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## Karen J. Brewer (1961–2014): A Bright Star that Burned Out Far Too Soon

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### 1.1 Introduction

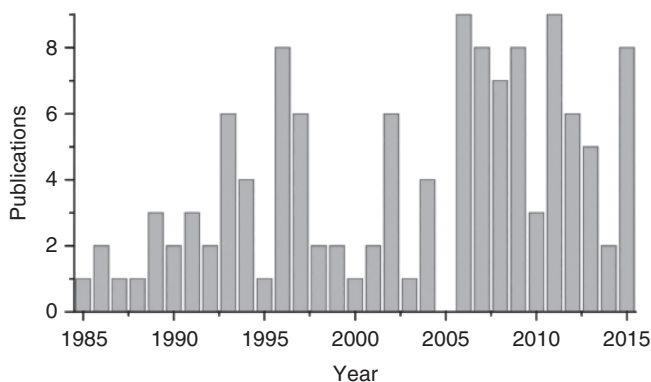
Over the span of her career, first at Washington State University (WSU) and later at Virginia Tech, Karen J. Brewer (Figure 1.1) earned international acclaim as a prolific and pioneering researcher in the photochemistry and photophysics of multimetallic complexes [1, 2]. Ranging from synthesis of new multimetallic complexes to the study of their ground- and excited-state properties, her contributions aimed to elucidate the effect of the specific assembly of such complexes on their respective spectroscopic and electrochemical properties. In the process, Karen studied the application of complexes to molecular photovoltaics, solar H<sub>2</sub> production, artificial photosynthesis, electrocatalysis, Pt-based DNA binders, and photodynamic therapy [1–6]. Publishing her first paper in 1985, she accumulated over 125 peer-reviewed research publications in her career, which have in turn garnered over 3000 citations to date [1, 2], and her research pace was as active as ever at the time of her premature death in 2014 (Figure 1.2) [1].



**Figure 1.1** Karen J. Brewer (1961–2014) in the Spring of 2014. (Courtesy of Virginia Tech.)

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**Figure 1.2** Publications per year from 1985 to 2015.

Although known specifically for her various research contributions, Karen was also an award-recognized educator. She was comfortable teaching chemistry at all levels, from first-year students in general chemistry to graduate students in special topics classes such as electrochemistry and the photophysics of transition metal complexes. Her enthusiasm in the classroom was infectious and she inspired students to change not only their view of chemistry but, in some cases, their major to chemistry [1].

For many, including this author, Karen will be remembered most for her role as mentor and role model. She had tremendous impact on everyone who transitioned through her research laboratory, from undergraduates to postdocs. Throughout her career, Karen was a strong advocate for women and minorities in chemistry and was a role model and mentor for many female students and researchers [1, 2, 5]. Her passion in the promotion of chemistry as a career choice for women was most evident in her extensive outreach efforts to K-12 students. Throughout her career, she regularly visited primary and secondary school classrooms and hosted students in her laboratories at Virginia Tech [1, 2, 5]. In the process, Karen provided a real-life role model for young girls and others with aspirations to work in the physical sciences [1, 5].

Over the years, Karen received significant recognition for her collective efforts in research, teaching, and outreach. This included a College of Arts and Sciences Diversity Award in 1996, shortly after arriving at Virginia Tech [1, 5], as well as various teaching awards [3] and a Popular Mechanics Breakthrough Innovator Award in 2010, which she shared with collaborator Dr Brenda Winkel [2–5]. Most recently, Virginia Tech recognized her outreach efforts with the 2014 Alumni Award for Outreach Excellence [1–4], which she shared with Dr Shamindri Arachchige, Virginia Tech instructor of chemistry and a former postdoctoral researcher from her research group [1, 5, 7].

## 1.2 Early Years

Karen Sonja Jenks was born on June 27, 1961, in Wiesbaden, Germany to parents Gerda and Henry Jenks [3, 4]. As the daughter of a career military man,



**Figure 1.3** Karen in kindergarten at age 5. (Courtesy of Elise Naughton and the Brewer family.)

Karen moved frequently in her youth (Figure 1.3) [2–4], which provided her the opportunity to see much of the United States and the world as a young girl [3, 4]. The family ultimately settled in Lancaster, South Carolina in 1974, where Karen graduated with honors from Lancaster High School in 1979 (Figure 1.4) [3, 4].

Karen then attended Wofford College in Spartanburg, South Carolina [2–4, 6] on a Reserve Officers' Training Corps (ROTC) scholarship [8]. It was an interesting time to attend Wofford College, as it had formerly been an all-male school and had transitioned to a coeducational institution only 3 years before she began her studies there [8]. Karen soon decided that the military was not what she wanted to do with her career and enrolled in Wofford's K-12 education program, where she was involved in teacher training at the middle school level [8]. Her father had instilled a love of learning and teaching [8] and this probably influenced her decision. Ultimately, however, she developed an interest in chemistry and she finished her undergraduate studies in the chemistry program. While at Wofford she also participated in women's basketball and became a member of both Alpha Phi Omega and the American Chemical Society during her senior year [2, 6]. The Wofford chemistry faculty thought highly of Karen as a student [9] and she received her BS degree in chemistry in 1983 [2–4, 6]. After the completion of her undergraduate studies, she married Ralph Gary Brewer (who went by Gary), with



**Figure 1.4** Karen in her senior year of high school at age 17. (Courtesy of Elise Naughton and the Brewer family.)

their wedding held on the same day as their Wofford graduation ceremonies on Sunday, May 15, 1983. Following her marriage, Karen was known both personally and professionally as Karen Jenks Brewer.

### 1.3 Graduate Studies and Clemson University

Karen then entered the Chemistry graduate program at Clemson University in the fall of 1983, where she began working under the supervision of Dr John D. Petersen (b. 1947, PhD University of California, Santa Barbara 1975) (Figures 1.5 and 1.6). Notable coworkers during her time in the Petersen group included Ronald Ruminski (Professor, University of Colorado Colorado Springs; PhD University of New Mexico 1980; Petersen postdoc 1981–1984) [10], Wyatt Rorer Murphy, Jr (Professor, Seton Hall University; PhD University of North Carolina at Chapel Hill 1984; Petersen postdoc 1984–1986) [11], and D. Brent MacQueen (PhD Clemson 1989) [12].

Karen began her research in the Petersen laboratory by joining ongoing efforts to develop bimetallic complexes capable of converting radiation to usable chemical potential energy. The basic design of such species included



**Figure 1.5** John D. Petersen (b. 1947). (Courtesy of John Petersen.)

three components (Figure 1.5): (i) a strongly absorbing, but photochemically unreactive, metal center (antenna complex); (ii) a second metal center capable of undergoing a useful chemical reaction from a nonspectroscopic excited state (reactive complex); and (iii) a bridging ligand (BL) that both couples the two metal fragments and facilitates intramolecular energy transfer between the two metal centers [12, 13]. While others had previously studied electron transfer in bimetallic complexes utilizing primarily monodentate BLs (Figure 1.7), the Petersen group focused on the application of bidentate BLs (Figure 1.8) as a method to increase stability of the bimetallic species during excitation. Karen's first publication was as fourth author on a 1985 paper published in *Coordination Chemistry Reviews* that presented this design and discussed the optimization of the three basic components [13].

Karen's research initially focused on evaluating the effect of bidentate BLs such as dpp on the photophysics of Ru(II)-based antenna complexes. This resulted in the publication of her initial first-author paper in 1986, which reported the synthesis of  $[\text{Ru}(\text{dpp})_3]^{2+}$  along with its photophysical and electrochemical properties [14]. The conclusion of this work was that in comparison to  $[\text{Ru}(\text{bpy})_3]^{2+}$ , the dpp analogue exhibited similar electronic absorption and emission spectra, as well as a similar luminescence quantum yield. As such, the application of dpp should allow the tethering of Ru(II)-based antenna complexes of reactive metal centers without the loss of the desired photophysical properties [12, 14].

The ultimate focus of the majority of her graduate work was the potential application of bimetallic complexes to the photochemical elimination of molecular hydrogen. These efforts began with an intermolecular sensitization study using  $\text{Fe}(\text{bpy})_2(\text{CN})_2$  as the donor and the dihydride species  $[\text{Co}(\text{bpy})(\text{PET}_2\text{Ph})_2\text{H}_2]\text{ClO}_4$  in order to evaluate the relative energy levels of the visible light accessible excited state of the Fe(II) antenna and the reactive

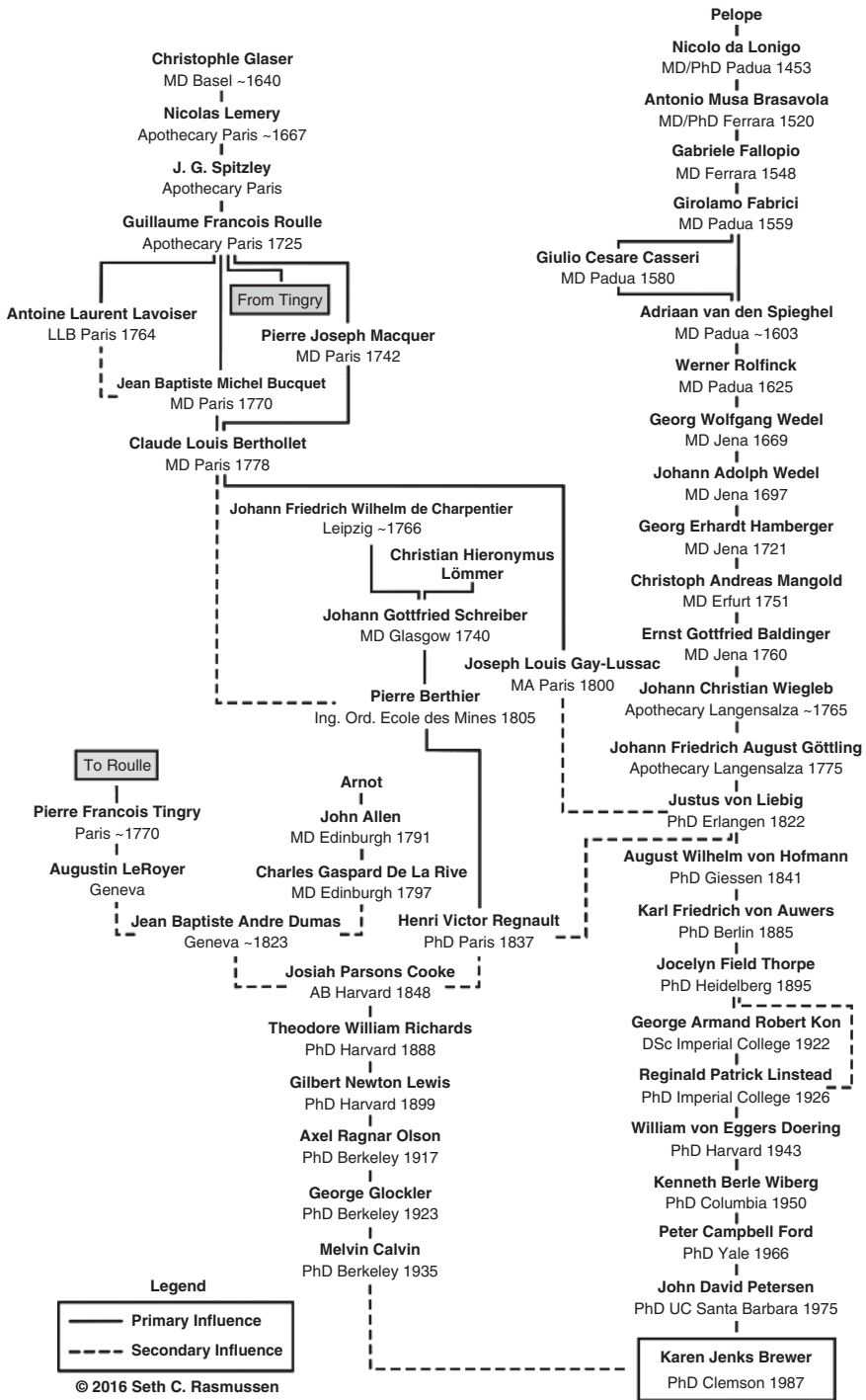
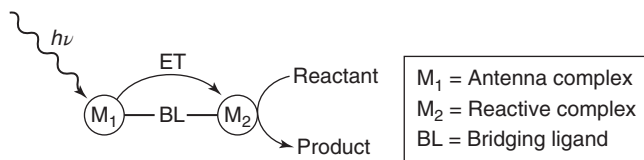


Figure 1.6 Karen Brewer’s academic genealogy.



**Figure 1.7** Basic design of bimetallic complexes capable of efficient photochemical processes.

<i>Terminal ligands</i>	<i>Monodentate bridging ligands</i>	<i>Bidentate bridging ligands</i>
 2,2'-bipyridine (bpy)	 pyrazine (pz)	 2,2'-bipyrimidine (bpm)
 1,10-phenanthroline (phen)	 4,4'-bipyridine (4,4'-bpy)	 2,3-bis(2-pyridyl)pyrazine (dpp)
 2,2';5'-2''-terpyridine (tpy)	 4-cyanopyridine (4-NCpy)	 2,3-bis(2-pyridyl)quinoxaline (dpq)

**Figure 1.8** Polypyridyl ligands referenced throughout the chapter.

state of the cobalt dihydride model reactive fragment [12, 15]. It was found that when either  $\text{Fe}(\text{bpy})_2(\text{CN})_2$  or  $[\text{Co}(\text{bpy})(\text{PEt}_2\text{Ph})_2\text{H}_2]^+$  was irradiated alone at 577 nm, no reaction occurred. Irradiation of a mixture of  $\text{Fe}(\text{bpy})_2(\text{CN})_2$  and  $[\text{Co}(\text{bpy})(\text{PEt}_2\text{Ph})_2\text{H}_2]^+$  at 577 nm, however, would result in the production of  $\text{H}_2$ . The hydrogen generated was due to the initial excitation of the  $\text{Fe}(\text{II})$  complex, followed by energy transfer to the  $\text{Co}(\text{III})$  dihydride and resulting in loss of molecular hydrogen. A limiting quantum yield of 0.13 mol/einstein was obtained for hydrogen production, which is within the experimental uncertainty of that obtained for the direct irradiation of the  $\text{Co}(\text{III})$  complex at 436 nm [12, 15]. These results demonstrated that visible light most certainly could be used to drive the photoelimination reaction of a transition metal dihydride.

A particular challenge in the choice of hydrogen production for the chemical reaction of the reactive complex was the necessity of working with molecular hydrogen. Here, the  $\text{Co}(\text{III})$  dihydride was generated via reaction of  $[\text{Co}(\text{bpy})(\text{PEt}_2\text{Ph})_2]^+$  with  $\text{H}_2$  and, of course, the photoelimination reaction

resulted in the production of H<sub>2</sub>. The highly flammable nature of hydrogen was an extra challenge at Clemson in the 1980s as smoking was still allowed in University buildings at that time, including in the chemistry research laboratories. Karen recounted on multiple occasions stories of people who would walk into the laboratory with lit cigarettes while she was working with hydrogen, even though she had posted clear warning signs of the danger on the door. It probably speaks to her care while working with sensitive materials that such events never resulted in fire or worse.

Karen then continued to study the effect of bidentate BLs on antenna complexes through the investigation of a series of monometallic and bimetallic Fe(II) cyano complexes containing either dpp or bpm BLs (Figure 1.5) [12, 16]. The bimetallic systems revealed that either bpm or dpp could successfully bridge two first-row transition-metal centers and the electrochemical data indicated good communication between the metal centers, supporting the model of possible energy transfer across the BL. The results also indicated that dpp may yield more promising results than bpm in the preparation of mixed-metal bimetallic complexes as it significantly lowers the steric crowding without reducing the communication between metal centers.

This investigation of BL effects on antenna complexes was then continued with bimetallic and tetrametallic Ru(II) complexes via dpp [12, 17]. The various tetrametallic complexes utilized the [Ru(dpp)<sub>3</sub>]<sup>2+</sup> core reported in her previous 1986 paper [14], which were then capped with three Ru(bpy)<sub>2</sub><sup>2+</sup>, Ru(phen)<sub>2</sub><sup>2+</sup>, or Ru(tpy)Cl<sup>+</sup> fragments. The results of the bimetallic systems were consistent with that previously observed for the analogous iron complexes. For the tetrametallic complexes, however, it was found that they were unstable when more than two electrons/mol are removed from the complexes. Still, the complexes allowed an overall predictability of the chromophore-based excited-state energies, as well as the ability to modulate the ground- and excited-state redox potentials by variation of metal center, BL, and terminal ligand. As a result, it was concluded that this structural motif provided significant promise for the further design and synthesis of heteropolymetallic complexes with specifically controlled ground- and excited-state properties [17].

Lastly, the ability to apply the previously designed multimetallic frameworks to heterometallic complexes was successfully demonstrated by the production of mixed-metal Ru(II)—Fe(II) bimetallic and tetrametallic complexes [12]. In these cases, the initial monometallic Ru(II) species [(bpy)<sub>2</sub>Ru(dpp)]<sup>2+</sup> or [Ru(dpp)<sub>3</sub>]<sup>2+</sup> were capped with Fe(CN)<sub>4</sub><sup>2-</sup> fragments. The synthesis of a bpm-bridged mixed Fe(II)—Co(II) bimetallic complex was also investigated.

By 1986, Karen had amassed a sizable amount of research and could reasonably have begun the preparation and defense of a relatively strong dissertation. However, that same year Petersen was awarded an Alexander von Humboldt research fellowship to spend a year at the Universitat Regensburg as a guest professor, where he began working in the laboratory of Arnt Vogler in December of 1986 [18]. At this point, Karen was the senior student in the Petersen group and he did not have a postdoc at the time, as Rory Murphy had left in August of 1986 to accept a faculty position at Seton Hall University [11]. As such, he really needed



to convince Karen to stay and supervise the group at Clemson until his return. As an incentive to wait to defend until after he returned from Germany, Petersen agreed to allow Karen to pursue some of her own research ideas while he was away.

Karen took advantage of this and began to develop ideas that she was interested in pursuing as part of her future career. These efforts resulted in the production and study of the Ir(III) complex  $[\text{Ir}(\text{dpp})_2\text{Cl}_2]^+$  [12]. The complex exhibited absorption in the visible regime, room temperature luminescence, as well as simple, stepwise electrochemical behavior. Overall, however, her interest in this species was the ultimate possibility of replacing the chlorides with hydride to produce a new reactive center for hydrogen production which could then be incorporated into multimetallic frameworks. Karen's development and synthesis of this complex was a critical moment in her career and this compound became the seed from which she grew the majority of her later independent research.

Petersen then returned to Clemson in August of 1987 [18] and Karen successfully defended her PhD dissertation entitled "The development of novel Fe, Co, Ir, and Ru complexes for the capture and utilization of solar energy" that same month before a graduate committee comprised of Petersen, Dr Kilian Dill, Dr James C. Fanning, and Dr Darryl D. DesMarteau [12]. Petersen commonly viewed Karen as the most successful PhD student of his career, stating in 2009 [6]:

"Karen was the most driven and most successful of the Ph.D. students I trained in chemistry."

Particularly after pursuing her own research ideas during Petersen's absence in Germany, Karen was eager to apply for faculty positions and begin her own independent career. However, an opportunity to work as a postdoc under Nobel Laureate Melvin Calvin (1911–1997) presented itself just as Karen finished and that was not an experience that she could pass up.

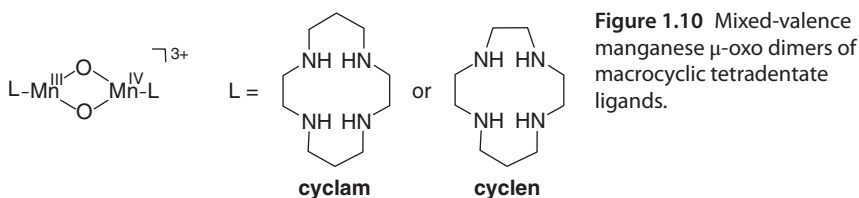
## 1.4 Postdoctoral Research and the University of California, Berkeley

After receiving her PhD from Clemson in 1987 [2–4, 6], Karen moved across the country to begin a postdoctoral fellowship with Melvin Calvin (PhD University of Minnesota 1935) (Figure 1.9) at the University of California, Berkeley [2–4]. Melvin Calvin was awarded the 1961 Nobel Prize in Chemistry for his work on the mechanistic study of photosynthesis, with an emphasis on the path of carbon during photosynthetic  $\text{CO}_2$  reduction, and his research had a strong focus on the electronic, photoelectric, and photochemical properties of metal chelate complexes [19]. As such, the focus and efforts of the Calvin group was synergistic with Karen's previous work under Petersen. Although she stayed at Berkeley for only 1 year, she accumulated three publications from her contributions to the group [20–22].

Her efforts in the Calvin group focused on metal chelates of macrocyclic tetradentate ligands, particularly 1,4,8,11-tetraazacyclotetradecane (cyclam)



**Figure 1.9** Melvin Calvin. (Photo courtesy of Lawrence Berkeley National Laboratory.)



**Figure 1.10** Mixed-valence manganese  $\mu$ -oxo dimers of macrocyclic tetradentate ligands.

and 1,4,7,10-tetraazacyclododecane (cyclen) [20–22]. The majority of this work focused on mixed-valence manganese  $\mu$ -oxo dimers (Figure 1.10) as potential homogeneous, multiple-electron redox catalysts [20, 21]. Of particular interest was the possibility of using such complexes for the catalytic oxidation of water to molecular oxygen. The electrochemistry of these complexes revealed them to be remarkably stable to both oxidation and reduction [20, 21] and that the redox potentials could be tuned by the choice of macrocyclic ligands [20]. In addition, it was found that cyclic voltammetry in the presence of water exhibited an additional process not observed in dry  $\text{CH}_3\text{CN}$ , which was ultimately determined to be consistent with the oxidation of water at the electrode following the electrochemical oxidation of the  $\text{Mn}(\text{III})$ – $\text{Mn}(\text{IV})$  dimer to the  $\text{Mn}(\text{IV})$ – $\text{Mn}(\text{IV})$  species [20]. It was later found that these species could be generated electrochemically via the oxidation of  $\text{Mn}(\text{SO}_3\text{CF}_3)_2$  in a water/acetonitrile solution in the presence of the ligand, which revealed that the oxygens of the  $\mu$ -oxo bridge came from water [21].

## 1.5 Washington State University: Beginning an Independent Career

Karen then moved to Pullman, Washington to join the Department of Chemistry at WSU as an assistant professor in the fall of 1988 [2, 6]. There she joined Professors John Hunt and Scot Wherland as part of the Inorganic Chemistry Division. At the time she joined the department, Karen became the second woman on the chemistry faculty [1, 5]. Karen had been assigned research space in one of the two new additions to Fulmer Hall, which were still in the final stages of construction at the time of her arrival [23]. As a result, she was assigned temporary laboratory space on the first floor of Fulmer Hall and it was there that she started to build her research group. The first student to join her research group was a third-year chemistry undergraduate, Seth Rasmussen, who had responded to a work-study position Karen had posted for a research assistant early in the fall of 1988. A second student, Eugene Yi, joined the group shortly thereafter.

During the spring of 1989, the laboratory transitioned to its permanent space in the ground floor of the new Synthesis Unit of Fulmer Hall and it was here that the Brewer Group really began to take shape and grow. Karen's personality and enthusiasm for research continued to draw undergraduates to the group and Karen recruited her first PhD student, Mark M. Richter (B.A. Gustavus Adolphus College 1989) in the summer of 1989. Thus, by the spring of 1990, the group had already grown to an appreciable size (Figure 1.11).

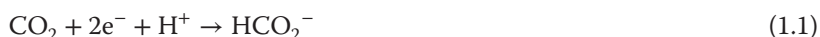
Karen's research at WSU began as an extension of the  $[\text{Ir}(\text{dpp})_2\text{Cl}_2]^+$  complex that she prepared during her final year at Clemson, with the synthesis



**Figure 1.11** Brewer Group, Spring 1990 (L to R): Eric Kimble (undergrad), Bob Williamson (undergrad), Seth Rasmussen (undergrad), Keith Blomgren (undergrad), Karen Brewer (Asst. Prof.), Sumner Jones (undergrad), Mark Richter (grad student), and Jon Bridgewater (undergrad). (Courtesy of Hannah Rodgers and the Brewer Group.)

and characterization of a series of Ir(III) and Rh(III) complexes of the type  $[\text{Ir}(\text{BL})_2\text{Cl}_2]^+$  and  $[\text{Rh}(\text{BL})_2\text{Br}_2]^+$  [24]. Here, the polypyridyl ligands consisted of one of four bidentate BLs, including the previously discussed bpm, dpp, and dpq (Figure 1.8), as well as the benzo-annulated analogue of dpq, 2,3-bis(2-pyridyl)benzoquinoxaline (dpb). Although her initial interest in such complexes back in 1986–87 was as potential reactive centers for hydrogen production, her focus had shifted to the application of these complexes as potential electrocatalysts for  $\text{CO}_2$  reduction [24]. This new interest in both electrocatalysts and  $\text{CO}_2$  reduction was most certainly a result of her time in the Calvin laboratory.

All of the Rh(III) and Ir(III) complexes successfully catalyzed the reduction of  $\text{CO}_2$  to formate ( $\text{HCO}_2^-$ ):



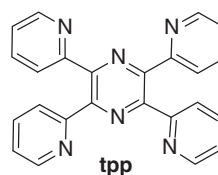
Current efficiencies for these catalytic reductions ranged from ca. 19 to 70%, with the Rh(III) complexes providing higher efficiencies than the analogous Ir(III) species [24]. These results confirmed that the application of the BLs did not significantly alter the desired catalytic activity of the metal previously observed in  $[\text{Rh}(\text{bpy})_2(\text{OTf})_2]^+$  (where  $\text{OTf}$  = trifluoromethylsulfonate). The application of the BLs thus provided the promise of developing multimetal systems that could ultimately allow the potential photochemical reduction of  $\text{CO}_2$ .

In addition to this initial work on group 9 complexes, efforts began in the study of osmium compounds of various BLs as new Os(II)-based antenna complexes for the eventual production of multimetallic complexes. These efforts began with the synthesis and study of a series of complexes of the form  $[\text{Os}(\text{bpy})_2\text{BL}](\text{PF}_6)_2$ , where BL consisted of dpp, dpq, or dpb [25]. This was then followed by the preparation and study of the  $\text{Ru}(\text{bpy})_2^{2+}$  and  $\text{Os}(\text{bpy})_2^{2+}$  capped bimetallic complexes  $[(\text{bpy})_2\text{Os}(\text{BL})\text{Ru}(\text{bpy})_2](\text{PF}_6)_4$  [26] and  $[(\text{bpy})_2\text{Os}(\text{BL})\text{Os}(\text{bpy})_2](\text{PF}_6)_4$  [27]. In general, the Os-based metal-to-ligand charge-transfer (MLCT) transitions occur at lower energy than the analogous Ru-based transitions and intervalence charge-transfer studies indicated that the metal–metal coupling is enhanced in the Os/Os systems relative to the Os/Ru mixed-metal analogues [26, 27]. Synthesis of the bis-BL species  $\text{Os}(\text{BL})_2\text{Cl}_2$  then allowed the production of the trimetallic complexes  $[\{(\text{bpy})_2\text{Ru}(\text{BL})\}_2\text{OsCl}_2](\text{PF}_6)_4$  [28].

Work also continued on the initial Rh and Ir complexes, with efforts focused on the addition of  $\text{Ru}(\text{bpy})_2^{2+}$  moieties to the two BLs of the central complexes. Purification of the resulting trimetallic complexes was challenging, such that although these efforts dated back to early 1990, the first report of these complexes was not until 1993. This report detailed the synthesis and characterization of a series of complexes of the type  $[\{(\text{bpy})_2\text{Ru}(\text{BL})\}_2\text{IrCl}_2]^{5+}$ , where BL included dpp, dpq, and dpb [29].

At the same time, the group began the investigation of multimetallic complexes of the terdentate BL 2,3,5,6-tetrakis(2-pyridyl)pyrazine (tpp, Figure 1.12). This began with the synthesis of  $\text{Ir}(\text{tpp})\text{Cl}_3$  and  $[\text{Ru}(\text{tpp})(\text{tpp})](\text{PF}_6)_2$ , before the ultimate synthesis of the mixed-metal bimetallic species  $[(\text{tpp})\text{Ru}(\text{tpp})\text{IrCl}_3](\text{PF}_6)_2$  [30]. It is perhaps not surprising that this study provided evidence that the

**Figure 1.12** The terdentate bridging ligand 2,3,5,6-tetrakis(2-pyridyl)pyrazine.



increased tridentate chelate of the tpp ligand provides excellent communication between the MLCT states centered on different metals.

While building her research group at WSU, this time in Pullman also brought changes to her nonacademic life. In the fall of 1989, Karen and Gary were looking forward to a trip to Hawaii that December to attend the International Chemical Congress of Pacific Basin Societies (Pacifichem 1989), with plans of exotic drinks and time on the beach. The details of these plans changed abruptly just a few weeks before the trip, however, when Karen discovered that she was pregnant, thus removing exotic drinks (at least those of the alcoholic kind) from the table. Their first child, Nicole Brewer, was born during the summer of 1990.

Karen's time in Pullman was somewhat short-lived, however, as she accepted an offer to move to Virginia Polytechnic Institute and State University (Virginia Tech) after only 4 years at WSU. Her choice to move her career was the result of several factors, including moving back closer to both her and Gary's families. In addition, she felt somewhat limited by what she perceived as a male-dominated culture within the department at WSU and thought things might be better at Virginia Tech. Even so, she left on good terms with her WSU colleagues, particularly Roger Willett with whom she continued to collaborate for years to come [31–34].

## 1.6 Move to Virginia Tech

Karen thus moved to Blacksburg, Virginia to become an assistant professor in the Department of Chemistry at Virginia Tech in the fall of 1992 [1–5]. Three of her graduate students from WSU, Sharon Molnar, Lisa Vogler, and Glen Jensen, moved to Virginia with her to become the core of her new research group there [35]. Mark Richter, who was close to finishing at the time, remained at WSU to finish writing his dissertation and was the only of Karen's graduate students to graduate from WSU. At the time that she joined Virginia Tech, she became one of two women on the faculty in the department [8] and was only the third woman ever hired in chemistry [1, 5].

At Virginia Tech, Karen's group continued to work on the synthesis, characterization, and photophysics/photochemistry of various multimetallic complexes. This included further work on the Rh- and Ir-based trimetallic complexes initially developed at WSU [36–38], as well as the eventual application of the Ir trimetallics as electrocatalysts for CO<sub>2</sub> reduction [39]. In comparison to the monometallic analogues, the trimetallics were found to be much better electrocatalysts. Not only were they found to be extremely selective toward the electrocatalytic reduction of CO<sub>2</sub> to CO but they also gave nearly quantitative current efficiencies and appeared quite robust under the electrocatalytic conditions [39].

In only 3 short years, Karen was promoted to associate professor in 1995 and she became the second woman granted tenure in the Department of Chemistry [1]. It was also about this same time that Karen and Gary welcomed another addition to their family with the birth of their second daughter, Kaitlyn Brewer. In the end, however, Karen's marriage did not last, eventually resulting in separation and divorce. Following the divorce, Karen took on the primary responsibility to continue raising Nicole and Kaitlyn. It has been said that Karen viewed her greatest achievement to be raising her two daughters [1].

Karen continued to be successful at Virginia Tech, not only in her research but also as an exceptional teacher and as a champion of science via numerous outreach activities. She was finally promoted to the rank of full professor in 2005 [1–4].

## 1.7 Collaboration with Brenda Winkel and the Study of Metal-DNA Interactions

Another landmark moment in her career occurred shortly after she arrived at Virginia Tech in August of 1992, when she met Brenda Winkel Shirley (now Brenda Winkel, Figure 1.13) at new faculty orientation [8, 40–42]. Like Karen, Brenda was a new faculty member at Virginia Tech and had just joined



**Figure 1.13** Karen J. Brewer and collaborator Brenda Winkel in 2005. (Courtesy of Virginia Tech.)

the Department of Biological Sciences and upon meeting her, Karen innocently asked her if she knew anything about DNA [42]. With initial training in chemistry and biochemistry, followed by a PhD in Genetics, Brenda was perhaps the perfect possible collaborator for the potential application of the inorganic species being developed in the Brewer laboratory to biological systems. The study of the interaction of multimetallic species with DNA then eventually became a major focus in the Brewer Group [8].

These efforts began by looking at ways to overcome some of the limitations of the widely used cancer drug cisplatin [*cis*-Pt(NH<sub>3</sub>)<sub>2</sub>Cl<sub>2</sub>] [40, 41]. As such, early efforts focused on the potential DNA binding of Pt bimetallic complexes of the form [(bpy)<sub>2</sub>M(dpb)PtCl<sub>2</sub>]Cl<sub>2</sub> (where M=Ru(II) or Os(II)) [43–45]. In fact, both complexes were shown to successfully bind to DNA and exhibited binding thought to be primarily intrastrand cross-linking in nature, similar to cisplatin [44, 45]. In contrast to cisplatin, however, the bimetallic Ru<sup>+</sup> and Os-based complexes exhibited a higher percentage of interstrand cross-links. These studies ruled out a purely intercalative mode of interaction and strongly suggested that these complexes form covalent bonds to DNA through the platinum metal site [45]. These bimetallic species then formed the basis of a new class of complexes that interact with DNA in a manner that is similar to but still observably different from the known anticancer agent cisplatin. In addition, the higher water solubility of the bimetallic complexes made them attractive as potential chemotherapeutic agents [41, 45].

Study of the Pt-based bimetallics was then expanded to include a greater diversity of BLs beyond the initially studied dpb [46]. In addition, the previous Ru(bpy)<sub>2</sub><sup>2+</sup> moiety was replaced with a Ru center capped with the terdentate ligand tpy, that is, Ru(tpy)Cl<sup>+</sup>. The chloride could then be substituted with monodentate phosphine ligands for greater structural and chemical diversity [47, 48]. As with the previous complexes, all of these species avidly bind DNA and occupy binding sites consistent with the covalent attachment of Pt [46, 48].

In addition to the successful Pt-based complexes, it was shown that previously studied Rh-based trimetallic complexes could successfully be used to photocleave DNA [49, 50]. In the absence of molecular oxygen, the DNA plasmid irradiated ( $\lambda \geq 475$  nm) in the presence of [(bpy)<sub>2</sub>Ru(dpp)]<sub>2</sub>RhCl<sub>2</sub>]<sup>5+</sup> exhibited conversion of the supercoiled DNA to the nicked form. While the mode of the DNA photocleavage was unclear, the cleavage observed was consistent with reactivity arising from the photogenerated Rh(II) site. This work was then expanded by tuning of the antenna species, including the use of Os(bpy)<sub>2</sub><sup>2+</sup> and Ru(tpy)Cl<sup>+</sup> fragments [50]. The photodynamic action of these complexes was reported to inhibit cell replication after exposure to light while displaying no impact on cell replication in the dark [51, 52].

These two approaches were then combined with the production of the tetrametallic complex, [(bpy)<sub>2</sub>Ru(dpp)]<sub>2</sub>Ru(dpp)PtCl<sub>2</sub>]<sup>6+</sup> [53]. This complex utilized the central [Ru(dpp)<sub>3</sub>]<sup>2+</sup> developed by Karen during her graduate work with Petersen [12, 14], coupled to two Ru(bpy)<sub>2</sub><sup>2+</sup> antenna complexes and the Pt center for DNA binding. As a result, this complex was shown to display both Pt-based DNA binding and Ru-based DNA photocleavage.

These efforts continued with the preparation and study of additional complexes, with an overall emphasis on photodynamic therapy. In particular, efforts focused on the production of materials that absorb efficiently within the therapeutic window of red light [54–56]. Ultimately, these efforts included an additional collaboration with John Robertson in biomedical engineering [8], as well as efforts to take their research into a clinical testing phase [40]. This also included a partnership with Theralase Technologies Inc., a developer of light sources capable of light treatment on deep tissue [40, 41]. It was reported in 2010 that when irradiated by lasers developed by Theralase Technologies, the complexes produced by the Brewer Group had been proved effective in destroying breast cancer cells in preclinical trials [57].

## 1.8 A Return to Where It All Started: Photochemical H<sub>2</sub> Production

As previously discussed, the photochemical process that was the focus of Karen's graduate work was that of H<sub>2</sub> production [12]. As such, it seems only natural that at some point Karen would return to this area of photochemical research. Thus, efforts began to apply the previously reported Rh-based trimetallic complex  $[(\text{bpy})_2\text{Ru}(\text{dpp})_2\text{RhCl}_2]^{5+}$  to the photocatalytic production of H<sub>2</sub> from H<sub>2</sub>O, which were first reported in 2007 [58]. In this initial communication, it was reported that the complex produced hydrogen catalytically when excited at 470 nm in the presence of dimethylaniline as a sacrificial electron donor, with a quantum yield of ca. 0.01. Following photolysis of this mixture for 4 h, 8.2 μmol of H<sub>2</sub> was produced representing 30 turnovers of the catalytic system with no reduction in the rate of H<sub>2</sub> production [58]. It was then shown in a follow-up report that the RhBr<sub>2</sub> analogue exhibited enhanced catalytic performance to generate 10.9 μmol of H<sub>2</sub> (38 turnovers) under the same conditions [59].

These initial efforts were then followed by a more expansive study in which the antenna complexes were varied via the capping of the  $[\text{Rh}(\text{dpp})_2\text{X}_2]^+$  core with either Ru(bpy)<sub>2</sub><sup>2+</sup>, Os(bpy)<sub>2</sub><sup>2+</sup>, Ru(phen)<sub>2</sub><sup>2+</sup>, Ru(tpy)Cl<sup>+</sup>, or Os(tpy)Cl<sup>+</sup> [60]. For comparison, the Ir-based complex  $[(\text{bpy})_2\text{Ru}(\text{dpp})_2\text{IrCl}_2]^{5+}$  was also evaluated and all but the Ir complex and the Os(tpy)Cl<sup>+</sup>-capped Rh complex demonstrated photocatalytic activity. Although the previously studied  $[(\text{bpy})_2\text{Ru}(\text{dpp})_2\text{RhBr}_2]^{5+}$  continued to provide the best catalytic performance [59, 60], the current study did illustrate that the use of phen terminal ligands in place of bpy had only minor effects on the photocatalytic activity.

In efforts to further tune the activity of the best photocatalyst, the potential effects of complex counterion (PF<sub>6</sub><sup>-</sup> vs Br<sup>-</sup>) was investigated, as well as the effect of pH and buffer acid [61]. While the use of Br<sup>-</sup> counterions does provide water solubility, this also resulted in a reduction in catalyst activity. In terms of pH, it was found that values near the pK<sub>a</sub> of the amine used for the electron donor gave a notable increase in H<sub>2</sub> production [61].

A shift to a Pt-based catalyst was then reported in 2011 with the tetrametallic species  $[(\text{phen})_2\text{Ru}(\text{dpp})_2\text{Ru}(\text{dpq})\text{PtCl}_2](\text{PF}_6)_6$  [62]. In contrast to the previous Rh-based complexes, this showed enhanced activity with the production



of 21.1  $\mu\text{mol}$  of  $\text{H}_2$  and 115 turnovers of the catalytic system when irradiated at 470 nm for 5 h.

About the same time, however, significant advances had been made in the applications of the previous champion photocatalyst,  $[\{(\text{bpy})_2\text{Ru}(\text{dpp})\}_2\text{RhBr}_2]^{5+}$  [63]. Through careful tuning of reaction conditions, it was found that  $\text{H}_2$  production was enhanced by the choice of solvent (DMF), increased electron-donor concentration, increased headspace, and purging of the system of  $\text{H}_2$ . Using such optimized conditions, 420 turnovers of the catalyst were achieved over 50 h, with a  $\Phi = 0.023$ . As a result, over 20 mL (810  $\mu\text{mol}$ ) of  $\text{H}_2$  could be photocatalytically produced over a period of 19.5 h. This was then further improved by replacing the terminal bpy ligands with 4,7-diphenyl-1,10-phenanthroline ( $\text{Ph}_2\text{phen}$ ) to increase the maximum  $\Phi$  to 0.073. As a result, this allowed the production of 44 mL (1640  $\mu\text{mol}$ ) of  $\text{H}_2$  in 20 h, corresponding to a catalyst turnover of 610 [64].

## 1.9 A Career Cut Tragically Short

For all of her professional career, Karen suffered from various health issues. By her teens, she had already been diagnosed with Crohn's disease [8], a relapsing systemic inflammatory disease that mainly affects the gastrointestinal tract, but can also include other health effects such as immune disorders [65]. Even during her graduate studies, her health was always on the edge, but she never complained or used it as an excuse [18]. Her constant battle with Crohn's resulted in various surgeries and a significant number of hospital stays throughout her life [8], and such health issues too often caused her to unexpectedly change plans or cancel speaking engagements. At one point, her struggles with her health even led to her needing a reduced teaching load while she worked to get her health under control [35]. The fact that she was able to accomplish so much during her career while dealing with such a handicap makes her successes just that much more impressive.

Unrelated to her Crohn's, Karen also had issues with her knees such that she finally had to give up basketball while she was attending Wofford [35]. As she got older, her knees continued to give her issues until she finally underwent knee-replacement surgery in June of 2012 [66]. Tragically, she did not recover from the surgery as expected, and it was eventually discovered that she was suffering from a serious infection related to the surgery. Treatment with intravenous antibiotics was not able to cure the infection, which ultimately required the removal of the knee replacement in order to treat the infection at the source in July of 2013 [35, 66]. As a result, she had to spend over a month without a physical knee while the infection was dealt with. It has been proposed that her various surgeries and hospital stays throughout her life led to such an antibiotic-resistant infection. Once the infection was dealt with, she underwent surgery once again in August of 2013 to replace the knee. In August of the following year, however, it was found that the infection had returned, thus requiring another knee surgery [66]. It was sometime in the months following this final surgery that it is believed that she developed a blood clot, resulting in a pulmonary embolism. As a result, Karen died unexpectedly in Blacksburg, Virginia, on October 24, 2014, at the

age of 53 [2–5]. Funeral services were held in Blacksburg on October 31, 2014, and she was laid to rest at Memorial Gardens of the New River Valley [3, 5].

## 1.10 Karen's Legacy

While there is no doubt that Karen left an extensive record of discoveries and top-notch research, which will be forever remembered and cited by anyone working in the field of multimetallic coordination chemistry, her true legacy is all of those that she trained over the years. As anyone who ever spent time in her group can confirm, the Brewer Group was family and every student or postdoc was far more than just the means to yet another publication. In the process, she did her best to instill in them everything that made her the scientist and teacher that she was. The success of this can be seen in the large number of Brewer Group members who remained in academia and are now faculty members, instructors, and research advisors themselves. This includes Seth Rasmussen (North Dakota State University), Mark Richter (Missouri State University), Sharon Molnar (West Virginia State University), Shawn Swavey (University of Dayton), Alvin Holder (Old Dominion University), Matthew Mongelli (Kean University), Matthew Milkevitch (Philadelphia University), Shamindri Arachchige (Virginia Tech), Michael Jordan (Oklahoma Baptist University), Avijita Jain (Indiana University of Pennsylvania), Jessica and Travis White (Ohio University), and I am sure even more that I have missed. All of these former members of the Brewer Group will then pass on aspects of Karen to their own students, thus guaranteeing that she will continue to live on in spirit and never be forgotten.

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