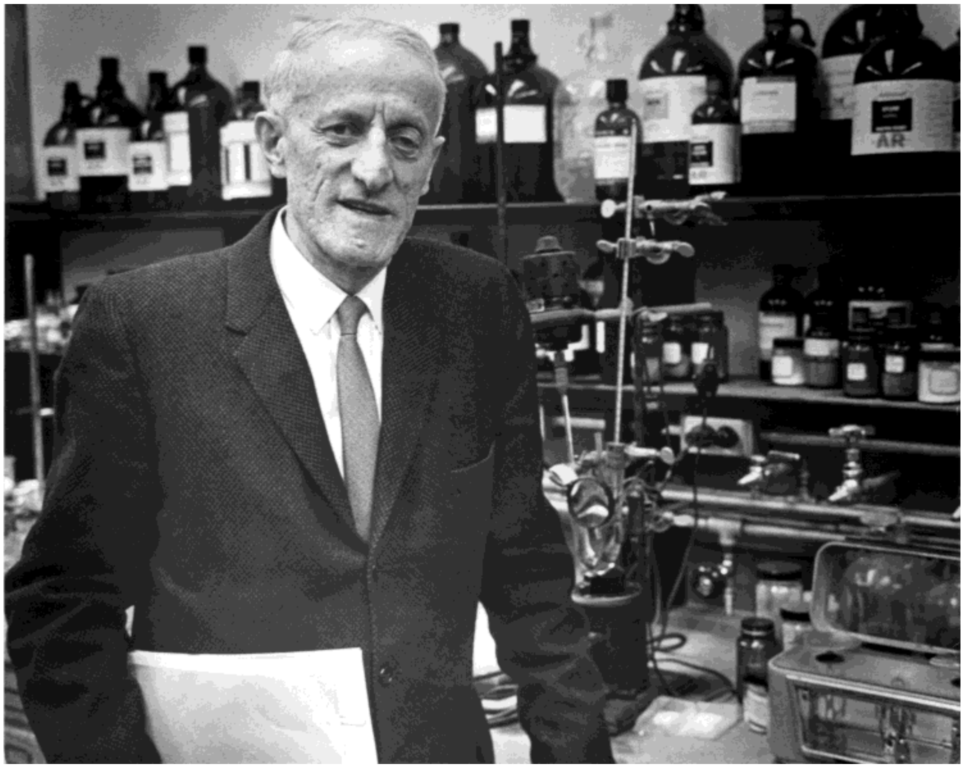


Figure 1. Henry Gilman at a student's research laboratory bench, ready for the daily oral report, a pose embedded in the mind of every Gilman student. (Photograph courtesy of the Iowa State University/Special Collections Department, which granted permission to reproduce this material.)

Organometallic Chemistry at the End of the 19th Century

Upon examining a copy of the American Edition of the classic Richter-Anschütz, *Organic Chemistry*, published in 1899, one finds in Volume I, Aliphatic Compounds, a scant 5 pages listing the properties of the alkyls of nine different main-group metals.[15] Scattered throughout the text are mentioned the occasional uses of zinc metal or its alkyls as reagents in organic synthesis (cf. supra). The impression conveyed was that the known metal alkyls are difficult to work with, being poisonous (Be, Hg, Pb, and Tl) and/or spontaneously flammable in air and explosively decomposed by water (Al, K, Mg, Na, and Zn) and should be considered as laboratory curiosities much like the fulminate of mercury. Contemporary general or inorganic chemistry textbooks from the turn of the century up to the 1920s make little mention of metal alkyls, although metal hydrides and metal carbonyls receive some attention. Clearly, organometallic chemistry then existed as a borderland between the thriving and mutually segregated disciplines of organic chemistry and inorganic chemistry, at most of marginal interest or relevance to either field. Indeed, broad acceptance of organometallics into organic chemistry proper did not occur until well into the 1950s in the United States. During the early years of my own academic career in the 1950s and 1960s my academic colleagues in organic chemistry at Michigan took the jocular but unsympathetic view that organometallic chemists were importing "peculiar elements" into the discipline of organic chemistry. However, academic organic chemists finally came to appreciate the enormous scope that organometallics brought to the science and art of synthesizing both naturally occurring organic compounds and artificial organic structures conceived in a chemist's unfettered imagination.

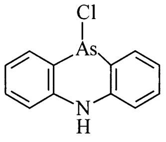
The Era of the Grignard Reagent and its Transplantation to the United States, 1900−1935

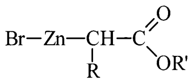
Slow Spread of Grignard's Findings. Although Victor Grignard discovered the class of reagents bearing his name in 1900 and pursued the applications of such reagents so diligently that he was awarded the Nobel Prize in 1912, the worldwide reverberations of his investigations were not felt in the chemistry community until after World War I. The reason for this delay in following Grignard's lead was that many of the chemists in countries of both the Allies and Central Powers were enlisted in the melancholy business of preparing for and conducting a war of unexpected duration and ferocity. Academic research gave way in part to priority programs directed to the production of high explosives, poison gases, and military vesicants. During and immediately after this war compounds containing carbon−arsenic bonds, and hence formally organometallic compounds, were developed as potential chemical warfare agents. In the United States, a young U.S. Army chemist, Roger Adams (of subsequent fame as the head of the Chemistry Department at the University of Illinois) prepared phenarsazine chloride, also eponymously called Adamsite (**1**), a poisonous vesicant used as an antipersonnel harassing agent. Adams was a young instructor at Harvard during Gilman's under-

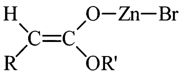
---

(15) von Richter, V. *Organic Chemistry*, 3rd American from the Eighth German Edition, translated by Smith, E. F.; Blakiston's Son: Philadelphia, 1899.

graduate study at Harvard and served as his research advisor on a senior project dealing with the phenyl esters of oxalic acid. Adams and Gilman then published these results, and this became Gilman's first scientific publication.[16]


1


2


3

Henry Gilman's awareness of the versatility and potential of Grignard reagents grew out of his undergraduate and graduate studies at Harvard University. Born into a middle-class family in Boston, Massachusetts, on May 9, 1893, Gilman was one of nine children of a merchant tailor who had considerable status because of his trade union activities. Already distinguished by his academic achievements in the English High School in Boston, the promising young man was sent to Harvard in neighboring Cambridge, where he received a Bachelor of Science degree, *summa cum laude*, in 1915. His experience in laboratory research with Roger Adams motivated him to apply for graduate study at Harvard. The eminent E. P. Kohler accepted him for postgraduate work and proposed for his doctoral studies a research problem concerning the preparation of brominated α-keto esters and their use in a modification of the Reformatskii reaction. This reaction of α-bromo esters with zinc, developed in the 1880s, was then thought to involve an organozinc intermediate and thus was Gilman's first apparent experimental work with organometallic reagents. It is ironic to note that investigations carried out about 50 years later have since shown that Reformatskii reagents have no actual carbon−zinc bonds, as indicated in **2**, but are rather zinc enolate salts of esters (**3**).[17] Through such work Gilman earned an M.A. degree in 1917 and a Ph.D. degree in 1918 in organic chemistry.[18]

Since Kohler is credited with having spread awareness of Grignard reagents and their use in the United States, Gilman's great interest in and curiosity about Grignard reagents must have stemmed from his graduate studies in Kohler's laboratories. However, a further travel experience during his doctoral work did much to heighten such curiosity. Because of his excellent performance in research, he was awarded a Sheldon Fellowship, which permitted him to spend a *Wanderjahr* in Europe. Brief periods of study were spent in Zurich at the Polytechnicum with Hermann Staudinger, at Oxford with William H. Perkin, Jr., and at the Sorbonne in Paris. Not only did his visit in France allow him to meet Victor Grignard personally, but he learned of the impressive advances in synthetic organic chemistry then made possible by such Grignard reagents. This advanced study proved decisive for him in finding his scholarly métier and in charting his course in academic research. His subsequent studies of the reactions of ketenes,[19] isocyanates, and isothiocyanates with Grignard reagents[20] signal the influence of his stay both in Staudinger's laboratory and at the Sorbonne. But Gilman's fascination with the Grignard reagent was to be the most abiding stimulus arising from his European travels and was to fix Grignard chemistry as the principal focus of his academic career for the first 15 years.

Henry Gilman Launches a Lifelong Academic Career at Iowa State College. Roger Adams left Harvard in 1919 to assume the headship of the Chemistry Department at the University of Illinois. With an eye for talent that would soon place his department at the forefront of organic chemistry in the United States, Adams offered Gilman a teaching and research instructorship at Illinois. Attracted by the prospect of working with his former mentor, Gilman accepted, but within a year a position offering greater independence and challenge came into prospect. Wishing to expand its chemistry program into doctoral studies, Iowa State College urged Gilman to join them as an assistant professor and to undertake improvements in the instruction and research in organic chemistry. The offer of a free rein and considerable responsibility was irresistible to Gilman, and in 1919 he accepted this position with alacrity. In 1919 The Iowa State College of Agriculture and Mechanical Arts in Ames was a modestly sized educational institution principally devoted to the farming and agricultural concerns of a largely rural state. Not until well after World War II with its heavy involvement in atomic energy research would Iowa State evolve, in substance and in name, into a major university. When Gilman arrived in Ames, he relates that "the chemistry program was very modest. Possibly 15 undergraduates and a dozen graduate students (master's candidates). But we were young and worked hard".[21] Indeed! As in whatever unleashed his enthusiasm and seemingly boundless energy, Gilman's performance at Iowa State was spectacular, and by 1923 he was promoted to full professor at the age of 30. He assembled initially a research group of students pursuing a master's degree and later doctoral students as well. His first publication stemming from work done at Iowa State with his student L. C. Heckert appeared in 1920 in the *Journal of the American Chemical Society* and was entitled "Mechanism of the Reaction between Ketenes and the Grignard Reagents".[19] This article can also be viewed as proclaiming his intentions of undertaking research focused on the mode of action of Grignard reagents. Gilman's then use of the word "mechanism" is not synonymous with what a physical organic chemist would mean by "reaction mechanism" in current usage. But it did signify that Gilman was interested in the experimental factors in the reaction and structural features in the reagents that promoted or retarded the reaction and determined which of several conceivable pathways would be followed. The use of "mechanism" even in this more limited meaning was an important concept in the organic chemistry of that time and was

---

(16) Adams, R.; Gilman, H. *J. Am. Chem. Soc.* **1915**, *37*, 2716.
(17) Vaughan, W. R.; Knoess, H. P. *J. Org. Chem.* **1970**, *35*, 2394.
(18) Kohler, E. P.; Gilman, H. *J. Am. Chem. Soc.* **1919**, *41*, 683.
(19) Gilman, H.; Heckert, L. C. *J. Am. Chem. Soc.* **1920**, *42*, 1010.
(20) Gilman, H.; Kinney, C. R. *J. Am. Chem. Soc.* **1924**, *46*, 493.
(21) Gilman, H. *News Iowa State* **1966**, *18* (5), May-June.

to play a prominent role in all of his scientific publications. Learning and understanding what empirical factors foster or hinder the course of any chemical reaction has become the basis for our modern electronic interpretation of reaction mechanisms.

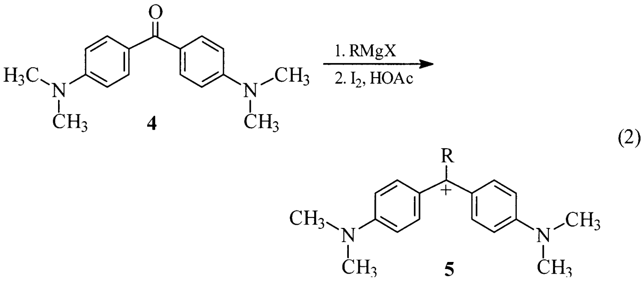
Soon after his arrival Gilman introduced the doctoral program of chemical studies, and by 1925 R. M. Pickens had become his first student to be awarded a Ph.D. The theme of his dissertation concerned the physiological action of various heterocycles, such as furan, thiophene, and pyrrole, as local anesthetics.[22] This subsidiary research interest of Gilman's in heterocycles and their physiological action undoubtedly stemmed from his affiliation with Iowa State and his interest in finding uses for chemicals derived from agricultural products. Later in his career he would intertwine his two strands of research interest through studies aimed at synthesizing new heterocyclic compounds by means of organometallic reagents.

Henry Gilman began his academic career at Iowa State College at a driving pace he was to continue. For 55 years he carried out chemical research and teaching with phenomenal vigor and success and until his formal retirement gave sought-after lectures to both undergraduate and graduate students. Over his career he directed the research of more than 140 doctoral, 50 master's, and 50 postdoctoral co-workers. His name became synonymous with chemistry at Iowa State, and in 1974, the now Iowa State University, in recognition of Gilman's worldwide renown, renamed the chemistry building as Gilman Hall.

Gilman's Laboratory Becomes the American Hearth of the Grignard Reaction. Motivated by a keen awareness of the Grignard reagent's potential in organic synthesis and by a focused curiosity as to how best it might be generated, Gilman and his group set out to give intensive scrutiny to the experimental factors that enhance or retard the ease and the extent of reaction between a given organic halide and magnesium metal (eq 1). In the hands of chemists other than those of Grignard's group, many such reactions had proved difficult to initiate or to conduct in high yield. Gilman realized that unless Grignard reagents proved to be consistently accessible in high yields and without elaborate experimental technique, chemists would be dissuaded from utilizing such "tricky" reagents in routine organic synthesis. In a subsequent review of these efforts by Gilman and his students, Kharasch and Reinmuth in 1954 surveyed the careful screening of the following experimental factors: (1) quality, quantity, and particle size of magnesium; (2) possible reaction activators and inhibitors; (3) nature and purity of the protective atmosphere; (4) structure and nature of the organic halide; (5) compatibility or interference of other functional groups in the organic halide; (6) structure and purity of the ether or other solvent; (7) rate of addition of the halide; and (8) the rate of agitating the reaction mixture.[23] At first inspection, such experimentation may seem unimaginative, boring, and blindly empirical. Yet exactly this kind of experimentation proved eminently suitable to answering the key question, How best can a given Grignard reagent be prepared in a convenient and a consistently reliable fashion? Furthermore, such experimental data have been most valuable in answering another vital question concerning the Grignard reaction, namely, How does the reaction take place, or in modern parlance, what electronic mechanistic pathway does formation of the Grignard reagent follow? Any chemist who has been following the research on Grignard reagent formation recently published variously by Whitesides, by Garst, by Walborsky, and by others can readily appreciate that the experimental factors explored by Gilman in these studies become crucially important in formulating mechanistic models of the reactions occurring on the surface of magnesium.[24] Gilman's pioneering contributions to such current mechanistic problems of heterogeneous organic reactions in general richly deserve recognition.

$$\mathrm{R{-}X} + \mathrm{Mg} \xrightarrow[\text{solvent}]{\text{atmosphere}} \mathrm{R{-}Mg{-}X} \qquad (1)$$

Since Gilman strove to attain optimal experimental conditions and a reliable procedure for the most diverse kinds of organic halides, he necessarily had to devise a qualitative test for the formation of a carbon−magnesium bond, which would have the sensitivity to detect even traces of the desired Grignard reagent. Once a given experimental variation was shown to generate even small amounts of R−Mg−X through a positive qualitative test, Gilman reasoned that the chemist would then know which experimental factors to modify further for increased yield. The most reliable qualitative test for detecting the presence of the C−Mg bond (or other active C−M bonds, such as those involving active metals such as sodium, potassium, lithium, calcium, barium, and strontium) is based upon the formation of a greenish-blue carbenium ion **5** from the reaction of RMgX with Michler's ketone (**4**) and subsequent protolysis (eq 2).[25]



(2)

Gilman found that the quantitative analysis of the total Grignard reagent in solution can be conveniently determined by hydrolysis of an aliquot of the ethereal solution with a known excess of standard aqueous HCl and back-titration with standard NaOH using phenolphthalein as an indicator.[26] Such assays have served as a rapid, reliable method for determining the yield of a given Grignard procedure (if moisture and dioxygen have been excluded during the reaction), since the overwhelming source of any base is the MgX(OH)

---

[22] Gilman, H.; Pickens, R. M. *J. Am. Chem. Soc.* **1925**, *47*, 245.

[23] Kharasch, M. S.; Reinmuth O. *Grignard Reactions of Nonmetallic Substances*; Prentice-Hall: New York, 1954.

[24] Lindell, W. E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 1, pp 156−166.

[25] Gilman, H.; Schulze, F. *J. Am. Chem. Soc.* **1925**, *47* (7), 2002.

resulting from hydrolysis (eq 3). For Grignard reagents

$$\mathrm{R{-}Mg{-}X} + \mathrm{H_2O} \longrightarrow \mathrm{HO{-}Mg{-}X} + \mathrm{R{-}H} \tag{3}$$

whose hydrolysis yields volatile alkanes, Gilman employed a Zerevitinov hydrolysis of the RMgX in di-*n*-butyl ether with the collection and measurement of the evolved gaseous alkane to measure the activity of the RMgX.[27] Such a measurement was especially useful in ascertaining the stability of RMgX solutions stored over months or years.

Through such meticulous experimentation over some 15 years, 1920−1935, Gilman and his students were able to present the chemistry community with a wide array of easily employed, highly reliable procedures for preparing the most structurally diverse kinds of Grignard reagents. Aware of how subtle changes in a given halide could retard Grignard reagent formation, Gilman was always pleased to learn when an unexplored, heteroatom-bearing halide had undergone successful conversion. As an inexperienced graduate student, I recall my surprise over how delighted Gilman was when I simply informed him that I had made the Grignard reagent from 3-bromo-*N*-ethylphenothiazine and converted it to its carboxylic acid.[28] In my naiveté, I thought that the bromo derivative was only reacting as it had been predestined to do!

As Gilman carried through such preparative studies on Grignard reagents, he was equally interested in how they could be applied for the synthesis of other organic compounds. Such studies extended Gilman's research into two different areas: one was the synthesis of the organometallic derivatives of other, less active metals (M = metals of groups 11, 12, 13, 14, and 15) by a metathetical alkylation (eq 4), while the other was the

$$\mathrm{MX_n} + \mathrm{n\,RMgX} \longrightarrow \mathrm{R_nM} + \mathrm{n\,MgX_2} \tag{4}$$

further application of Grignard reagents in organic synthesis. The first research focus would extend Gilman's efforts into the study of a wide variety of carbon−metal bonds of both main-group and transition metals. This research would continue over Gilman's entire professional career and would constitute his *magnum opus*. We wish to defer discussion of this great body of work until we consider how Gilman shifted his focus from the Grignard reagent to the analogous lithium reagent (cf. section on the Era of the Organolithium Reagent).

As to the applications of Grignard reagents in organic synthesis, Gilman was confronted with extensive contributions that Grignard himself, together with his many students and followers, had already made to this area. At the very start of his career and in collaboration with C. J. West, he compiled a complete bibliography on all such previous work, which was published by the U.S. National Academy of Science in 1922.[29] From this vantage point, then, he was able to identify what potential applications of Grignard reagents were not adequately explored or, more significantly, what Grignard reactions took an anomalous, unexpected course. Gilman's interest in the atypical courses of Grignard reactions was a relatively new approach to organic chemical research, which in its 19th Century Golden Age had focused on simply determining what overall structural change took place in the typical "name" reaction under carefully controlled conditions. In his very first publication from Iowa State,[19] Gilman strove to differentiate between two different possible courses for the reaction between diphenylketene (**6**) and phenylmagnesium bromide (**7**), which should involve chemically distinct intermediates (Scheme 1): addition to the ethylenic bond (path a, Staudinger's view) or addition to the carbonyl bond (path b, Gilman's hypothesis). In either event, hydrolysis would yield the observed isolated ketonic product **10**. Proposing that **8** and **9** were separate, noninterconverting intermediates, Gilman sought to learn which path was followed by capturing **8** or **9** through benzoylation. Since **11** was isolated from such a reaction, Gilman concluded that path b, carbonyl group addition, was the actual pathway. What neither Gilman nor any other chemist in the 1920s knew is that **8** and **9** are not distinguishable structures, being at best limiting tautomeric forms that might readily interconvert via one enolate anion (**12a** and **12b**). But although this modern hindsight may weaken the validity of Gilman's conclusion, it does not detract from the originality and ingenuity that Gilman showed in attempting to address such fundamental, subtle, and complicated questions of reaction mechanism.

Extensive studies were carried out on known Grignard reactions such as additions to carbonyl derivatives, treatments with X_2, O_2, CO_2, or S_8, and 1,4-additions to conjugated systems, with each investigation attempting to establish optimal experimental conditions for yielding the main desired product and minimizing the extent and kind of side products. In such work Gilman was able to recognize the pronounced effect of impurities, such as oxygen, peroxides, transition metals, or organic isomers, on the course of a given reaction. On the theme of transition-metal promotion of anomalous and highly unusual reactions of Grignard reagents Morris Kharasch and his students made pioneering and outstanding contributions as well.[30] The conclusions reached in many such investigations were that free organic radicals are often generated under such conditions. This hypothesis of free-radical generation in Grignard reactions has been repeatedly confirmed in most recent research.[31]

Other unusual Grignard reactions that Gilman's group scrutinized during this period were the following: (1) 1,4-additions to α,β-unsaturated carbonyl derivatives (eq 5 via **13**);[32] (2) addition to isocyanates or to isothiocyanates (eq 6);[20] (3) reduction of azobenzene (eq 7)[33] and nitroso- and nitroaromatics (eq 8);[34] (4) rearrangement products from reactions of benzylic

---

[26] Gilman, H.; Wilkinson, P. D.; Fishel, W. P.; Meyers, C. H. *J. Am. Chem. Soc.* **1923**, *45*, 130.

[27] Gilman, H.; Fothergill, R. E. *J. Am. Chem. Soc.* **1927**, *49*, 2815.

[28] Gilman, H.; Eisch, J. *J. Am. Chem. Soc.* **1955**, *77*, 3862.

[29] West, C. J.; Gilman, H. *Natl. Acad. Sci.-Natl. Res. Council, Reprint Circ. Ser.* **1922**, 24.

[30] Kharasch, M. S.; Reinmuth O. *Grignard Reactions of Nonmetallic Substances*; Prentice-Hall: New York, 1954; pp 116−131.

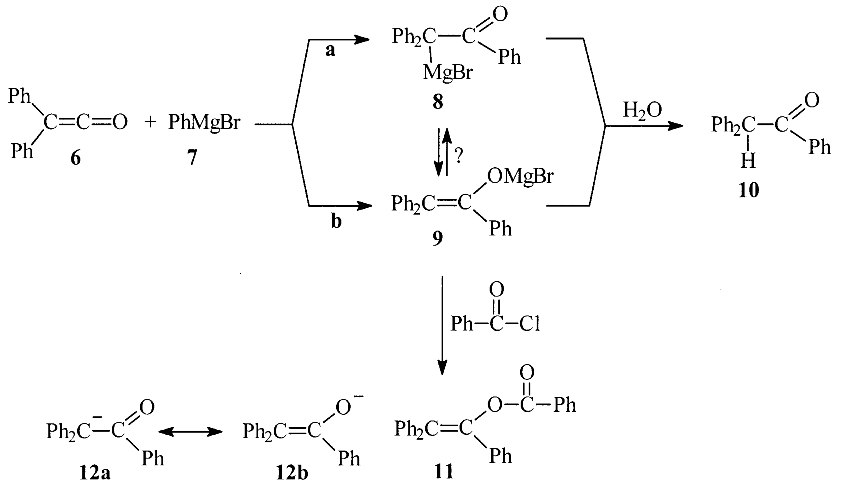
[31] Lindell, W. E. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 1, pp 192−193.

[32] Gilman, H.; Kirby, J. E.; Kinney, C. R. *J. Am. Chem. Soc.* **1929**, *51*, 2252.

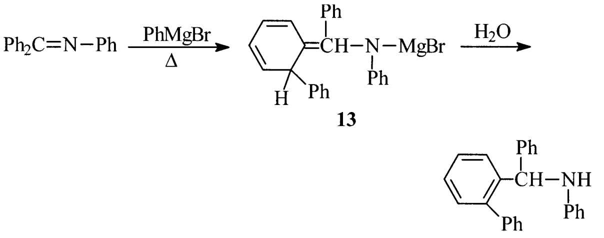
[33] Gilman, H.; Adams, C. E. *J. Am. Chem. Soc.* **1926**, *48*, 2004.

[34] Gilman, H.; McCracken, R. *J. Am. Chem. Soc.* **1929**, *51*, 821.

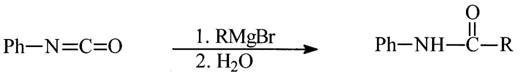
Scheme 1



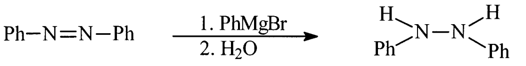
Grignard reagents (eq 9 via **14**);[35] and (5) periodic claims from other laboratories that unconjugated olefinic linkages do undergo additions of Grignard reagents (proposed eq 10). In every instance of such a claimed carbomagnesiation of an isolated olefinic linkage, the careful reinvestigation by Gilman's group was able to demonstrate the invalidity of the report because the authors had overlooked side reactions not stemming from RMgX.[36] Some 40 years later, when my own research uncovered such an apparent carbomagnesiation, I was accordingly most skeptical until I had reproduced the reaction many times (Scheme 2).[37] Because the cumulative efforts of Kharasch, Gilman, Ziegler, Birch, Cooper, and Finkbeiner and others had shown how profoundly transition-metal salts could alter the reactions of main-group organometallics, we even prepared reagent **15** from triply sublimed magnesium and were still able to achieve the same carbomagnesiation.[38] After we published our results, Gilman immediately sent congratulations. Investigation of the mechanism for the formation of **18** demonstrated that special circumstances prevailed in this unprecedented addition: diallylmagnesium (**15**) in Schlenk equilibrium with the Grignard reagent first led to the formation of adduct **16**. This intramolecular juxtaposition of the C−Mg and C=C bonds undoubtedly fostered the ensuing carbomagnesium to yield **17**. The retarding effect of ethers proved to be consistent with electrophilic attack of the magnesium center on the olefinic π-base.[39] Without Gilman's prior research, I would have had no appreciation of the unusual nature or significance of our observations.



(5)

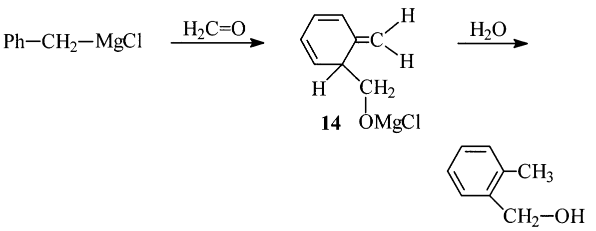


$$\text{Ph–N=C=O} \xrightarrow[\text{2. H}_2\text{O}]{\text{1. RMgBr}} \text{Ph–NH–}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{–R} \qquad (6)$$

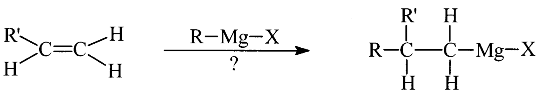


(7)

$$\text{Ph–NO}_2 \xrightarrow[\text{2. H}_2\text{O}]{\text{1. PhMgBr}} \text{Ph}_2\text{NH} + \text{Ph–Ph} + \text{PhOH} \qquad (8)$$



(9)



(10)

One C−C bond-forming reaction that received Gilman's continuing attention was the reaction of dialkyl sulfates with RMgX or isolated R_2Mg (eqs 11 and 12).[40]

$$\text{R–R}' + \text{RMgOSO}_3\text{R}' \xleftarrow[\text{eq. 12}]{\text{R}'_2\text{Mg}} \text{R}_2\text{SO}_4 \xrightarrow[\text{eq. 11}]{\text{R}'\text{MgX}} \text{R–R}' + \text{R–X} + \text{Mg(OSO}_3\text{R}')_2$$

The value of such a reaction is in the cross-coupling of different organic groups, still a topic of keen current interest in organic synthesis, as is evident in diverse cross-coupling of R−M and various organic derivatives R−E catalyzed by transition-metal complexes. Whether the cross-coupling method is termed Kharasch, Kumada, Stille, Suzuki, or another name(s), these methods find their common origin in the seminal work of Morris

---

[35] Gilman, H.; Kirby, J. E. *J. Am. Chem. Soc.* **1932**, *54*, 345.

[36] Gilman, H.; Leermakers, J. A. *Rec. Trav. Chem.* **1929**, *48*, 577.

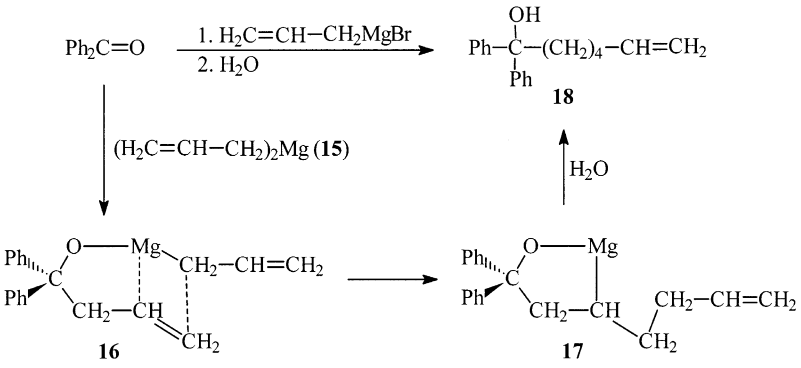
[37] (a) Eisch, J. J.; Husk, G. R. *J. Am. Chem. Soc.* **1965**, *87*, 4194. (b) Eisch, J. J.; Merkley, J. H. *J. Organomet. Chem.* **1969**, *20*, 27.

[38] Reagent **15** derived from triply sublimed Mg reacted somewhat slower than **15** derived from ordinary Mg turnings and markedly slower than **15**, to which catalytic amounts of $Ni(acac)_2$ had been added. Therefore, this carbomagnesiation is also catalyzed by transition metals.

[39] (a) Eisch, J. J. Merkley, J. H.; Galle, J. E. *J. Org. Chem.* **1979**, *44*, 587. (b) Eisch, J. J.; Merkley, J. H. *J. Am. Chem. Soc.* **1979**, *101*, 1148.

[40] Gilman, H.; Hoyle, R. E. *J. Am. Chem. Soc.* **1922**, *44*, 2621.

Scheme 2

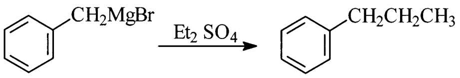


Kharasch in the 1930s on the transition-metal-promoted couplings involving Grignard reagents.[30] Prior to that discovery, it was known that the uncatalyzed reaction of a Grignard reagent with its own halide (eq 13) was

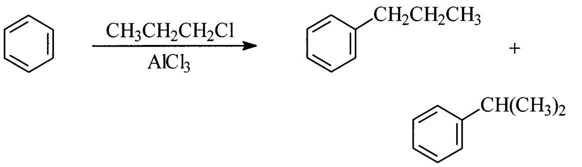
$$R{-}X + Mg \longrightarrow R{-}Mg{-}X \xrightarrow[\text{rate ?}]{R-X} R{-}R + MgX_2 \qquad (13)$$

too slow for fruitful coupling to R−R in most cases (with allylic and benzylic halides and some alkyl iodides being notable exceptions). It is readily apparent that *if* such coupling were relatively *fast*, the preparation of *RMgX* would be *impossible*.

In light of this, Gilman appreciated the utility of being able to substitute the magnesium by a primary alkyl group from R_2SO_4 in high yield (eq 14).[40] It should be noted that generally *n*-alkyl groups cannot be introduced cleanly into aromatic nuclei by the conventional Friedel−Crafts reaction because of an interfering rearrangement (eq 15).[41]



(14)



(15)

In all of these studies carried out over the first 15 years of his career, Henry Gilman established with his investigations of the Grignard reagent an exemplary paradigm of how an experimental chemist should determine the nature and scope of a chemical reaction. In a corpus of 125 publications he elucidated the preparative possibilities and limitations in forming the various Grignard reagents, the relative reactivities of various functional groups toward the carbon−magnesium bond, the compatibility or interference of functional groups in the presence of the C−MgBr bond, possible intermediates and reaction pathways, and the quantitative estimation of Grignard reagents in solution. Gilman himself followed his own *modus operandi*, formed in such Grignard studies, as he gradually and successively expanded his investigations to encompass organometallic compounds of lead, tin, beryllium, mercury, lithium, sodium, potassium, silicon, copper, aluminum, zinc, and, in some degree, most other main-group organometallics. In pioneering studies Gilman and his students demonstrated that with the few exceptions of copper and platinum (cf. infra) ordinary alkyls of transition metals are generally too unstable to be isolated at room temperature.

What was pivotal in aiding Gilman's studies of the preparations and reactions of other organometallic compounds was the discovery of a convenient preparation of a much more potent alkylating or arylating agent for metal salts (cf. eq 4) than organomagnesium compounds, namely, organolithium reagents. In 1930 Ziegler and Colonius described the first promising preparation of organolithium compounds in hydrocarbon and, in some cases, ether media.[42] Gilman immediately recognized the great potential of such lithium reagents as much more reactive organometallics than Grignard reagents and already in early 1932 published a markedly superior procedure for the preparation of alkyl and aryl organolithium reagents in diethyl ether.[43] Moreover, in that article and a succeeding publication[44] he stressed that special glass-sealed apparatus was not required, as previous work with alkali metals had prescribed but that ordinary apparatus used in Grignard preparations was directly suitable. Though the lithium reagents proved to be less stable in ethers, these donor solvents exhibited distinct advantages: subsequent studies showed that ethers accelerate the rates of many important organolithium reactions such as hydrogen−lithium, halogen−lithium, and metal-lithium exchange processes (cf. infra). Since Gilman's contributions to organolithium chemistry are inextricably bound up with those of two outstanding contemporaries working in Germany, Karl Ziegler and Georg Wittig, fairness and accuracy now require us to give pertinent biographical detail on these men as well.

The Era of the Organolithium Reagent, 1930−2000

Two Stellar Academicians from Marburg. Both Karl Ziegler (1898−1973) and Georg Wittig (1897−1987) studied chemistry at the University of Marburg and

---

[41] Price, C. C. *Organic Reactions*; Adams, R., Ed.; Wiley: New York, 1946; Vol. 3, Chapter 1.

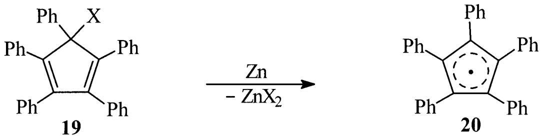
[42] Ziegler, K.; Colonius, H. *Liebigs Ann. Chem.* **1930**, *479*, 135.

[43] Gilman, H.; Zoellner, E. A.; Selby, W. M. *J. Am. Chem. Soc.* **1932**, *54*, 1957.

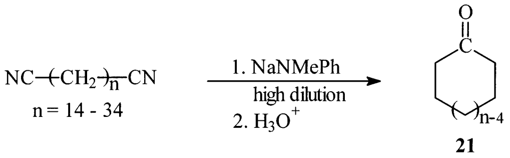
[44] Gilman, H.; Zoellner, E. A.; Selby, W. M. *J. Am. Chem. Soc.* **1933**, *55*, 1252.

conducted their doctoral research in organic chemistry under the direction of the renowned Karl von Auwers. Both came from educated families; Ziegler's father being a Lutheran pastor in Marburg and Wittig's father a professor of art in Kassel. Both Ziegler and Wittig evinced an early interest in science, and each set up a home laboratory in which to gratify his curiosity in chemical experimentation. This study permitted them to progress rapidly through their individual doctoral programs. Ziegler was somewhat ahead in his studies since he did not serve in the army as Wittig did. They remained close friends for the rest of their lives, seeking the opinion of the other on current chemistry issues in general and their own research projects in particular. In his academic career Ziegler attained a worldwide reputation while still in his 30s, while Wittig was well into his 50s before his research earned him recognition outside Germany. Yet again, both won the Nobel Prize in Chemistry, Ziegler in 1963, shared with Giulio Natta, and Wittig in 1979, shared with Herbert Brown, for contributions not directly concerned with organolithium chemistry but indirectly based on their fundamental studies with organolithium reagents. Many of the results of such studies were published during the period of 1933−1945, when the German government was preparing for and conducting war or in the aftermath of World War II, 1945−1950, and hence were disseminated worldwide only with serious delay. This led to similar organolithium experiments being conducted both in Gilman's laboratory and in the laboratories of his two German colleagues without each other's knowledge.

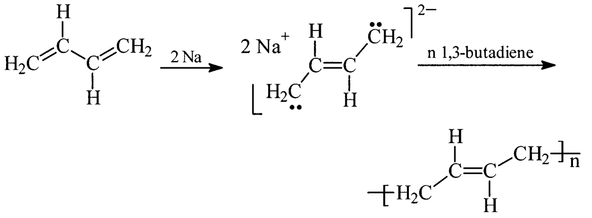
Karl Ziegler's Contributions to Organolithium Chemistry. Karl Ziegler launched a prodigious career by receiving his doctoral degree at the astonishing age of 21.[45] Only four years later, he had completed an independent research project at Marburg and submitted the results for his *Habilitation*, a degree necessary for scholars aspiring to a university teaching position. After a brief stay at the University of Frankfurt, Ziegler began a fruitful 10 years at the University of Heidelberg (1926−1936), where the three basic themes of his life's research had their start and where he would attain international recognition while still relatively young. These ongoing research topics proved to be (1) reactive and persistent carbon free radicals, such as the highly stable, monomeric **20**, prepared by the dehalogenation of halide **19** with alkali metals (eq 16); (2) the formation of medium-sized and many-membered organic rings (**21**) by base-promoted cyclization at high dilution (eq 17); and (3) the action of alkali metals and their organometallic derivatives on olefins, diolefins, and polyunsaturated hydrocarbons, such as involved in the sodium-catalyzed polymerization of butadiene discovered by Harries in 1910 (eq 18).



19 **20** (16)



21 (17)

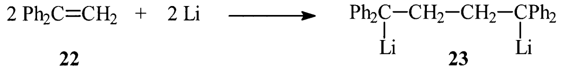


(18)

The last-mentioned research, subsequently continued while he was *Ordinarius Professor* at the University of Halle (1936−1943) and finally when Direktor of the Kaiser-Wilhelm (later, Max-Planck)-Institut für Kohlenforschung (1943−1969 at retirement), was to lead to Ziegler's keen interest in the reactions of organolithium reagents with simple olefins. Such research prompted Ziegler to explore in turn the analogous reactions of aluminum alkyls with olefins. In these last-mentioned studies, conducted in the early 1950s, Ziegler and coworkers made the serendipitous discovery that early transition-metal salts, such as those of titanium or zirconium, and aluminum alkyls caused the polymerization of ethylene without requiring heat or pressure.[45,46] This discovery, which earned for Ziegler the Nobel Prize, stemmed directly from his organoaluminum research and his prior organolithium studies.

Initially, Ziegler wished to compare the reactivity of lithium and its organolithium derivatives with that of sodium and potassium in butadiene polymerization. Hence, he required a convenient preparation of RLi types. Organolithium compounds of two extreme types were known to be accessible by methods developed by Schlenk before Ziegler published his general method in 1930. In one approach the diorganylmercury derivative was shaken with finely cut lithium metal in a hydrocarbon medium (eq 19), while in the other a conjugated hydrocarbon, such as **22**, added lithium metal and, in this case, dimerized to **23** (eq 20). In 1930 Ziegler and Colonius then showed that alkyl and aryl halides (X = Cl, Br, I) reacted smoothly in benzene or cyclohexane with lithium pieces to give the lithium reagent in high yields (eq 21).[42] Less satisfactory results were obtained in ether. By employing *n*-butyl chloride in hexane their method has remained eminently suitable for the commercial production of *n*-butyllithium, indefinitely stable in hexane. As previously mentioned, in 1932 Gilman introduced the procedure for the rapid preparation of the same RLi reagents, including methyllithium, in

$$(CH_3CH_2)_2Hg \ + \ 2\,Li \longrightarrow 2\,CH_3CH_2Li \ + \ Hg \qquad (19)$$



$$\underset{\textbf{22}}{2\,Ph_2C{=}CH_2} \ + \ 2\,Li \longrightarrow \underset{\textbf{23}}{Ph_2\underset{\displaystyle Li}{C}{-}CH_2{-}CH_2{-}\underset{\displaystyle Li}{C}Ph_2} \qquad (20)$$

$$R{-}X \ + \ 2\,Li \longrightarrow R{-}Li \ + \ LiX\downarrow \qquad (21)$$

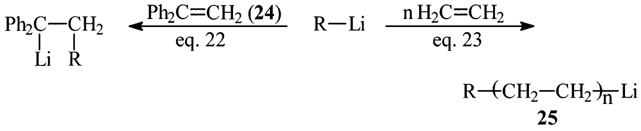
---

(45) A short biographical discussion of Karl Ziegler's career and scientific contributions to both pure and applied chemistry has been published by the present author: Eisch, J. J. *J. Chem. Educ.* **1983**, *60*, 1009.

(46) (a) Ziegler, K.; Holzkamp, E.; Breil, H.; Martin, H. *Angew. Chem.* **1955**, *67*, 541. (b) Ziegler, K.; Martin, H. *Makromol. Chem.* **1956**, *18/19*, 186.

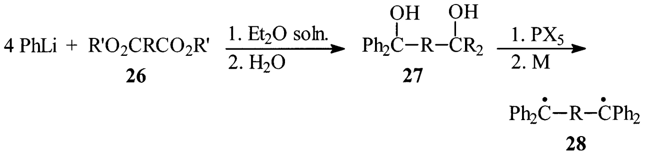
ether solution in yields that for aryllithium reagents generally were >85%, and >80% for alkyllithiums. Because of their reactivity toward ethers, such reagents have to be used promptly but can be stored for a time at 0 °C.[43,44]

In exploring the great reactivity of such novel RLi reagents Ziegler's principal finding was the generality of the carbolithiation by RLi of carbon–carbon double bonds, ranging from the highly conjugated, such as in 1,1-diphenylethylene (**24**), fulvenes, or azulenes (eq 22),[47–49] to the isolated olefinic linkage of ethylene (eq 23) to generate oligomer **25**.[50] Further noteworthy was the finding that the carbolithiation of eq 22 is markedly accelerated in diethyl ether over its rate in benzene: the reaction in benzene requires several days for completion, the reaction in ether, minutes. Since the carbolithiation product of a single ethylene in eq 23 is itself an alkyllithium, RCH_2CH_2Li, repeated carbolithiation could lead to an oligomerization of ethylene. This observation led Ziegler to investigate the action of aluminum alkyls on ethylene and thus to his unexpected discovery of the low-pressure polymerization of ethylene.

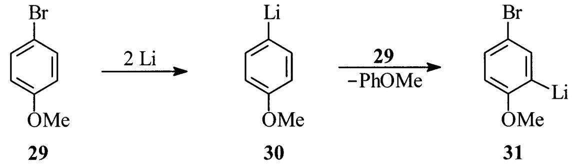


Georg Wittig's Discoveries in Organolithium Chemistry. After being awarded a doctorate in 1923 for research on aryl quinones, Wittig remained at Marburg to complete his *Habilitation* on chromones and coumarins in 1926 and to undertake independent research as a *Privatdozent* until 1932.[51] During this period he developed research foci in stereochemistry, free radicals, ring strain, and the preparative potential of organometallic derivatives of groups 1 and 2. Like his close colleague, Karl Ziegler, Georg Wittig found that his great passion for research lay in the fundamentals of what we would now term physical organic chemistry and the role of reactive intermediates. But his approach to such studies was less focused than Ziegler's, and he permitted unexpected experimental discoveries to guide his future experimentation. His subsequent academic appointments at Braunschweig (1932–1937), Freiburg (1938–1944), Tübingen as Ordinarius (1944–1956), and finally Heidelberg as Head of the Chemical Institute (1956–1967 at retirement) gradually narrowed and concentrated his interest upon organolithium reagents in organic chemistry and was to make the two decades of 1932–52 a most fruitful period of significant discoveries, centered on arynes, carbenes, anionic rearrangements, ylides, and hypervalent organometallics.

Scheme 3

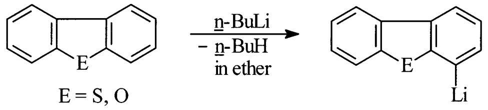


Scheme 4



Wittig was drawn to organolithium compounds in a search for a reagent to convert diesters (**26**) more efficiently into glycols (**27**), which were intermediates in novel biradical systems he was attempting to make (**28**). Noting that in 1930 Ziegler had discovered a highly convenient route to organolithium compounds, Wittig treated the diester **26** with phenyllithium in ether and found it greatly superior to the Grignard reagent for preparing the glycol **27** (Scheme 3).[52,53] When he attempted to use this approach for attaching *p*-anisyl groups to carbonyl centers, Wittig encountered the unexpected: *p*-bromoanisole (**29**) was converted, in part, not only into *p*-anisyllithium (**30**), but also into 2-bromo-5-anisyllithium (**31**) (Scheme 4).[54]

Wittig correctly deduced that a hydrogen–lithium exchange had taken place between **29** and **30** to generate **31** and anisole. Such lithiations at an unactivated C–H bond had been discovered in Henry Gilman's research group in 1934 and had been published in both a master's thesis[55a] and a doctoral dissertation.[55b] Gilman and Bebb finally did publish such lithiations of dibenzothiophene in the *Journal of the American Chemical Society* in 1939[56] and Gilman, Moore, and Baine a lithiation of dibenzofuran in 1941 (eq 24).[57] Thereafter, Gilman's group pursued this lithiation reaction in a systematic and consequential manner.[58] Wittig's discovery, which was published in 1938,[54] deserves to be recognized as a parallel, independent contribution, even though his group did not pursue their initial observation as thoroughly as did Gilman.



(24)

It is of further interest to note that in the same article[54] Wittig also reported the discovery of the halogen-lithiation exchange reaction, when he observed that phenyllithium reacted smoothly with 4,6-dibromoresorcinol dimethyl ether (**32**) in the manner shown in eq 25 to yield **33**. Thus, he was co-discoverer with

---

(47) Ziegler, K.; Crössmann, F.; Kleiner, H.; Schäfer, O. *Liebigs Ann. Chem.* **1929**, *473*, 1.

(48) Ziegler, K.; Schäfer, W. *Liebigs Ann. Chem.* **1934**, *511*, 101.

(49) Hafner, K.; Weldes H. *Angew. Chem.* **1955**, *67*, 302. N.B.: Hafner was a co-worker of Ziegler in the joint discovery of a new synthesis of azulenes: Ziegler, K.; Hafner K. *Angew Chem.* **1955**, *67*, 301.

(50) Ziegler, K.; Gellert, H. G. *Liebigs Ann. Chem.* **1950**, *567*, 195.

(51) The role of chemical fantasy in the pioneering contributions of Georg Wittig to the modern reality of organic and organometallic chemistry has been portrayed by the present author: Eisch, J. J. *J. Organomet. Chem.* **1988**, *356*, 271.

(52) Wittig, G.; Leo, M.; Wiemer, W. *Ber. Dtsch. Chem. Ges.* **1931**, *64*, 2405.

(53) Wittig, G.; Leo, M. *Ber. Dtsch. Chem. Ges.* **1931**, *64*, 2395.

(54) Wittig, G.; Pockels, U.; Dröge, H. *Ber. Dtsch. Chem. Ges.* **1938**, *71*, 1903.

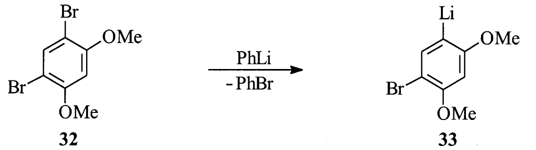
(55) (a) Hayes, D. M. M.S. Thesis, Iowa State College, 1934. (b) Bywater, W. G. Doctoral Dissertation, Iowa State College, 1934.

(56) Gilman, H.; Bebb, R. L. *J. Am. Chem. Soc.* **1939**, *61*, 109.

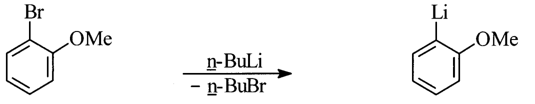
(57) Gilman, H.; Moore, F. W.; Baine, O. *J. Am. Chem. Soc.* **1941**, *63*, 2479.

(58) Gilman, H.; Morton, J. W., Jr. *Organic Reactions*; Adams, R., Ed.; Wiley: New York, 1954; Vol. 8, p 258.

Henry Gilman of an extremely important organolithium transformation, for in the same year Gilman described the conversion of **34** into **35** by *n*-butyllithium (eq 26).[59] Here again, Gilman and co-workers mapped out the scope and limitations of this unusual reaction in a masterly series of investigations (cf. infra).[60,61]



32 **33** (25)

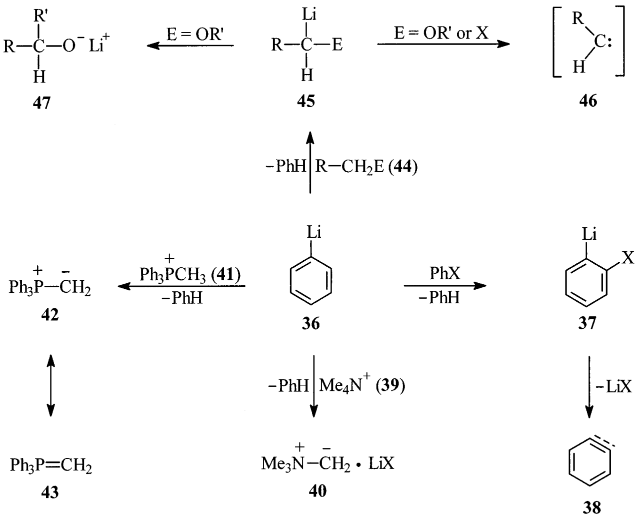


34 **35** (26)

In Wittig's hands, phenyllithium (**36**) now served as the "master key" for opening up hidden possibilities in the area of unusual, highly reactive carbanionic intermediates (Scheme 5).[62] Through the proton-abstracting ability of phenyllithium toward weak carbon acids, Wittig was able to convert haloarenes into *o*-lithiohaloarenes (**37**), which were shown to serve as aryne precursors (**38**);[63] quaternary ammonium salts (**39**) were converted in trialkylammonium methylides (**40**);[64] phosphonium salts (**41**) were analogously transformed into phosphonium ylides (**42**) or phosphoranes (**43**);[65] and alkyl ethers or halides (**44**, E = OR or X) underwent α-lithiation to **45**.[66] The lithiated intermediate **45** was shown to undergo either α-elimination to produce carbenes[67] (**46**) or rearrangement in the case of ethers to yield alkoxides (**47**).[68] The latter novel transformation has been recognized in the chemical literature as the Wittig ether rearrangement.[69]

Besides carbanionic rearrangements, however, all other transformations depicted in Scheme 5 have had a profound impact on different aspects of modern organic chemistry, once such findings were merged with contemporaneous studies conducted in Henry Gilman's laboratory before, during, and in the aftermath of World War II. Delays in scientific publication appreciably retarded widespread awareness of advances made in organolithium research during this period, such as Henry Gilman's important contributions to the lithium–hydrogen and lithium–halogen exchange reactions, diverse transmetalation reactions, and solvent effects. These important discoveries now merit our attention.

Scheme 5



Henry Gilman's Promotion of Organolithium Compounds as Versatile Reagents in Organic and Organometallic Synthesis. What clearly differentiates the contributions of Henry Gilman to organolithium chemistry from those of Georg Wittig or Karl Ziegler was Gilman's focused interest in the carbon–lithium bond in all of its structural variants, be they alkyl, aryl, allylic, acetylenic, or heterocyclic. Ziegler was particularly concerned with the addition of lithium alkyls to C=C bonds (carbolithiation, eqs 22 and 23), while on the other hand, Wittig sought to learn what variety of reactive intermediates could become accessible by lithiating various organic substrates with phenyllithium (lithium–hydrogen exchange, Scheme 5). From his first investigations of organolithium reagents in 1932, Gilman sought to understand how the R group in the RLi reagent influenced both the kind of reaction undergone by the organic substrate and the relative *rate* of such a reaction. Such findings have proved indispensable in making particular RLi compounds highly efficient, selective, and convenient for organic synthesis.

A second important discovery by Gilman was that RLi reagents with the most various R groups were superior reagents to RMgX compounds in the alkylation–arylation reaction depicted in eq 5, whereby a new carbon–metal bond can be generated and a different organometallic compound synthesized (eq 5a). This general

$$MX_n + n\,RLi \longrightarrow R_nM + n\,LiCl \qquad (5a)$$

method has proved applicable in many cases where the substitution involving the corresponding Grignard reagent failed (eq 5). Moreover, owing to the many preparative routes to the specific RLi reagent now possible, the organolithium compound required is often readily accessible while the requisite Grignard reagent is not.

With such greatly improved access to every type of main-group organometallic compound and some transition-metal examples as well, Gilman was then able to compare the chemical reactivity of the different organometallics generated. From such observed reactivities he then attempted to discern correlations based upon the individual metal's position in the periodic table. We shall examine each of the foregoing aspects resulting

---

(59) Gilman, H.; Jacoby, A. L. *J. Org. Chem.* **1938**, *3*, 108.

(60) A further defined and optimal procedure for preparing *n*-butyllithium for use in halogen–lithium exchange was finally published in 1949: Gilman, H.; Beel, J. A.; Brannen, C. G.; Bullock, M. W.; Dunn, G. E.; Miller, L. S. *J. Am. Chem. Soc.* **1949**, *71*, 1499.

(61) Jones, R. G.; Gilman, H. In *Organic Reactions*; Adams, R., Ed.; Wiley: New York, 1951; Vol. 6, p 339.

(62) Wittig, G. *Naturwissenschaften* **1942**, *30*, 696.

(63) Wittig, G.; Merkle, W. *Ber. Dtsch. Chem. Ges.* **1942**, *75*, 1491.

(64) Wittig, G.; Wetterling, M. H. *Liebigs Ann. Chem.* **1944**, *557*, 193.

(65) Wittig, G.; Rieber, H. *Liebigs Ann. Chem.* **1949**, *562*, 177.

(66) Wittig, G.; Löhmann, L. *Liebigs Ann. Chem.* **1942**, *550*, 260.

(67) Schöllkopf, U.; Eistert, M. *Liebigs Ann. Chem.* **1949**, *562*, 192.

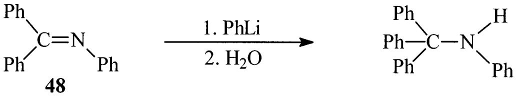
(68) Wittig, G.; Döser, H.; Lorenz, I. *Liebigs Ann. Chem.* **1949**, *562*, 192.

(69) Schöllkopf, U. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 763.

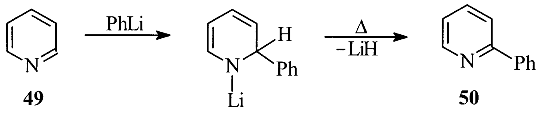
from Gilman's research with organolithium compounds. Such considerations give substance to the opinion that Henry Gilman has been the outstanding integrating pioneer in modern organometallic chemistry.

Henry Gilman: the Great Systematizer of Organometallic Chemistry

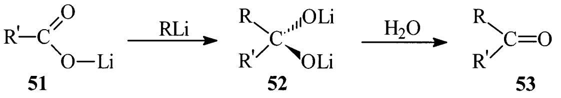
Organolithium Compounds as "Super Grignard Reagents". After the publication of more convenient, general preparations of alkyl- and aryllithium reagents in the early 1930s by Ziegler[42] and by Gilman,[43,44] studies of their reactions toward typical organic substrates showed that the lithium reagent undergoes all of the reactions of its Grignard counterpart but more rapidly and completely. Furthermore, in certain cases the RLi and RMgBr reagents have been shown to behave differently. Gilman and Kirby found that phenyllithium readily adds to benzophenone anil (**48**) in the expected 1,2-manner (eq 27),[70] which contrasts sharply with phenylmagnesium bromide, which requires higher temperatures to react and then adds only in a 1,4-fashion (eq 5 via intermediate **13**).[32] Similarly, Ziegler and Zeise had observed that phenyllithium adds readily to the supposedly deactivated, aromatic C=N bond of pyridine (**49** → **50**, eq 28), while the phenyl Grignard reagent fails to react.[71,72] Gilman also discovered that RLi reagents could add to other systems usually inert toward RMgX. An example is the addition of RLi to lithium salts of carboxylic acids (**51**), a useful synthesis of ketones (**53**) (eq 29) via the stable salt **52**,[73] which has become known as the Gilman−Van Ess reaction.[74]



(27)



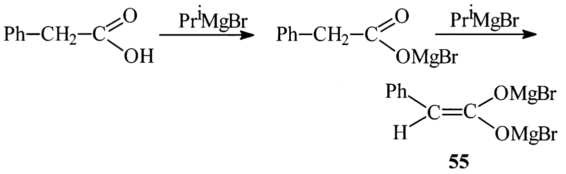
(28)



(29)

However, another reaction achievable with Grignard reagents and only few Brønsted acids, namely, the metalation or the metal−hydrogen exchange reaction, was to attain extraordinary scope and utility when organolithium reagents were employed. Magnesiations by Grignard reagents have been shown to be limited to terminal alkynes (**54**, eq 30), cyclopentadienes, indenes, and enolizable carbonyl derivatives, such as that involved in preparing the Ivanov reagent (**55**, eq 31).[23] (It should be noted that such enolate salts as **55** and as the Reformatskii reagent shown earlier (**3**) are not genuine organometallics, since they lack a C−M bond.)

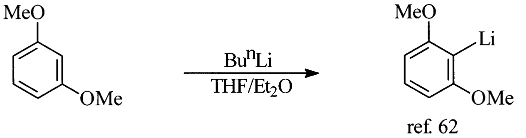
$$CH_3CH_2MgBr + \underset{\mathbf{54}}{Ph{-}C{\equiv}C{-}H} \longrightarrow Ph{-}C{\equiv}C{-}MgBr + C_2H_6\uparrow \qquad (30)$$



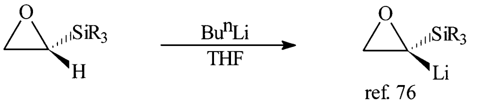
(31)

Because of such limitations in the magnesiation reaction, it has proved to be of decisive importance that both Gilman and Wittig independently discovered the facile lithiation of polar sp^2-hybridized and sp^3-hybridized C−H bonds in ether solution and at lower temperatures. In our previous discussion we have already learned how Wittig utilized such lithiations to generate precursors to carbenes, arynes, and ylides, as well as initiators of elimination or rearrangement reactions. But it was Henry Gilman who undertook and completed a masterly survey of the scope and limitations of the lithiation reaction itself. He thus established lithiation as versatile and invaluable methodology in organic synthesis and thereby encouraged other organic chemists to explore the power of this novel reaction.[61] His use of THF to enhance the rate of such lithiations and his careful determination of the temperatures and times for which such RLi reagents will be stable proved of crucial importance for applications in organic synthesis.[75]

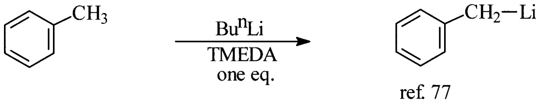
A wide array of preparatively useful lithiations by *n*-butyllithium is offered in eqs 32−36. In determining the fostering effect of Lewis-base solvents or promoters



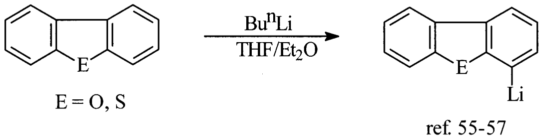
(32)



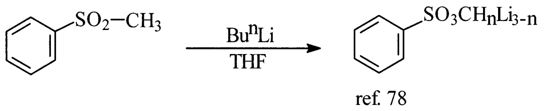
(33)



(34)



(35)



(36)

---

[70] Gilman, H.; Kirby, R. H. *J. Am. Chem. Soc.* **1933**, *55*, 2609.

[71] Ziegler, K.; Zeiser, H. *Ber. Dtsch. Chem. Ges.* **1930**, *63B*, 1847.

[72] Prolonged heating in ether of more reactive Grignard reagents, such as allylmagnesium bromide, leads to small amounts of 1,4-addition product: Gilman, H.; Eisch, J.; Soddy, T. *J. Am. Chem. Soc.* **1957**, *79*, 1245.

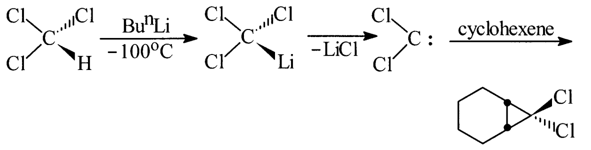
[73] Gilman, H.; Van Ess, P. R. *J. Am. Chem. Soc.* **1933**, *55*, 1258.

[74] Schöllkopf, U. *Methoden der Organischen Chemie (Houben-Weyl)*; Müller, E., Ed.; Thieme Verlag: Stuttgart, 1970; Vol. XIII/1, p 184.

[75] (a) Mallan, J. M.; Bebb, R. L. *Chem. Rev.* **1969**, *69*, 693. (b) Schöllkopf, U. *Methoden der Organischen Chemie Houben-Weyl*; Müller, E., Ed.; Thieme Verlag: Stuttgart, 1970; Vol. XIII/1, pp 97−126.

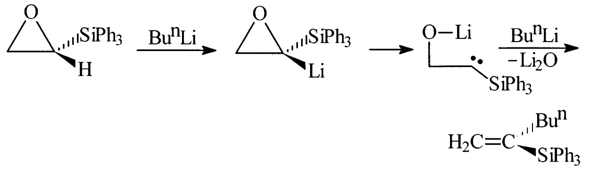
on such lithiations, Gilman, Wittig, H. Normant, Langer, and others had helped to achieve a more rapid lithiation of the organic substrate without the undesirable destructive lithiation of the solvent.

Both Gilman's and Wittig's particular contribution to the lithiation reaction has been to encourage researchers to generate reactive intermediates by lithiation under mild conditions as a powerful probe of organometallic reaction mechanisms. A variety of such studies for carbenes (eqs 37, 38) and arynes (eqs 39, 40) give a vivid impression of the power of this approach.



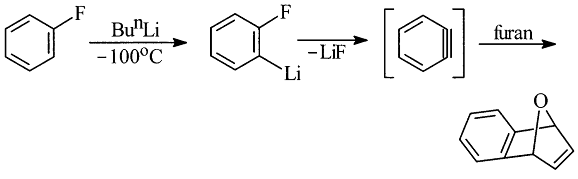
(37)

ref. 79, 80



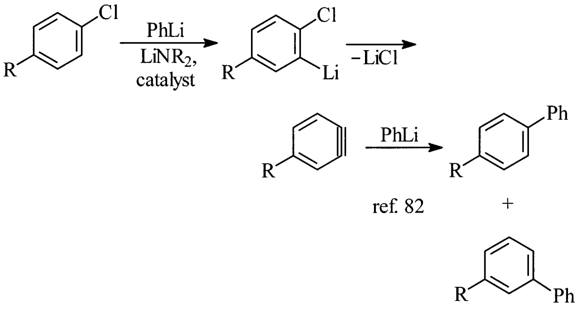
(38)

ref. 76b



(39)

ref. 81

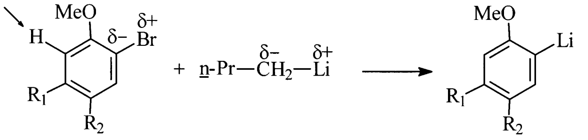


(40)

Another reaction of organolithium compounds that has set them apart from the corresponding Grignard reagent is the lithium−halogen exchange reaction, which is generalized in eq 41.

$$\mathrm{R{-}Li} + \mathrm{R'{-}X} \longrightarrow \mathrm{R{-}X} + \mathrm{R'{-}Li} \quad (41)$$

In the foregoing discussion of the lithiation reaction we have seen how even the slight positive polarization of the hydrogen of the carbon−hydrogen bond permits rapid reaction. Even though hydrogen is formally a nonmetal, Pauling's initial electronegativity scale in the 1930s had assigned carbon a greater electron-attracting power (C, 2.50 vs H, 2.2). Accordingly, the exchange of hydrogen for lithium does not violate expectations based on bond polarities. But, as mentioned above, in 1938 an exchange reaction incongruous with the accepted bond polarities of carbon−halogen bonds was reported independently by the laboratories of Henry Gilman[59] and those of Georg Wittig.[54] In each case, an *o*-bromoanisole (**56**) was treated with *n*-butyllithium in ether. Instead of the expected lithiation *ortho* to the methoxyl group (arrow), lithium−bromine exchange occurred. Noteworthy are the assumed polarities of the C−Br and C−Li bonds in light of Pauling electronegativities (C, 2.5 vs Br, 2.8) (eq 42). Subsequently, in pioneering and

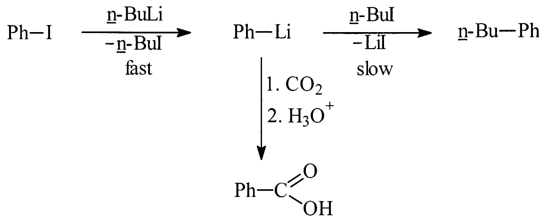


(42)

56, R_1, R_2 = H (Gilman)
R_1 = MeO; R_2 = Br (Wittig)

comprehensive studies by Gilman's group this exchange was found to proceed more readily with organic iodides and more slowly with chlorides. Furthermore, this reaction proved to be a kinetically controlled forerunner of an ultimately thermodynamically determined lithium-alkyl exchange or coupling.[61] Illustrative of these two processes is the interaction of *n*-butyllithium and iodobenzene depicted in Scheme 6. The initial lithium−iodine exchange occurs rapidly in ether even at low temperatures to produce phenyllithium, which can be trapped by CO_2, but at prolonged time and at 25 °C ultimate coupling leads to *n*-butylbenzene. It should be noted that in the latter coupling the expected bond polarities do accord with the observed reaction.

Scheme 6



The lithium−halogen exchange has been shown to provide highly selective and often unique access to a wide variety of lithium derivatives, difficult to produce by any other method. The following transformations survey the considerable scope of the method (eqs 43−47).[61] In principle, at any site on a vinylic chain or an aromatic or heterocyclic ring where a Br or I substituent can be introduced, this lithium−halogen exchange permits a lithium−carbon bond to be generated.

With the realization that a simple polar view cannot explain lithium−halogen exchange, much study has been devoted to this mechanistic conundrum over the last six decades. Evidence suggesting the role of *ate*-complexes (**58**), especially with iodides, and/or of radical-

---

(76) (a) Eisch, J. J.; Galle, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 4646. (b) Eisch, J. J.; Galle, J. E. *J. Organomet. Chem.* **1976**, *127*, C9. (c) Eisch, J. J.; Galle, J. E. *J. Org. Chem.* **1976**, *41*, 2615.

(77) (a) Eberhardt, G. G.; Butte, W. A. *J. Org. Chem.* **1964**, *29*, 2928. (b) Langer, A. W., Jr. *Trans. N. Y. Acad. Sci* **1965**, *27*, 141.

(78) (a) Eisch, J. J.; Galle, J. E. *J. Org. Chem.* **1980**, *45*, 4534. (b) Eisch, J. J.; Dua, S. K.; Behrooz, M. *J. Org. Chem.* **1985**, *50*, 3674.

(79) (a) Hoeg, D. F.; Lusk, D. I.; Crumbliss, A. L. *J. Am. Chem. Soc.* **1965**, *87*, 4147. (b) Köbrich, G. *Angew. Chem.* **1967**, *79*, 15.

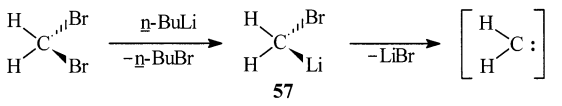
(80) Closs, G. L.; Closs, L. E. *J. Am. Chem. Soc.* **1960**, *82*, 5723.

(81) Gilman, H.; Soddy, T. S. *J. Org. Chem.* **1957**, *22*, 1715.

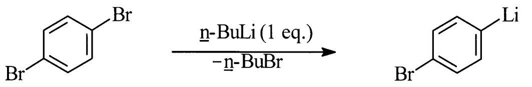
(82) Huisgen, R.; Sauer, J. *Angew. Chem.* **1960**, *72*, 91.

(83) (a) Kirmse, W. *Angew Chem.* **1961**, *73*, 540. (b) Eisch, J. J.; Kovacs, C. A.; Chobe, P. *J. Org. Chem.* **1989**, *54*, 1275.

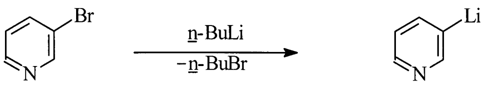
Generation of carbenes from carbenoid sources (**57**):[83a]


(43)

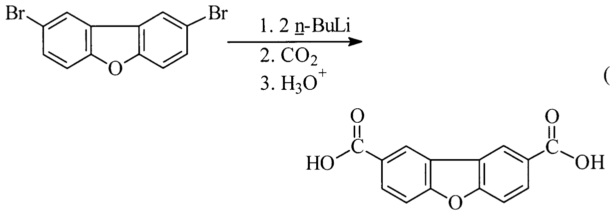
Selective exchange of one halogen:


(44)

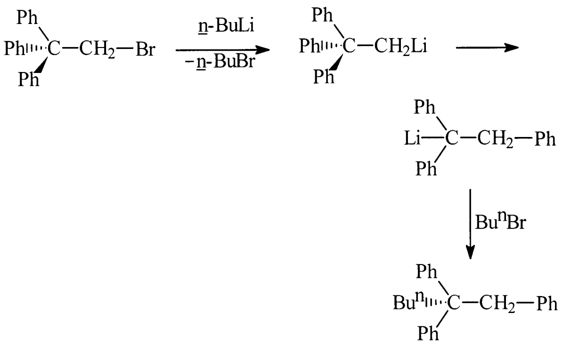
Formation of 3-pyridyllithium without RLi-addition to the C=N bond:


(45)

Alternative to Grignard formation with aryl halides:


(46)

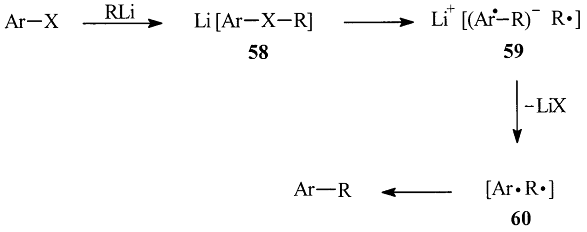
Generation of intermediates to carbanionic rearrangement:[83b]


(47)

anions (**59**)[84–86] has been obtained and some type of electron transfer may be involved, possibly as shown in Scheme 7, where radical-anion, **59**, generates a radical pair trapped in a solvent cage (**60**) until coupled.[87,88]

Despite such mechanistic complexities Gilman brought the same masterly focus to his study of lithium–halogen exchange as he had applied to the lithiation reaction. His explorations of the scope and limitations of both processes were invaluable in advocating the use of these reactions in organic synthesis and in the study of reaction mechanisms. Although he was the sole discoverer of neither the lithium–hydrogen exchange, Schlenk and Ziegler having made initial observations, nor of the lithium–halogen exchange, where Wittig shared in the discovery, his significant, intensive, and pioneering investigations transformed both exchange reactions into reliable methodology. His personal accounts of his logical and useful studies appear in the authoritative series *Organic Reactions*.[58–61] In assessing Henry Gilman's contributions to the lithium–hydrogen exchange reaction in light of Ziegler's prior work and Gilman's key discoveries to the lithium–halogen exchange reaction compared with Wittig's contemporaneous studies, we stress that Gilman regularly employed *n-butyllithium*, in contrast to Ziegler and Wittig, who chose *phenyllithium* as the reagent in these reactions. Gilman thereby established what chemists now have come to recognize: from a standpoint of reaction rates and thermodynamics, *n*-butyllithium is far superior to phenyllithium in establishing C–Li bonds from a wide variety of C–H and C–X linkages. In view of this background, this writer suggests that there is substantial merit in referring to such reactions as the Gilman lithiation and the Gilman-Wittig lithium–halogen exchange, respectively.

Scheme 7



Organolithium Compounds as Superior Alkylating or Arylating Agents. Since the thermodynamic driving force for any metal–metal exchange reaction lies in the greater stability of the inorganic products, this exchange would be expected to be favored for organolithium reagents over organomagnesium compounds (eqs 48a, 48b). The greater lattice energy of *n* moles of lithium halides over *n*/2 mol of magnesium halides would be decisive for the reactions leading to metal salts in their solid state. For such reactions generating products in solution, the greater thermochemical heat of formation of such lithium salts in solution would be determinant. Actually, organoalkali reagents of sodium or higher group 1 metals would be even more suitable alkylating or arylating agents from a thermodynamic standpoint. The difficulty with their use lies in their insolubility in or reactivity toward any potential solvent. Hence, organolithium reagents, which can be dissolved in hydrocarbons or, even for short periods, in ethers, have proved to be eminently applicable to Gilman's alkylation studies in homogeneous media. Furthermore, from the greater number of preparative routes available for the lithium reagents, compared with Grignard reagents, the nature of the R in RLi could be varied almost ad libitum for transfer to the new metal center (eq 48). In cases where the lithium reagent proves too reactive and leads to complete arylation (eq 49b), the Grignard reagent then is to be preferred (eq 49a).[89] In other instances, the desired organometallic product may

$$R_nM \underset{\textbf{b}}{\xleftarrow[-n/2\,MgX_2]{n/2\,R_2Mg}} MX_n \underset{\textbf{a}}{\xrightarrow[-nLiX]{n\,RLi}} R_nM \qquad (48)$$

---

(84) (a) Eisch, J. J. *Res. Chem. Intermed.* **1996**, *22*, 145. (b) Panek, E. J. *J. Am. Chem. Soc.* **1973**, *95*, 8461.

(85) Reich, H. J.; Green, D. P.; Phillips, N. H. *J. Am. Chem. Soc.* **1991**, *113*, 1414, and references therein.

(86) Winkler, H. J. S.; Winkler, H. S. *J. Am. Chem. Soc.* **1966**, *88*, 964, 949.

(87) Lepley, A. R.; Landau, R. L. *J. Am. Chem. Soc.* **1969**, *91*, 748.

(88) Schöllkopf, U. *Methoden der Organischen Chemie Houben-Weyl*; Müller, E., Ed.; Thieme Verlag: Stuttgart, 1970; Vol. XIII/1, p 150.

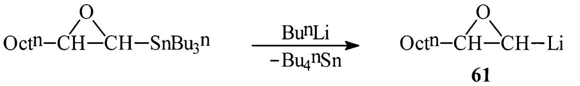
(89) Gilman, H.; Brannen, C. G. *J. Am. Chem. Soc.* **1950**, *72*, 4280.

form stable complexes with ethers (eqs 50b), so that the availability of the lithium reagent in hydrocarbon solution (used stoichiometrically, eq 50a) offers obvious advantages. Furthermore, transmetalation reactions can occur between lithium reagents and organometallics of less active metals, as first observed by Schlenk[90] and extensively developed by Gilman, Seyferth, and Nesmeyanov.[91−93] Two examples of such preparatively useful metal−metal exchanges for generating difficultly accessible lithium reagents themselves are given in eqs 51 and 52.[93,94]

$$(2\text{-}C_{10}H_7)_4Si \underset{\mathbf{b}}{\xleftarrow[\text{4 equiv., – 4 LiCl}]{\text{2-Naphthyllithium}}} SiCl_4 \underset{\mathbf{a}}{\xrightarrow[\text{3 equiv., – 3 PhMgBr}]{\text{2-Naphthyllithium}}} (2\text{-}C_{10}H_7)_3SiCl \qquad (49)$$

$$Bu^n{}_3Al \cdot OEt_2 \underset{\mathbf{b}}{\xleftarrow[\text{in ether}]{3\ Bu^nMgBr}} AlCl_3 \underset{\mathbf{a}}{\xrightarrow[\text{in hexane}]{3\ Bu^nLi}} Bu^n{}_3Al \qquad (50)$$

$$(H_2C{=}CH)_4Sn \xrightarrow[-Ph_4Sn]{4\ PhLi} H_2C{=}CHLi \qquad (51)$$



61

(52)

Alkylations or arylations with lithium or Grignard reagents were employed by Gilman and co-workers over a period of 50 years to prepare a great array of organometallic compounds of beryllium and main-group metals of groups 11, 12, 13, 14, and 15, as well as certain transition metals such as copper and platinum bearing a variety of organic groups. Attempts to synthesize homoleptic alkyl derivatives of many transition metals were uniformly unsuccessful because of rapid thermal decomposition of such labile R_nM_t compounds at room temperature. The results of Gilman's studies of such alkylations or arylations have appeared in several hundred publications, and the interested reader is referred to an extensive review published by Jones and Gilman for the principal findings of such studies up to 1954.[96] Detailed evaluation of Gilman's transmetalation work is therefore neither necessary nor appropriate here, but it is worthwhile to point out that certain transmetalations studied by Gilman have gained in significance and value in subsequent research. First of all is the metal−metal exchanges already cited in eqs 51 and 52 as an important route to both useful and highly unstable lithium reagents, such as **61**. Second, of the two reactive organocopper compounds, **62** and **63**, first prepared by Gilman,[97,98] **63** was later found by Whitesides, by House, and by Corey to be an excellent cross-coupling reagent with organic bromides or iodides (forming **64**)[99] and an alkylating agent capable of conjugate addition to α,β-unsaturated carbonyls forming **65**.[100] In such reagents, R can be other than Me (Scheme 8). Corey has advocated that $[R_2Cu]Li$ compositions, lithium diorganylcuprates, be termed Gilman reagents.

Third, conversion of Grignard reagents into the corresponding organozinc compound was found by Blaise[101] to yield a reagent for the efficient conversion of acid chlorides into ketones (**66**) (Scheme 9). But in 1936 Gilman and Nelson[102] demonstrated that organocadmium derivatives generated by the RMgX alkylation of cadmium halides proved more satisfactory. This approach was taken up by Cason and developed into an efficient synthesis of unsymmetrical ketones from acyl chlorides,[103] which methodology could properly be then named the Cason−Gilman reaction.[104]

Fourth, by treatment of copper(I), silver(I), and gold(III) halides with Grignard and lithium reagents Gilman was able to isolate or detect unstable phenylcopper, phenylsilver, and trimethylgold and to determine that thermal stability decreased in the order Cu > Ag > Au.[97,105,106]

Fifth, in an attempt to prepare new methylplatinum(IV) derivatives and hexamethyldiplatinum, Gilman found that the reaction of $PtCl_4$ with MeMgI (eq 53) took an unexpected and complicated course. In addition to the verified formation of Me_3PtI and Me_2PtI_2, Gilman concluded from analytical data that Me_4Pt and $Me_3Pt{-}PtMe_3$ were formed as well.[107] Despite Gilman's claimed synthesis of $Me_3Pt{-}PtMe_3$ according to eq 54[108] and despite supposedly corroborative data from Rundle's group (later proved wrong),[109,111] prevailing opinion is that authentic Me_4Pt and $Me_3Pt{-}PtMe_3$ have not yet been prepared.[111] Again, the thermal instability of the carbon−transition metal bond leads to organometallic reactions of great complexity. In a related study the thermal instability of the nine late transition-metal phenyl derivatives formed according to eq 55 was assessed by the yield of biphenyl formed at −20 °C. Similar studies were carried out on the thermal insta-

---

(90) Schlenk, W.; Holtz, J. *Ber. Dtsch. Chem. Ges.* **1917**, *50*, 271.

(91) Leading reference: Gilman, H.; Moore, F. W.; Jones, R. G. *J. Am. Chem. Soc.* **1941**, *63*, 2482.

(92) Leading reference: Seyferth, D.; Vaughan, L. G. *J. Am. Chem. Soc.* **1964**, *86*, 883.

(93) Survey of transmetalation: Schöllkopf, U. *Methoden der Organischen Chemie (Houben-Weyl)*; Müller, E., Ed.; Thieme Verlag: Stuttgart, 1970; Vol. XIII/1, pp 130−134.

(94) Seyferth, D.; Weiner, M. A. *J. Am. Chem. Soc.* **1961**, *83*, 3583.

(95) Eisch, J. J.; Galle, J. E. *J. Organomet. Chem.* **1988**, *341*, 293.

(96) Jones, R. G.; Gilman, H. *Chem. Rev.* **1954**, *54*, 835.

(97) Gilman, H.; Straley, J. M. *Rec. Trav. Chim.* **1936**, *55*, 821.

(98) Gilman, H.; Jones, R. G.; Woods, L. A. *J. Org. Chem.* **1952**, *17*, 1630.

(99) Corey, E. J.; Posner, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 3911.

(100) Posner, G. H. In *Organic Reactions*; Dauben, W. G., Ed.; Wiley: New York, 1972; Vol. 19, p 1.

(101) Blaise, E. *Bull. Soc. Chim. Fr.* **1911**, *9* (4), 1.

(102) Gilman, H.; Nelson, J. F. *Rec. Trav. Chim.* **1936**, *55*, 518.

(103) Cason, J.; Prout, F. S. *Org. Synth.* **1948**, *28*, 45.

(104) Shirley, D. A. In *Organic Reactions*; Adams, R., Ed.; Wiley: New York, 1954; Vol. 8, p 28.

(105) Gilman, H.; Parker, H. H. *J. Am. Chem. Soc.* **1924**, *46*, 2823.

(106) Gilman, H.; Woods, L. A. *J. Am. Chem. Soc.* **1948**, *70*, 550.

(107) Gilman, H.; Lichtenwalter, M.; Benkeser, R. A. *J. Am. Chem. Soc.* **1953**, *75*, 2063.

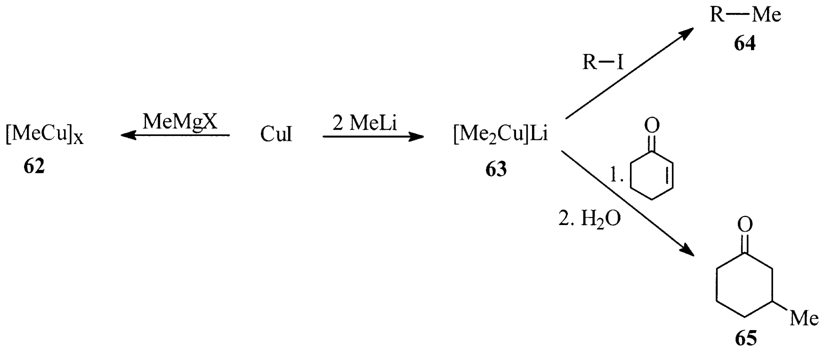
(108) Gilman, H.; Lichtenwalter, M. *J. Am. Chem. Soc.* **1938**, *60*, 3085.

(109) Rundle, R. E. *J. Am. Chem. Soc.* **1947**, *69*, 1327.

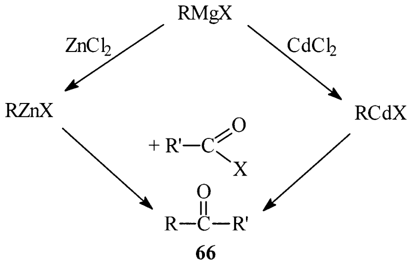
(110) Rundle, R. E. *J. Am. Chem. Soc.* **1947**, *69*, 1561.

(111) Hartley, F. R. In *Comprehensive Organometallic Chemistry*; Wilkinson, G., Stone, F. G. A., Abel, E. W., Eds.; Pergamon: Oxford, 1982; Vol. 6, p 585.

Scheme 8



Scheme 9



bility of early transition and lanthanide methyl and ethyl derivatives as well (M_t = Ti, Zr, and La).[112–114]

$$PtCl_4 + n\,MeMgI \longrightarrow Me_3PtI + Me_2PtI_2 + Me_4Pt\,(?) + Me_3Pt\text{–}PtMe_3\,(?) \tag{53}$$

$$2\,Me_3PtI + K \xrightarrow{\text{benzene}} Me_3Pt\text{–}PtMe_3\,(?) \tag{54}$$

$$MtX_n + n\,PhMgBr \longrightarrow [M_tPh_n] \longrightarrow \underset{98\text{-}100\%\ (\text{except Os, Ir, Pt})}{Ph\text{–}Ph} \tag{55}$$

M_t = Fe, Co, Ni, Ru, Rh, Ag, Ir, Pt, Au

In all these variants of the alkylation reaction, the work of Gilman and students has established the pioneering precedents in making such lithium–metal exchanges of comparable importance to lithium–hydrogen and lithium–halogen exchanges in organic synthesis. Furthermore, such alkylations in organometallic synthesis have made available organometallic derivatives of most main-group metals, whose R ligands can be of almost any desired character. Gilman was to study the relative reactivities of such organometallic derivatives toward organic substrates as a function of the metal, the R ligands on the metal, and the reaction solvent. Such studies would constitute his *magnum opus*.

Relative Reactivities as an Integrating Principle in Organometallic Chemistry. Shortly after Gilman developed his procedure for the convenient preparation of organolithium compounds in ether,[43,44] he decided to assess their reactivity and modes of reaction compared with those of organomagnesium compounds. For example, he was greatly interested in their different behavior toward benzophenone anil (eq 5 versus eq 27).[32,70] The methodology developed by Gilman for making this specific comparison of organolithium reagents with those of organomagnesium compounds was to be very effective in establishing reactivity gradations for main-group organometallics in general.

In 1933 he began to publish a series of studies entitled “The Relative Reactivities of Organometallic Compounds”, which initially would compare the modes and rates of reaction of Grignard reagents with those of their organolithium counterparts. Thus in the first publication Gilman and Kirby examined the reaction of organomagnesium and organolithium reagents with typical substrates, such as benzonitrile, benzyl chloride, dialkyl sulfates, anils, furfural, and hindered ketones.[76] In all cases, phenyllithium proved to be much more reactive than phenylmagnesium bromide, and *n*-butyllithium was shown to surpass phenyllithium in reactivity. Since the state of association and solvation of most organometallic compounds was unknown at the time, the different rates of reaction and modes of reaction of PhMgBr and PhLi were suggested to stem from steric factors, which would hinder approach of the bulkier Grignard reagent to the organic substrate. The greater reactivity of *n*-butyllithium over that of phenyllithium was likewise imputed to steric factors.

These comparative reactivity studies were to be gradually extended to many other organometallic derivatives of groups 1, 2, 11, 12, 13, 14, and 15 and were to be published over the next 20 years in more than 70 subsequent articles. These results comprise an invaluable body of empirical information not only for organolithium reagents but for almost every other main-group organometallic or organometalloid compound as well. From this wealth of experimental observations made in both Gilman’s laboratory and those of his contemporaries, Gilman formulated a series of 10 empirical rules of carbon–metal bond reactivity exhibited in typical addition reactions to carbonyl and cyano substrates.[115] Expressed in terms of the Mendeleev periodic groups and families, these reactivity trends would eventually thus lend themselves to the same electronic explanation that might be conceived for interpreting the periodicity shown in the properties of the elements themselves or their compounds. For example, Rule 1 states that the organometallic compounds in the A-families of the first three groups of Mendeleev’s periodic table (groups 1, 2,

---

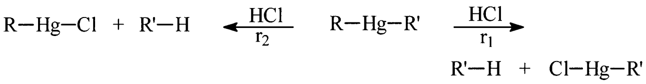
(112) Gilman, H.; Lichtenwalter, M. *J. Am. Chem. Soc.* **1939**, *61*, 957.

(113) (a) Gilman, H.; Jones, R. G. *J. Org. Chem.* **1945**, *10*, 505. (b) Studies with rhenium salts: Gilman, H.; Jones, R. G.; Moore, F. W.; Kolbezen, M. J. *J. Am. Chem. Soc.* **1941**, *63*, 2525.

(114) Gilman, H.; Jones, R. G.; Woods, L. A. *J. Am. Chem. Soc.* **1954**, *76*, 3615.

(115) Gilman, H. In *Organic Chemistry: An Advanced Treatise*, 2nd ed.; Gilman, H., Ed.; Wiley: New York, 1943; Vol. 1, p 489.

Scheme 10



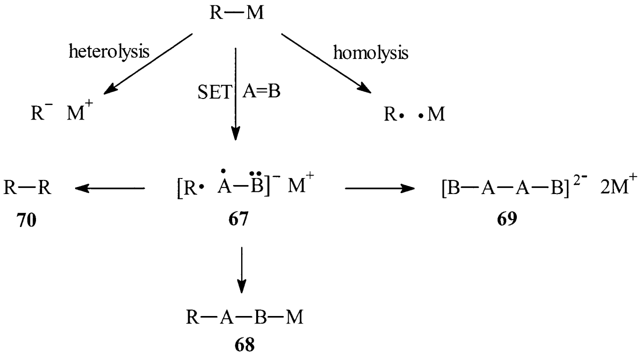
and 13 (partly) in our modern terminology) increase in reactivity with increasing atomic weight or atomic number. This rule reflects the observed trends: (1) Li, Na, K, Rb, Cs; (2) Be, Mg, Ca, Sr, Ba, (Ra, proposed); and (3) B, Al (with Ga, In, and Tl considered as B-family members). Further, Rule 2 observes that the organometallic compounds of the B-families of the first three groups (groups 3, 11, and 12 in modern terms) generally decrease in reactivity with increasing atomic weight. The experimentally observed gradations are (1) Cu, Ag, Au; (2) Zn, Cd, Hg; and (3) In, Ga, Tl (with Ga being an exception). Finally Rule 3 has also proved to be of enduring value: in the A-families of the first three groups the reactivity of the organometallics in a given period decreases with the group number. Thus, the reactivity trends are (1) Li, Be, B; (2) Na, Mg, Al; and (3) K, Ca, Sc(?).

The other seven rules either are subsidiary to the first three rules or by Gilman's admission are based upon much more limited experimental data, especially for transition-metal organometallics and main-group metalloid derivatives. In an important addendum and in rule 10, however, Gilman observed that the nature of the organyl group on a given metal could markedly alter the reactivity of the C−M bond (cf. supra,[70] where *n*-butyllithium is shown to be more reactive than phenyllithium).

The similar importance of ligands in organometallic reactivity was also demonstrated by Morris Kharasch in his studies on the competitive cleavage reactions of organomercurials by HCl (Scheme 10).[116] The reactivity of the cleaved R−Hg bond was found to decrease as R = *o*- and *p*-methoxyphenyl, *o*- and *p*-tolyl, phenyl, *o*- and *p*-chlorophenyl, various alkyls, benzyl, 2-phenylethyl. Although Kharasch's attempt to explain such ease of cleavage by what he terms the "electronegativity of a radical" is no longer considered valid, such empirical data did eventually form the basis for proposing the interplay of inductive and resonance contributions of substituents on a benzene ring.[8]

These correlations of relative reactivity, especially those based on Mendeleev's periodic table or on incipient notions of electronegativity, have proved to be invaluable in subsequent attempts to understand the electronic nature of carbon−metal bonding and the heterolytic or homolytic nature of such bond rupture in organometallic reaction mechanisms. Gilman's decades-long harvesting and ordering of extensive data on the reactivity of organometallics have provided physical organic chemists with a bumper crop of correlated observations, which when combined with the theoretical insights of Bohr, Lewis, and Langmuir on atomic and molecular structure, has led to our modern electronic theory of organometallic reaction mechanisms. Such mechanistic infrastructure has permitted chemists to make experimental tests of such mechanisms in terms of expected outcome by change of solvent or catalyst and to probe organometallic reactions for transient intermediates such as carbenes, radical-anions, or other paramagnetic participants.

Scheme 11



Gilman's Contributions to Understanding the Nature of the Carbon−Metal Bond. When Gilman began his professional career in 1919, the valence bonds used to connect atoms in organic structures had barely no more fundamental significance than the coupling of the imaginary "hooks" postulated by the Roman poet Lucretius in 50 B.C. as the "glue" of atom union. But when the implications of Thomson's discovery of the electron and Bohr's model for atomic structure for the nature of chemical valence were recognized by Langmuir in 1921 and G. N. Lewis in 1923, such valence bonds began to be appreciated as electron pairs. In the case of the organometallic compounds of groups 1 and 2, such a suitably ionized carbon−metal bond, $Ar_3C^- M^+$, was viewed as an excellent explanation for the salt-like physical properties of these compounds, such as solubility in aprotic Lewis bases and the electrical conductivity of the resulting solutions. Accordingly, by the 1930s Gilman, Ziegler, and Wittig recognized that R−Li and R−MgX reagents would tend to react with polar bonds in substrates generally with heterolysis of the carbon−metal bond. With organometallics having polar but un-ionized bonds, such as those of boron, aluminum, tin, lead, copper, zinc, and the few known derivatives of transition metals, their solubility in hydrocarbons and the nonconductivity of their solutions in ethers were consistent with covalent bonding. Moreover, the thermal decomposition of especially methyl derivatives to metal and free radicals (detectable by the Paneth technique), especially facile with lead alkyls and transition-metal alkyls, spoke for an evident homolysis of the carbon−metal bond. To add to the problem of understanding how such a bond ruptures when reacting with a substrate, Blicke and Powers put forward the hypothesis in 1929 that neither simple heterolysis nor homolysis occurs, but bond ruptures could also occur by single electron transfer (SET).[117] As depicted in Scheme 11 R−M could donate an electron to substrate A=B to form an ion pair **67**, consisting of M^+ and a solvent-caged radical−radical anion pair. Collapse of the ion pair then would lead to the observed final product **68**, although under certain conditions the radicals and radical-anions could escape to form telltale products **69** and **70**. From our present understanding, some 75 years later, we now know that any one of these reaction

---

[116] Kharasch, M. S.; Reinmuth, O.; Mayo, F. R. *J. Chem. Educ.* **1934**, *11*, 82.

[117] Blicke, R. R.; Powers, L. D. *J. Am. Chem. Soc.* **1929**, *51*, 3378.

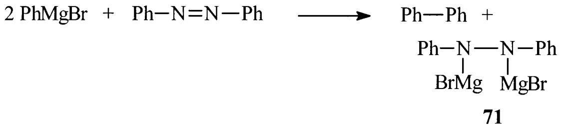
pathways may be operative with a given organometallic compound, depending strongly upon the specific substrate and experimental conditions.[84,118] But before World War II Gilman and his colleagues were generally inclined to favor organometallic reaction mechanisms involving radicals, rather than ions. Certain reactions of Grignard and organolithium reagents were considered as polar, especially by Wittig, but in the absence of clear evidence, radicals were considered more likely. Indeed, in 1940 Gilman pointed out that the relative reactivities of organoalkali compounds did not correlate as well with their electrical conductivities (i.e., their ionic character), determined by Hein and co-workers,[119] as they did in an inverse sense with the ionization potentials of the respective metals. Thus the metal in the most reactive organoalkali compound, RCs, has the lowest ionization potential of 3.87.[120] Such a correlation would be more consistent with the Blicke–Powers hypothesis of SET bond cleavage (Scheme 11).

Especially as Gilman's research focus shifted after 1945 away from magnesium and lithium reagents and toward C–M bonds of low polarity and heightened kinetic reactivity such as those involving heavier metals of groups 13–15 and the transition metals did his preference for homolytic processes grow. Since the early 1920s Gilman made use of RMgX and then RLi reagents in alkylation reactions to prepare and study the thermal stability of less reactive organometallics (eq 5). Beryllium, lead, mercury, tin, zinc, cadmium, and copper organometallics received Gilman's primary attention before 1941, even though forays into preparing every type of main-group organometallic were made as part of his relative reactivity studies (cf. supra). Gilman's interest in organoberylliums clearly stemmed from his desire to compare this congener's derivatives with the corresponding Grignard reagents. But his studies of almost all other organometallic compounds, both main-group and transition-metal, were, in his own opinion, strongly motivated by the discovery in 1922 by Midgley and Boyd of the antiknock properties of Et_4Pb in combustion-engine fuels.[121] With the hypothesis that the metal and organic groups would have a great influence on the homolysis of the C–M bond, Gilman prepared such heavier metal alkyls, aryls, and heterocyclic derivatives from the individual metal halide and the requisite RMgX or RLi (cf. eq 5). In this research Gilman was able to utilize all the reliable methods he had discovered for magnesium and lithium organometallics, to prepare a large and diverse variety of many other main-group organometallics. For preparing the more reactive organometallics, such as those of potassium, calcium, strontium, barium, and aluminum, Gilman broke no new ground but adhered to known, reliable procedures, such as the metal displacement reaction with mercury derivatives (eq 56).[122] More than any other investigator before or since, Gilman remains the dominant figure in such preparative organometallic chemistry.

$$\mathrm{M} + \mathrm{R_2Hg} \longrightarrow \mathrm{R_nM} + \mathrm{Hg}\downarrow\ (\text{or Hg–M}) \qquad (56)$$

As with many an experimentalist, however, Gilman's attempts to prepare and isolate transition-metal alkyls encountered, with the few exceptions of copper, gold, and platinum, almost complete failure. Yet in such failure Gilman clearly defined the low limits of stability of carbon–transition metal bonds to spontaneous rupture at room temperature. Unfortunately, he did not conduct such studies at sufficiently low temperatures to prevent decomposition. This facile rupture of such $C{-}M_t$ bonds became thereafter so predictable that Gilman, Wittig, and preeminently Morris Kharasch utilized it for the efficient coupling with RMgX or RLi (eq 57).[30] It is pertinent here to note that Gilman and Adams observed a similar coupling of the Grignard reagent R groups when azobenzene was used in place of M_tCl_2. The attendant formation of hydrazobenzene salt **71** is a clear indication of C–Mg bond homolysis and the involvement of an SET pathway (eq 58).[33,84]

$$2\,\mathrm{RMgX} + \mathrm{M_tX_2} \xrightarrow[-\mathrm{MgX_2}]{} [\mathrm{R{-}M_t{-}R}] \xrightarrow[-\mathrm{M_t}]{} \mathrm{R{-}R} \qquad (57)$$



$$2\,\mathrm{PhMgBr} + \mathrm{Ph{-}N{=}N{-}Ph} \longrightarrow \mathrm{Ph{-}Ph} + \mathrm{Ph{-}\underset{BrMg}{N}{-}\underset{MgBr}{N}{-}Ph} \qquad (58)$$

71

The reputed reliability of such coupling reactions induced Kealy and Paulson to attempt the synthesis of the desired bicyclopentadienyl **73** by the coupling reaction between $FeCl_2$ and the cyclopentadienyl Grignard reagent **72** (Scheme 12). As is now well-known, the failure of this reaction to produce **73** made it one of the most successful "abortive experiments" in modern chemistry, for it led instead to the first sandwich π-complex, ferrocene (**74**), and helped usher in the era of transition-metal π-complexes.[132]

---

(118) Eisch, J. J. *Pure Appl. Chem.* **1984**, *56*, 35.

(119) Hein, F.; Segitz, F. A. *Z. Anorg. Allg. Chem.* **1926**, *158*, 153.

(120) Gilman, H.; Jones, R. G. *J. Am. Chem. Soc.* **1940**, *62*, 2353.

(121) Considine, W. J. *Ann. N. Y. Acad. Sci.* **1965**, *125*, 4.

(122) Exemplary publications showing Gilman's use of known methods (eq 56) for the preparation of more active organometallics are cited here; naturally Gilman invariably optimized the preparative procedures in such studies: (a) Ca, Sr, B: Gilman, H.; Haubein, A. H.; O'Donnell, G.; Woods, L. A. *J. Am. Chem. Soc.* **1945**, *67*, 922. (b) Al, Zn: Gilman, H.; Marple, K. E. *Rec. Trav. Chim.* **1936**, *55*, 133. (c) Ga: Gilman, H.; Jones, R. G. *J. Am. Chem. Soc.* **1940**, *62*, 980. (d) In, Tl: Gilman, H.; Jones, R. G. *J. Am. Chem. Soc.* **1940**, *62*, 2353, 2357.

(123) Kealey, T. J.; Pauson, P. L. *Nature* **1951**, *168*, 1039.

(124) Robert E. Rundle (1915–1963) served on the Chemistry Faculty and on the research staff of the Ames Laboratory of the Atomic Energy Institute from 1941 until his passing. During his relatively short career he contributed prominently to our understanding of chemical bonding in organometallics, uranium and other heavy metals, and starches through his pioneering X-ray crystallographic structure determinations and his theoretical insights into electron-deficient bonding. He received both national and international recognition for his scientific publication and was named Distinguished Professor at Iowa State in 1963.

(125) (a) West, R. *Pure Appl. Chem.* **1984**, *56*, 163. (b) Okazaki, R.; West, R. In *Advances in Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic Press: San Diego, 1996; Vol. 39, p 232.

(126) Brook, A. G.; Brook, M. A. In *Advances in Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic Press: San Diego, 1996; Vol. 39, p 71.

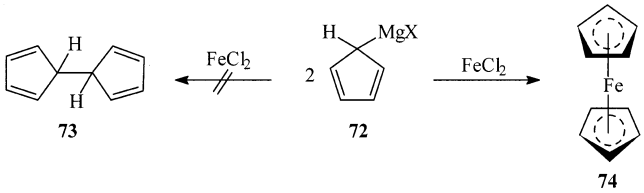
(127) (a) For a historical account of the controversy over the structure of the dimer of triphenylmethyl, consult: McBride, J. M. *Tetrahedron* **1974**, *30*, 2009. (b) For ^{1}H NMR spectral evidence on the quinoidal structure of supposed "hexaphenylethane", consult: Lankamp, H.; Nauta, W. T.; MacLean. *Tetrahedron Lett.* **1968**, 249.

(128) Gilman, H.; Schwebke, G. L. In *Advances in Organometallic Chemistry*; Stone, F. G. A., West, R., Eds.; Academic Press: New York, 1964; Vol. 1, p 1.

(129) Gilman, H.; Winkler, H. J. S. In *Organometallic Chemistry*; Zeiss, H., Ed.; American Chemical Society Monograph Series; Rheinhold: New York, 1960; p 270.

(130) Bachmann, W. E. In *Organic Chemistry, An Advanced Treatise*, 2nd ed.; Gilman, H., Ed.; Wiley: New York, 1943; Vol. 1, p 624.

Scheme 12

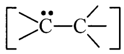
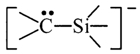
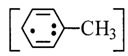
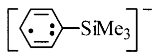


It is important to mention that Gilman enjoyed the collaboration of his brilliant younger colleague at Iowa State, Robert Rundle, whose pioneering XRD studies on the trimethylaluminum dimer, the dimethylberyllium polymer, the real structure of supposed "tetramethylplatinum" and phenylmagnesium bromides, and his theory of electron-deficient bonding did much to clarify the multifaceted nature of the carbon–metal bond. His premature death in 1963 at the age of 47 was a keen loss to his many admirers in organometallic chemistry.[124]

Gilman's Leading Contributions to the Chemistry of Group 14 Organometallic Compounds

Gilman's systematic studies on preparing covalent carbon–metal bonds from every known metal by use of RMgX or RLi by the alkylation reaction (eq 5) were conducted continually throughout the first half of his career into the mid 1950s. But after 1945 Gilman's interest was captured by organosilicon compounds, undoubtedly due to the exciting postwar commercialization of silicone polymers. At first Gilman seemed to view organosilanes as an extreme type of organometallic compound that would be formed by a metalloid, but where the carbon–silicon bond exhibited both unusual thermal and oxidative stability. Eugene Rochow, inventor of the direct synthesis of the methylchlorosilane precursors for methylsilicone polymers, has observed that any chemist would be impressed to learn that tetraphenylsilane can be distilled at 425 °C under an atmosphere of air without decomposition. Certainly such stability of a C–M bond represents the other extreme of the C–M bonds Gilman had unsuccessfully tried to make from most transition metals. But another aspect of organosilanes also piqued Gilman's curiosity, as it had Kipping's a generation earlier: What similarities or differences in properties would emerge when one or more silicon atoms were substituted for carbon in an organic structure, as for example in the tetraarylsilanes, Ar_4Si, compared with Ar_4C, or in hexaphenyldisilane, $Ph_3Si{-}SiPh_3$, compared with $Ph_3C{-}CPh_3$. In such studies the metallic character of silicon was of less interest than its carbon-like properties. Thus Gilman was interested to what extent organosilanes resembled their all-carbon analogues and wished to evaluate the reactivity not only of C–Si bonds but of Si–H and Si–Si bonds as well. Furthermore, from the previous studies of Kipping and Stock, silicon was known to form chains and rings of silicon atoms very readily, and Gilman set out to explore how such concatenation might resemble the similar formation of carbon skeletons. In such silicon–silicon bonding the question of multiple bonding had been raised by previous investigators and would remain an unsolved problem during Gilman's research as well. Building on Gilman's findings, however, younger colleagues were to synthesize sterically hindered disilenes containing Si=Si bonds (R. West)[125] and silylene–carbene compounds, containing Si=C bonds (A. G. Brook),[126] respectively.

Table 1. Reactive Intermediates of Organic and Organosilicon Chemistry

Radicals	$R_3C\bullet$	$R_3Si\bullet$
Cation	R_3C+	R_3Si+
Anion	$R_3C:^-$	$R_3Si:^-$
Divalent Compound	$R_2C:$	$R_2Si:$
Carbanion with Neighboring Atom		
Radical-anion		

Over and above such organosilane skeletons and their resemblance to their all-carbon counterparts, Gilman hoped to synthesize and compare organosilane intermediates analogous to the active intermediates of organic chemistry as depicted in Table 1. Although Gilman's work did not address or establish the existence of all these intermediates, in his search for silicon-centered radicals, silylenes, and anions, Gilman clearly posed the fundamental experimental questions in such studies and by his findings showed how the detection of such intermediates could be undertaken. Finally, to the extent to which any "organic-like" character would be exhibited by organosilanes, Gilman was prompted to carry out comparative studies on the organic derivatives of the congeners of group 14, namely, germanium, tin, and lead. In seeking to make such an intrafamily comparison of "organic-like" character, Gilman again was able to discern Mendeleevian trends, which have been of considerable significance in establishing an electronic basis for carbon–metal and metal–metal bonding.

As we have seen, Gilman was always inclined to accept free radicals and carbenes as probable reaction intermediates. Therefore, in his initial studies with organosilanes he appears to have been influenced by the work of Viktor Meyer on steric hindrance, by Julius Nef on divalent carbon, and profoundly by Moses Gomberg on the difficulty of preparing tetraarylmethanes and the dissociation of highly substituted ethanes into free radicals. In addition, noting the comparative stability of the C–Si bond, he studied which reagents and experimental conditions would actually cause cleavage. In the course of such investigations he established that steric hindrance was less a problem in preparing silanes

---

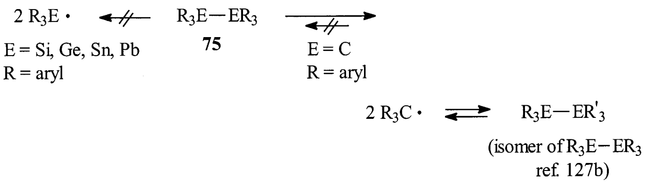
(131) (a) For leading references on group 14 analogues of Ph_3SiM: (a) Ph_3GeM: Gilman, H.; Gerow, C. W. *J. Org. Chem.* **1957**, *22*, 334. (b) Ph_3SnM: Gilman, H.; Rosenberg, S. D. *J. Org. Chem.* **1953**, *18*, 680. (c) Ph_3PbM: Gilman, H.; Bindschadler, E. *J. Org. Chem.* **1953**, *18*, 1675. (d) As many a first-year graduate student with Gilman during this period, this chemist was assigned the three-step sequence given below, as his introduction to a demanding laboratory procedure. He notes that he had to repeat the sequence *four times* with guidance from a postdoctoral associate, to obtain a satisfactory outcome. After the introduction of THF as a solvent, the preparation of Ar_3SiLi reagents became remarkably easy on the *first attempt.*

$$2\ Ph_3SiCl \xrightarrow{Na} Ph_3Si{-}SiPh_3 \xrightarrow{2\ NaK} 2\ Ph_3SiK \xrightarrow{2\ Me_3SiCl} 2\ Ph_3Si{-}SiMe_3$$

(132) Overview of Gilman's extensive research on perfluoro-organometallics: Gilman, H. *J. Organomet. Chem.* **1975**, *100*, 83.

with four bulky aryl groups than it was with the corresponding methane. The synthesis of tetra-2-naphthylsilane with the lithium aryl and $SiCl_4$ was easily achieved, whereas the analogous methane has not been made (eq 49b).[89]

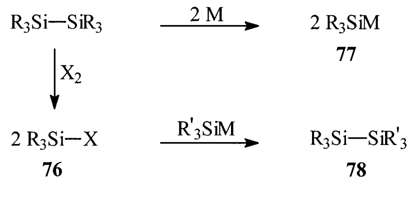
But Gilman's studies on the dissociation and cleavage of the hexasubstituted derivatives of group 14 analogues of ethane proved most fruitful in pointing out the similarities and the contrasts of such elements with carbon and in providing syntheses for group 14 concatenated derivatives. Such investigations applied to silicon permitted the following conclusions to be drawn (eq 59):



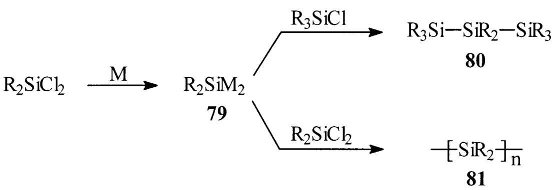
(1) no hexaaryl derivative of type **75** dissociates into radicals reversibly under the mild conditions possible for the carbon analogues;[127a] (2) the Si−Si bond can be cleaved by halogens and by alkali metals to give reactive silyl halides **76** and silylmetallics **77**, which proved to be useful cross-coupling partners to yield new Si−Si bonds **78** (Scheme 13); and (3) by extension, alkali metal derivatives R_2SiM_2 (**79**) could be coupled with R_3SiCl or with R_2SiCl_2 to produce linear (**80**) or cyclic (**81**) polysilanes (Scheme 14). Thus the ground was firmly laid for the rational system of silicon-skeletal organosilanes.[128]

The heart of Gilman's pioneering contribution to organosilicon chemistry lies in his research on silylmetallic reagents, R_3SiM, especially those where R = aryl.[129] Although prior work by C. A. Kraus and by Razuvaev with trialkylsilyl- and trialkylgermylmetallics had demonstrated the existence of such reagents in the reactions of silyl or germyl chlorides, R_3SiCl, or disilanes, $R_3Si-SiR_3$, with alkali metals,[128] Gilman pioneered in finding reliable, high-yield routes to aryl-containing silylmetallic reagents from either disilanes or silyl chlorides and alkali metals. Such Ar_nR_{3-n} reagents ($n = 1-3$) proved of great significance from three vantage points: (1) by comparing the reactivity of R_3CM and R_3SiM toward organic substrates the role of silicon as a nonmetal like carbon could be clearly evaluated; (2) R_3SiM and R_2SiM_2 reagents proved to be excellent coupling agents with R'_3SiCl and R'_2SiCl_2 for the stepwise formation of Si−Si bonds in linear or cyclic arrays; and (3) the action of R_3SiM reagents on organic substrates was shown to be a versatile and facile method for forming Si−C bonds. Just as organomagnesium halides permitted Victor Grignard to convert variegated organic substrates into a vast array of carbon−carbon bonded derivatives, so too did such silylmetallic reagents allow Henry Gilman access to countless novel organosilicon derivatives through newly formed Si−Si or Si−C bonds. Therefore, Gilman's silylmetallics will continue to have a great impact on developments in organosilicon chemistry.

Scheme 13



Scheme 14



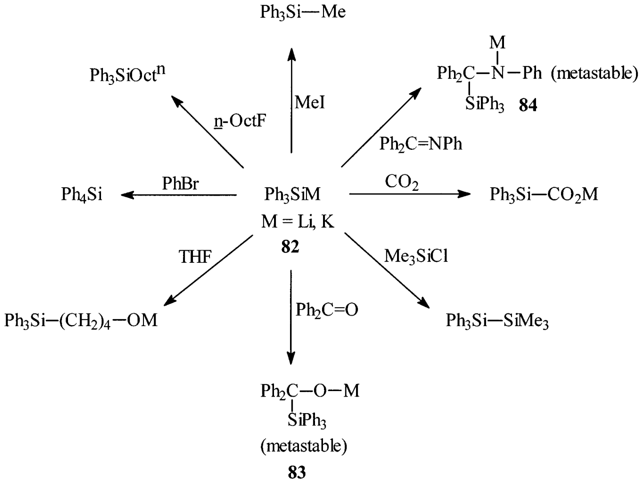
Overriding the three aspects of copious empirical information provided by Gilman's studies of silylmetallics is the greater question of what the many unusual reactions observed tell us about the nature of the silicon−carbon and the silicon−alkali metal bonds in R_3SiM. Gilman's findings present intriguing challenges to existing electronic interpretations of organic structure and reaction mechanisms.

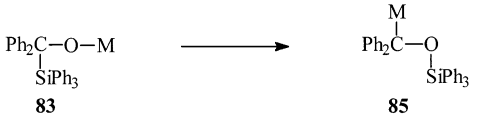
Triorganosilylmetallics, exemplified by triphenylsilylpotassium, have been extensively studied by Gilman and co-workers, who had as their original purpose, a detailed comparison of $Ph_3Si^-M^+$ (**82**) with its carbon congener, $Ph_3C^-M^+$ (**83**).[129] The silyl anion **82** does in fact react with various substrates in ways quite analogous to those exhibited by the carbanion **83**, which has been generally viewed as a nucleophile attacking an electrophilic substrate (eq 60).

$$\underset{\mathbf{83}}{Na^+\,Ph_3C\!:^-} + \overset{\delta+}{CH_3}-\overset{\delta-}{I} \longrightarrow Ph_3C-CH_3 + Na^+\,I^- \qquad (60)$$

Although an analogous nucleophilic attack could explain the reactions of Ph_3SiM with CH_3I, CO_2, Me_3SiCl, and carbonyl substrates, such a mechanism cannot account for the facile attack of **82** on aryl halides, ethers, aliphatic fluorides, or certain unsaturated hydrocarbons (Scheme 15), all of which are unresponsive toward Ph_3CM. Furthermore, the normal adducts with carbonyl or azomethine substrates (**83** and **84** in Scheme 15) were found to easily rearrange to the abnormal adducts (e.g., **85** in eq 61). These observations have compelled chemists to consider other mechanisms.

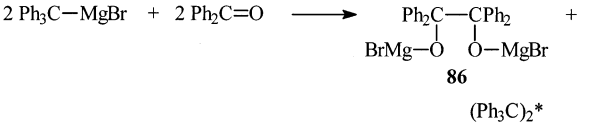
Scheme 15





(61)

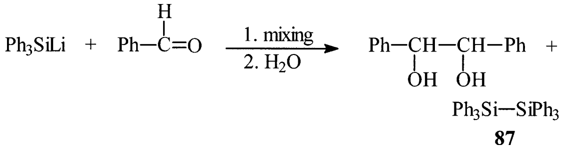
At this juncture we should recall that even Ph_3CMgBr reacts with an organic substrate like Ph_2CO in an abnormal manner (eq 62), yielding reduced dimer **86**[130] and the rearranged dimer of the Ph_3C radical.[127a] This reaction can readily be explained through the operation of a single-electron-transfer mechanism (SET).[84] In a strikingly similar manner, the most common side-product of Ph_3SiM reactions is the analogous dimer, hexaphenyldisilane (**87**). Consider the following (eqs 63 and 64): The generation of major proportions of **87** in both reactions and the reductive coupling in eq 64 provide compelling evidence that the reactions of Ph_3SiM in large part react by way of SET pathways with the silyl anion functioning as a single-electron donor[91] (Scheme 16). Such a view would not only accommodate all the normal, supposedly "nucleophilic" displacements and additions (Scheme 16) but would make much more rational the ease of reaction by Ph_3SiM on such unlikely "electrophilic" substrates as Ph−X, R−F, hydrocarbons, and R−O−R′ (eqs 65−68).



(62)

*For the structure of this dimer, cf. ref. 127a

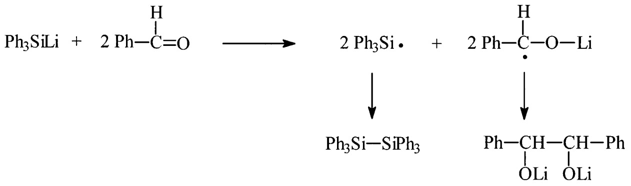
$$Ph_3SiK + PhCl \longrightarrow \underset{12\%}{Ph_4Si} + \underset{\mathbf{87},\ 77\%}{Ph_3Si{-}SiPh_3} \qquad (63)$$

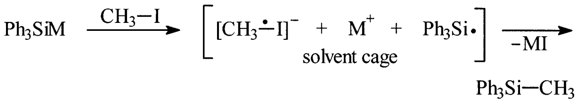


(64)

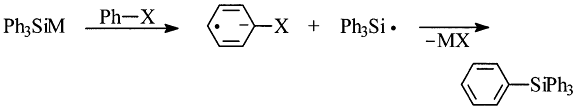
Finally, SET processes and their reversal can explain both the normal addition of Ph_3SiM to C=O and C=N linkages and the facile rearrangement of such adducts to the abnormal products (eq 61). Gilman's comprehensive studies of the reactions of triarylsilylmetallics with diverse organic substrates have therefore provided us with convincing evidence for the importance of SET mechanisms in this branch of organometallic chemistry. In retrospect, it is understandable why Ph_3SiM reagents are constitutionally better suited to react as SET agents than as nucleophiles. First and perhaps foremost, the three phenyl ligands make the silicon center sterically impeded for close approach to the substrate. Second, the unshared electron pair on silicon in $[Ph_3Si:]^-$ is less stabilized by the nuclear charge on Si or by delocalization over the phenyl π-clouds than is the carbon center in $[Ph_3C:]^-$. Both factors lower the electron affinity in the Ph_3Si^- anion and thus favor SET.

Scheme 16

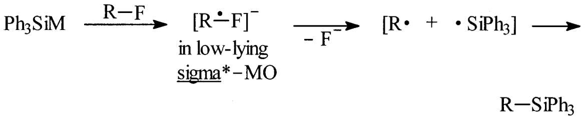




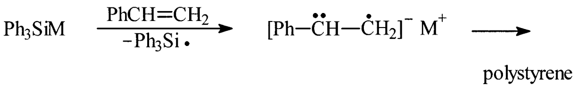
(65)



(66)



(67)



(68)

In a systematic fashion Gilman's group prepared metallics of the group 14 congeners of silicon, such as Ph_3GeK (following prior work of Kraus and of Razuvaev for R_3GeM reagents), Ph_3SnK, and Ph_3PbNa, generally in a manner similar to that employed for Ph_3SiK, namely, by the cleavage of the hexaphenyldimetalloid derivative by alkali metal, in early studies with Na−K alloy and in later work with Li metal in THF (eq 69).[131a]

$$Ph_3M'{-}M'Ph_3 + 2M \xrightarrow{\text{donor solvent}} 2\ Ph_3M'M \qquad (69)$$

From this chemist's own experience in Gilman's laboratory in 1953, before the advent of THF as solvent, achieving the starting of such a cleavage reaction with Na−K alloy was a most demanding test of experimental technique. All reagents had to be absolutely pure, dry, and both halogen- and oxygen-free.[131b] In the course of such studies Gilman's students finally determined that strong donor ethers such as THF or DME have an accelerating influence on M′−M′ bond cleavages. In light of the SET nature of such reactions, this solvent effect is readily understandable.

Over the last two decades of Gilman's career he conducted research with such silylmetallic reagents which proved capable of producing a wide range of highly phenylated and/or fluorinated silicon derivatives of linear, branched, or cyclic structure, which possess remarkable thermal stability in air, and which have been of ongoing interest to the U.S. Air Force as high-temperature lubricants for jet engines.[132] In sum, then, Henry Gilman's research with silanes has uncovered much fundamental information on the preparation and properties of organosilicon compounds, which has greatly expanded our understanding of the electronic basis of structure and reaction mechanisms. In addition, the extensive and widely applicable preparative procedures emanating from his laboratory over the years have fostered the whole field and range of organosilicon polymers. In recognition of his important contributions and leadership Henry Gilman was named the first recipient of the Frederic Stanley Kipping Award in Organosilicon Chemistry upon its establishment in 1962 by the American Chemical Society.

It is of historical interest to note that when Gilman wrote his chapter, “Organometallic Compounds”, in his treatise in 1943, he did not include any discussion of organosilicon chemistry,[115] nor did Coates in his second edition of *Organometallic Chemistry* published in 1960.[133] In other words, silicon was considered more as a nonmetallic analogue of carbon and its compounds rather than as an “organometallic”. The researches of Gilman, Sommer, Eaborn, Rochow, West, Seyferth, and many other Kipping awardees have emphasized the differences between carbon and silicon while clarifying silicon’s metallic properties. As a consequence, comprehensive treatments of organometallic compounds now include organosilanes as a matter of course. A similar development can be traced with other metalloids such as boron, arsenic, and tellurium, where each has become the subject of its own branch of “organic-like” chemistry. Especially in organoboron chemistry, where the boron atom is even more closely similar to carbon in electronic properties, do we observe close parallels with their all-carbon analogues. Indeed, such branches of “organic-like chemistry” owe a significant debt for their development to Gilman’s prior studies of group 14 organic chemistry. His research in this area was undertaken from the perspective of a professional organic chemist, whose goal generally was to attach variously functionalized organic groups to the metalloid center. In this manner Gilman sought to learn how the metalloid atom would modify the reactivity of a given functionality compared with the all-carbon analogue.

The Impact of Gilman’s Character and Personality on the Growth of Modern Organometallic Research

For the trio of young chemists, Henry Gilman, Georg Wittig, and Karl Ziegler, who launched their teaching and research careers in the early 1920s, organometallic chemistry at that time was not *terra incognita* but certainly was *terra obscura*. What this field and its growth have brought to modern science and technology was not even foreshadowed then. Rather all three possessed the faith that rich rewards of important knowledge awaited those who would have the patience, hope, and determination to undertake the study of these “unnatural”, exotic carbon−metal compounds. In Ziegler’s words, what drew him into such research was “the joy of finding, somehow or somewhere, something really novel”.[134] Scientific knowledge, even before its exact nature and implications were known and recognized, was deemed by these pioneers worthy of a lifetime of labor and ardor.

Before considering the positive impact that Henry Gilman’s character and personality have had on organometallic chemistry, it should be noted that he played no principal role in the third period of development in organometallic chemistry, the rise of organotransition-metal chemistry in the early 1950s. He was then about 60 years old, leading a large group of some 15 graduate students and postdoctoral associates and with some 20 years of activity still in prospect. Although experienced in preparing all types of stable and labile organometallics, he chose not to become involved in the burgeoning area of π-complexes. Why this was so this author does not know, but some reasonable speculation can be considered. It might have been that he was already fully occupied with his researches on organolithium reagents and on group 14 organometallic derivatives with a special focus on solvent effects on organometallic reactions. The apparent opportunity may also have invoked his sense of scientific priority or ethics: one pursues scientific discoveries made in one’s own laboratory and does not rashly intrude into a colleague’s area of specific discovery. Finally, Gilman’s focus in his organometallic research had always been the reactions of a carbon−metal bond; he was decidedly less interested in the global structure of organometallic compounds. With their lack of a specific carbon−metal bond, transition-metal π-complexes apparently offered him little attraction. But his pioneering work in developing reliable procedures for preparing main-group organometallic reagents was of special importance in permitting rapid growth in preparative transition-metal organometallics in the period of 1950−1980.

In the shaping and development of modern organometallic chemistry as a whole, it has been Henry Gilman’s unquenchable curiosity and untiring zeal that has been a major force. His research program on organometallics at Iowa State, conducted over a 55-year period, engaged a total of at least 250 graduate and postdoctoral co-workers, whose findings are reported in over 1000 publications. Although many of his publications were shorter in length and less in factual content than most modern publications, they invariably presented improvements in experimental procedures and significant reaction observations of immediate use to practicing organic chemists.[135] From youth to age the extraordinary demands he made of himself and of his students remained undiminished and has become the stuff of legend.[136] Gilman assumed that any student working in his laboratory would equally share his passion for chemical experimentation as a morning-noon-and-night, seven-days-a-week occupation. During my time with Gilman I was such a zealot and hence worked in harmony with his expectations. But those fellow students who viewed their graduate study in more realistic and practical terms could be scorched by Gilman’s ardor and hunger for new results. A hapless graduate student who had not completed the identifica-

---

(133) Coates, G. E. *Organometallic Compounds*, 2nd ed.; Methuen: London, 1960.

(134) Ziegler, K. *Glückauf* **1955**, *91*, 1266.

(135) A detailed assessment of Gilman’s scientific bibliography, which had been undertaken both by Professor Colin Eaborn and by this author, has led us to the following consensus: There is much overlap of content and fragmentary publication of research results among Gilman’s scientific research reports over the years. Other researchers might have been inclined to have combined such brief reports into a noticeably smaller number of longer papers, possibly one-half the number actually published. Such a practice would not be consistent, however, with Gilman’s firmly held belief that positive experimental results should be shared with the chemistry community without delay.

(136) Accounts of Henry Gilman’s public persona and his demanding interactions with co-workers, “warts and all”, have been published by Professor Robert A. Benkeser, his former graduate student (*J. Org. Chem.* **1968**, *33*, 5), and in a much more extensive treatment that is based upon commentary of former co-workers, by his colleague, Professor Colin Eaborn (*Biographical Memoirs of Fellows of the Royal Society* **1990**, *36*, 151). Both present the legendary Henry Gilman in a most engaging and affectionate manner without however assessing the particular scientific contributions of this most zealous of researchers. This author hopes that the present account will identify the specific achievements in chemistry for which Henry Gilman deserves to be remembered.

tion of a reaction product because his lunchtime had taken precedence was reproved by an incredulous Gilman with the query, “What, man, have you ice water in your veins?” On his daily rounds of his large research group (cf. Figure 1) Gilman greeted each student with the urgent general question of “What’s new?”, followed by meticulous inquiry into each project Gilman recalled as being underway under that student’s responsibility. Answers on such progress indicating that failure or little headway had resulted evinced quiet dismay from Gilman punctuated by a drawn-out “Oh”. The unproductive student was given the unmistakable impression that he was reporting on a disappointing and unacceptable performance. On the other hand, the student who had much to report to Gilman certainly received his lavish congratulations. In the next breath, however, Gilman would make a stream of suggestions for further experimentation. Thus the unproductive student and the productive student alike felt after Gilman’s visit that he should have done *more*. Inevitably, all Gilman students came to appreciate the work-ethic inculcated by Gilman at Iowa State, but for not a small number that appreciation did not crystallize until years later in their careers, when they were to learn that not only talent and knowledge but also diligence and dedication were required for success in their profession.

If Gilman’s standards of performance were high for his students, he expected no less of himself. He followed the research progress of his students in minute detail and retained it, even when the Gilman group comprised 20 or more doctoral candidates. He did not insulate himself from them through postdoctoral associates, who in many present-day research groups often handle day-to-day research direction. He spent long hours with the chemical literature and maintained a masterly command of contemporary research reported throughout the world. Astonishing as this performance is, it pales in the light of one burden Gilman had to bear for 40 years: diminished and dwindling eyesight. In 1947 he suffered retinal detachments that severely impaired and, coupled with glaucoma, ultimately deprived him of his vision. Thus, for over half his professional career he labored under this handicap but did not give up. Unrelenting, he had the chemical literature read to him many hours daily and actually published more than 500 scientific contributions *after* 1947. That surely attests to an indomitable courage and professional commitment far above human expectations.

In his scientific publications and public lectures Gilman contributed greatly to making organometallic chemistry into a vital and valuable branch of modern science and technology. Not only through his primary publications but also by his review chapters and articles on specific types of organometallics, he elucidated the scope and limitations of the preparations and reactions of all known main-group organometallics.

His professional activities in editorial work and writing contributed greatly to the growth of both organometallic chemistry and organic chemistry in the United States. He served as associate editor of both the *Journal of the American Chemical Society* and *Chemical Reviews*. He collaborated with Morris Kharasch in founding the *Journal of Organic Chemistry* and also served as chairman of the editorial board. He was sought out as a member of numerous editorial or advisory boards, such as that of the *Journal of Organometallic Chemistry*, *Advances in Organometallic Chemistry*, and *Organometallic Syntheses*. He was editor of Volume VI and Collected Volume I of *Organic Syntheses*. With his major work, “Organic Chemistry: An Advanced Treatise”, in four volumes, Gilman conceived a collaborative, edited work that was to serve as a literary model for future comprehensive chemistry reference books: a carefully coordinated and edited sequence of chapters on important topics by recognized experts. It is a tribute to Gilman’s stature and sense of collegiality that he was able to persuade various prominent research chemists to engage in this new, unprecedented publishing venture. His own chapter on organometallic compounds in this series is a model of lucid exposition, and the same clarity and care are evident in the editing and cross-references of the entire treatise. It can be observed that with this treatise Henry Gilman assured that thereafter organometallic chemistry would be regarded a vital and indispensable part of organic chemistry.

In his professional life Gilman’s respect for his colleagues and his students manifested itself in many ways. His concern for the personal welfare and future plans of co-workers was evident in daily conversations during their time at Iowa State and was maintained through frequent correspondence after they set out into the world. Help with stipends, job placement, changes in positions, and professional contacts was Gilman’s way of fostering the careers of his research students. Ever ready to hear a student’s opinion or to engage in discussions ranging far from chemistry, he never tried to dominate any discussion, nor did he engage in negative comment about others. In his publications he explicitly recognized and generously praised the prior work of his colleagues. His papers remained free of polemic or derogation of others’ work. When called upon by his results to differ from a published statement, he did so with mildness and courtesy. Such tact stemmed not from mere good manners, but from his deep respect for others.

His respect for others was also colorblind. Dr. Nathaniel Calloway, the first black student to receive a Ph.D. degree in chemistry west of the Mississippi, studied with Henry Gilman. Subsequently, Gilman welcomed many other black students into his laboratory and trained them for leading positions in teaching and research. Far ahead of his time, he served on the Board of Trustees of the Carver Foundation and the Tuskegee Institute and was a proponent of equal opportunity for blacks when the issue was unpopular. In the words of Martin Luther King, he judged men by the quality of their minds and the content of their characters, rather than by the color of their skin.

His impact on chemistry has received wide recognition. The Midwest has shown its gratitude to its adopted son by honoring Henry Gilman with the Midwest Gold Metal Award of the American Chemical Society in 1951, the Iowa Award in 1951, and the Iowa Governor’s Science Metal in 1977. He was the first chemist from a land-grant institution elected to the National Academy of Sciences (1945); he was chosen an Honorary Fellow of the Chemical Society of London and a Foreign

Member of the Royal Society; and he was awarded the Priestley Metal of the American Chemical Society in 1977, the highest honor in U.S. Chemistry. Many of his colleagues and former students had hoped for an even greater recognition of his achievements, the Nobel Prize in Chemistry.

Perhaps the most lasting recognition and remembrance of Henry Gilman will come from the very discipline of organometallic chemistry, which he helped to shape both in the United States and throughout the world. The great store of knowledge that he gathered and the many students he has inspired are his own memorial to his role in 20th century chemistry. Christopher Wren, the architect of St. Paul's, London, chose for his epitaph "*Si monumentum requiris, circumspice*". Similarly, Henry Gilman could have justly said, "If you seek my memorial, look about you in the field of organometallic chemistry". At his death on November 7, 1987, at the age of 93 he was universally acclaimed as a great leader of modern organometallic chemistry. The fruits of his 75 years of research continue to attract younger generations of chemists to the ever-bright prospects of organometallic chemical research.

Acknowledgments. Direct and personal knowledge of the careers and research of Henry Gilman and Karl Ziegler stem from my residence in their laboratories as a graduate research assistant and as a postdoctoral research fellow, respectively. My admiring familiarity with Georg Wittig's research developed out of valuable, professional contacts with him over the years. Further insight into the scientific contributions of these great men has come from colleagues, such as Professors Adrian G. Brook and Robert A. Benkeser for Henry Gilman, Professor Günther Wilke for Karl Ziegler, and Professor Manfred Schlosser for Georg Wittig. The Department of Chemistry of the Iowa State University, through the good offices of Professors David K. Hoffman and Walter S. Trahanovsky, has provided me with helpful biographical material on Henry Gilman, including a complete list of his scientific publications and the personal photograph used in this article. I am deeply grateful for the ready assistance that these and other colleagues have provided me in this demanding but rewarding task. Finally, the final manuscript has profited greatly from the discerning redaction of Dietmar Seyferth and anonymous referees, who have helped to eliminate unsubstantiated attributions and opinions, as well as luxuriant prose, from previous drafts.

OM0109408