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# Playing with Excited Double Bonds. Isomeric Triplets, Upper Excited States, One-Way Isomerization & Hula-Twist

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When I started to do research in Hammond's group at Caltech, I was indeed incredibly naive. Fortunately, Nick Turro, Jack Saltiel and Angelo Lamola were already there. I am including Angelo with the two more senior members of the group for the simple reason that he was far ahead in research experience than the rest of us in his class. And, at that time he was already quite ready to give out directions. For a green horn like me, I was quite happy to receive suggestions from them or anybody else. To a large extent, it was the interaction with them and other members of the research group that allowed my hurried transformation from a complete novice to a full fledge member of the "Hammond Mafia".

From Nick, I learned all the basic things including how to pack a gc column. In fact, later on after Nick left for Harvard I was promoted to the post of the caretaker of the Beckman Megachrome gc, one of the few working units in the country. While I floundered in the beginning, Angelo kept on telling me to try new things on my own instead of waiting to be told what to do. So, one day I roamed around the chemical stockroom and found a bottle of isoprene. With my newly acquired gc and photochemical techniques, I irradiated a sample of the diene in the presence of benzophenone. I detected seven new peaks! A wiser man probably would have abandoned such a complex system and looked for a greener pasture. But not knowing better, I found the new result quite a nice green pasture. In fact, with the Megachrome, I was able to separate close to gram quantities of all seven dimers. I was quite proud of myself with the quality of the NMR spectra obtained on the old Varian 60 MHz spectrometer.

At that time, Jack was completing his Saltiel plot, stilbene isomer composition versus triplet energy of sensitizers. I borrowed his idea and struggled through the rather complex mixtures of isoprene dimers and came up with a plot of percentages of C4 dimers versus sensitizer energies and submitted my first progress report to GSH. It was near the end of my first summer at Caltech. The following Monday morning George showed up in my lab with a smile on his face and proceeded to explain to me his new idea of isomeric diene triplets. I did not quite follow everything he said; but certainly I was very happy that my data generated such enthusiasm on his part. Soon, he left my lab saying that he would tell Nick about it. (You see before my isoprene work, Nick had in his hand some "unusual" butadiene dimer results where benzophenone gave a very different product mixture from that of biacetyl). Wow, I got the news from the Cat's mouth before Nick. It certainly produced a warm feeling that I might be allowed to stay in Caltech. My mood reached a new high when in the following week, a manuscript on isomeric triplets of dienes was ready for JACS.

Of course, now it looks very odd that in that communication George Hammond, such a clear thinker, had chosen this terribly complex isoprene system to demonstrate the concept of isomeric triplets of dienes. But, the choice was not his; I was simply too fond of a system that worked for me. Later on, Nick did save the pain of the textbook writers of later years by completing the Saltiel plot of the simpler butadiene system.

One thing bothered me with the isoprene dimer work. When anthracenes were used as sensitizers, the cyclobutane dimers were inexplicably more (not by much, but the difference was real) than those from the high energy sensitizers. Soon after I joined the Central Research Department of duPont, I came across the exciting report by the group of chemists (Reid Kellogg, Peter McCartin and Dick Bennett) of the old Radiation Laboratory that described the assignment of the $T_2$ level of anthracene being very close to $S_1$. The exact position of $T_2$ depends on the nature of the substituents on the aromatic rings, but it was clear that intersystem crossing involved the population of $T_2$. It did not take long for me to associate their findings with the isoprene results by invoking $T_2$ sensitization and selective $T_1$ quenching of the cisoid triplets. But the catch was how to rule out the concept of non-vertical excitation, something made very popular by Saltiel and Hammond in their stilbene isomerization work. Fortunately, I had in my hand a set of fluorinated barrelenes which were shown to undergo triplet sensitized rearrangements. The rigid bicyclo[2.2.2]octatriene structure negates any possibility of non-vertical excitation. So with some patience, $T_2$-sensitization became a reality. (I used to say that the process was so inefficient that only an industrial chemist not faced with the "publish or perish" dilemma can afford to tackle the project). Helping along the chemical study was the unique, seemingly uphill process of naphthalene phosphorescence sensitized by anthracene (I solicited the help of Reid Kellogg for this experiment). Perhaps the chemical community was getting weary of the idea of non-vertical excitation; there was virtually no resistance toward the case of $T_2$ sensitization, even though it was an obvious violation of the Kasha's Rule. Using chemical kinetics, we determined the lifetimes (sub-nsec) of such upper states, which later were verified by spectroscopists with the advent of more sensitive and better time-resolved instruments.

The next thirty years at Hawaii went through in a blur. The program for preparation of new stereoisomers of vitamin A started with Ramamurthy's discovery of one-way triplet sensitized isomerization of β -ionol. In spite of being a physical chemist at heart, he took up the synthetic challenge that led to many hindered 7-cis precursors of vitamin A. Strangely, it was only after successful characterization of the hindered, previously unknown 7-cis geometry and well on our way to new isomers of vitamin A, that we discovered an early paper by L. Pauling stating that such hindered 7-cis isomers were supposed to be too unstable for isolation. (I am not sure what is the moral of this story as far as encouraging students to keep up with the literature.) But, of course Pauling's conclusion is still valid if it is limited to comparing relative thermodynamic stability of the isomers rather than predicting their kinetic stability at room temperature.

Murthy departed in 1974 for a post-doc position with Paul de Mayo. He left with me partially separated synthetic mixtures of new 7-cis isomers of retinal. Soon after, a communication by Nakanishi appeared in which the use of 20 micron silica gel was mentioned for separation of isomers of a retinal analog. So, I packed a 7 ft "hplc" column. With that awkward setup, pure 7-cis isomers of retinal were isolated for the first time. Subsequently, after a coaching session with

Allen Kropf, separation of retinal isomers on commercial columns with silica gel particles of progressively smaller sizes became a routine matter.

The program later led to all previously unknown isomers of vitamin A and A2. These new stereoisomers allowed us to demonstrate regioselective or adiabatic isomerization, quantum chain processes and to probe for the stereospecificity of the binding site of opsin. The flexible binding site argued for possible inclusion of substituted vitamin A as the chromophore. Subsequently, many fluorinated and alkylated retinal analogs were prepared for information on specific protein-substrate interactions. Recently, we finally took up the courage to tackle the larger and more sensitive fluorinated carotenoids.

A few years ago, Al Asato prepared a series of compounds that we called "Mini-carotenes". Tomas Gillbro of Umea turned them into a wonderful set of compounds that systematically violated the Kasha's Rule -- by emitting from $S_2$ with varying intensity. Even azulene has played an important role in our work. Al prepared several series of highly colored azulenic retinal analogs that led to the first NIR absorbing analogs of bacteriorhodopsin and other polarized polyenes. And, Rajeev's recently prepared 1,3-difluoroazulene now has the record for high quantum yield of $S_2$ emission (0.20) and lifetime (9.5 ns) as claimed by our collaborator Ron Steer.

In considering conditions for regiospecific isomerization of polyenes, we came up with the "Hula-twist" model -- simultaneous twisting of a pair of adjacent double and single bonds, a process that seemingly violates the NEER Principle. We thought it could only be a high energy process taking place in a confined medium. For a while it remained as an unlikely high energy process because there were no new experimental evidence supporting the idea. It was a surprise to me that a decade later, high level calculations showed that the low energy pathway for deactivation of an excited singlet polyene, via conical intersection, followed such a two-bond twisted process (M. Olivucci *et al*). Photoisomerization of vitamin D compounds was shown to yield "Hula-twist" products (W. Fuss) and isomerization data of exocyclic dienes suggested simultaneous two-bond twist (W. Leigh). When taken together with the early low temperature photochemical work of interconversion of S-trans, S-cis conformers of 1,3-butadiene and 1,3,5,7-octateraene (M. Squillacote & B. Kohler), there appear to be room again for this conceptually simple process (although admittedly I was guilty of being excessively optimistic in presenting the model).

In looking back, I can honestly say that when I started my job at Hawaii, I never envisioned the type of complex systems that we later worked on. The program simply evolved with the help of many capable associates. The polyene photochemical program was initiated by Yondani Butt and V. Ramamurthy. Synthetic value of this observation was subsequently realized through the effort of my long term associate, Al Asato, joined by Aravinda Kini, Dennis Mead, Achla Trehan, Rong-Liang Chen, Jin Liu and Rajeev Muthyala along the way. Hiro Matsumoto brought biochemical expertise into the group. Marlene Denny provided reliable analytical and photochemical work, Tara Mirzadegan in computer graphics, Letty Colmenares in her all around effort of bioorganic and protein NMR studies, S. Ganapathy and Bao-Wen Zhang in quantitative retinal photochemistry and Xiao-Yuan Li and Yun Zhu in spectroscopic and analog studies. It has been fun to learn with my people, and to share the fruit of their efforts including the

occasional reward of the dawning of simple explanations out of the initial, seemingly chaotic sets of data. To them I am most grateful.

Bob Liu,

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