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President's Letter

Dear EPA members

Writing a letter in the last month of the year is difficult to accomplish without sending any season´s greetings. For a photochemist, the light deprivation of winter time carries perhaps a particular burden. Fortunately, today, the first snow fell in Bremen, which caused some nice scattering effects to make days brighter – and giving me a pleasant surrounding while writing my first letter as EPA President.

Please take the time to read our December 2012 Newsletter, which is thematically dedicated to photochemical techniques in organic synthesis, resulting in a very comprehensive and multifaceted collection of interesting articles by leaders in the field. Of particular interest to all of us, you will read about the history of the IUPAC Symposia of Photochemistry, compiled by Silvia Braslavsky, where you will also find good reasons why this symposium series is traditionally being held in Europe. In general, historical content related to photochemistry is very well placed in our Newsletter and I invite everybody to share important knowledge from the past. The recent publication on the history of EPA, which has been prepared for a book series by Ugo Mazzucato, has also been highlighted in this issue by Angelo Albini.

Reports on recent EPA-associated conferences and workshops are included in this Newsletter. The XXIV IUPAC Symposium on Photochemistry in Coimbra was the international conference highlight in 2012. Our association contributed to the symposium by awarding the EPA PhD Prize to Karl Borjesson and the EPA-PPS Prize to Mike Heilemann, each accompanied by a lecture and a laudatio held by Eric Vauthey. Our new EC has been constituted by the EPA General Council held during the same symposium. We have now a new General Treasurer: Alexandre Fürstenberg is looking forward to cooperate with the national EPA representatives and is also prepared to receive directly membership applications, which can be paid conveniently by credit card. Please advertise EPA and convince colleagues and coworkers to join EPA – it´s easy, and there are immediate benefits, such as reduced registration fees at conferences. Also the Newsletter Editor is new in

office, please feel free to submit content to Maurizio D'Auria or our Associate Editor, Julia Pérez-Prieto. Finally, we will also have a new EC member, Roberto Improta, responsible for "new information technologies". You will find a first subtle indication on the direction this may lead to in the "Follow us …" section of our Newsletter. The "Follow us …" section is new, it is supposed to not only make each member look forward to the next issue, but also to allow all members to contribute articles related to upcoming themes. With two issues per year, one online and one printed, there is always sufficient time to make a contribution to the upcoming issue.

We are particularly looking forward to receive Technical Notes to be featured in our Newsletter. Remember there is a prize for the best Technical Note composed by a PhD student or postdoctoral researcher. In the next four issues of the Newsletter, you will find a series of notes on optical spectroscopic methods, written up by John Gilchrist. The technical note featured in this issue will help you decide, for example, which type of scattering the one mentioned from snow needs to be classified as. And if you are curious what you need to do if you would like to apply to the International Foundation of Photochemistry for funding, you will also need to study this issue of the EPA Newsletter very carefully.

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PUBLICATIONS

The history of the European Photochemistry Association

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Not everybody of the present day readers of the EPA Newsletter is familiar with the history of this association. An outline[1] is now available for the interested people, thanks to the work of one of the prominent figures of European photochemistry, Ugo Mazzucato. The lively activity in this field in the late Sixties and the interest generated, also among industrial chemists, led to the foundation of the association in 1970 under the auspices of the Council of Europe. A working party had carried out a preparatory work, suggesting that the new body should organize meetings on the model of Gordon conferences, publish an European journal of photochemistry and promote the mobility of European researchers. Scientists from ten European countries and G. Quinkert as IUPAC representative participated into the founding meeting in Strasbourg on September 10th and the first president was D. Bryce-Smith.[1] EPA participated to the organization of following photochemical meetings (Bordeaux, 1971; Reading, 1972) and began to circulate typewritten letters with information on photochemistry, which in 1978 developed into the printed edition of the EPA Bulletin. The following history of the association, chaired by K. Schaffner (from 1972), J. Jussot-Dubien (1976), F. De Schryver (1980), F. Wilkinson (1984), V. Balzani (1988), J. Verhoeven (1992), J Wirz (1996), J. Waluk (2000), D. Phillips (2004), D. Markovitsi (2007), E. Vauthey (2010) is then summoned up, with the various important initiatives, from the organization of meetings and summer schools (from 1974), the publication of directories of photochemical laboratories, the establishment, after several attempts, of Photochemical ad Photobiological Sciences, the contacts with the Inter-American Photochemical Society (IAPS) and the Japanese and then the Asian and Oceanian Photochemical Association. The portrait offered, based on personal experience, is vivid and sincere.

1. Mazzucato, U. *Photochemistry* **40**, 197-229 (2012).

Brief history of the IUPAC symposia on Photochemistry[1]

The IUPAC Symposium on Photochemistry was started in 1964 by the initiative of George Hammond, and held in Strasbourg, France.[2] It was then called International Symposium on Organic Photochemistry. Since 1967 its name is IUPAC Symposium on Photochemistry and it is regularly held in even years usually at the end of July.[3] This Symposium was only once held outside Europe in 2006 in Kyoto, Japan (see attached Table for a list of sites, chairmen and local organizers) and is planned to be again in Japan in 2016. The number of Japanese participants in the Symposia has been very large over many years.

In fact, 1964 was a banner year for photochemistry in that the Gordon Conference series and the IUPAC series were both started that year. However, the physical photochemists already had two series going: (1) the series which later became the International Conference on Photochemistry (ICP) which started in 1962,[4] and (2) the Informal Conference on Photochemistry, started by Francis Blacet in 1952 and held in North America every two years[5] until 2000 in San Juan, Puerto Rico.[6]

The rationale behind having the IUPAC Symposium on Photochemistry always (almost) in Europe is as follows. The "International Conference on Photochemistry, ICP" (in odd years, the next one will be in Leuven)[7] is held around the world, in Canada, USA, Japan, China, Russia, Europe, etc. The Gordon Conference on Organic Photochemistry is held in the USA since 1964, in odd years since 1965 (to alternate with the IUPAC Symposium on Photochemistry), and re-named Gordon Conference on Photochemistry since 2001. This Conference, together with the I-APS (Inter-American Photochemical Society)[8] Conference (every year in early January), serve the North-American Photochemical Community very well.

There is also an I-APS meeting in Latin-America every five years, the last one in 2011 in Mendoza, Argentina and the previous one in 2006 in Salvador de Bahia, Brazil. Information on the history of these meetings and of ELAFOT (Encuentro Latinoamericano de

Fotoquímica, which is the Encounter of Latin-American Photochemists) up to 2005 has been summarized in an article by Braslavsky and Simon.[9] The last ELAFOT was held in Córdoba, Argentina, in October 2012.[10]

The Asian and Oceanian Photochemistry Association (APA) holds regular meetings in the area.[11] The 7th Asian Photochemistry Conference 2012 (APC2012) was held in Osaka, Japan, in November 2012.[12]

Within Europe, the increasing contacts between the national sections of EPA (European Photochemistry Association)[13] have led to the support by EPA of various bi- and multi-lateral small European meetings,[14] among them a series called Central European Photochemical Conference (CECP), started in 1998.[15] But the Europeans do not have an extra "European Photochemical Conference" and the IUPAC Symposium serves also the purpose of hosting the European photochemical community; the General Council of EPA usually meets at these symposia, and EPA occasionally sponsors plenary lectures.

The chair of a given IUPAC Symposium on Photochemistry chooses, after adequate consultation, the chair of the Symposium four years later. The selected chair chooses the location and local organizer, requests the support by IUPAC and is responsible for the scientific standard and quality control of the Symposium, together with the selected scientific committee for that Symposium. Although the Symposia were held all in Europe (with the mentioned exception in 2006 in Kyoto), 10 of the first 20 Scientific Chairmen were from the USA, alternating with those from Europe. The decline in this practice reflects both declining USA participation, mainly due to the reduced support by the North American funding agencies, as well as simplified logistics when the Scientific Chair is located near the conference site.

During the Symposium there is usually a regular meeting of the Sub-Committee of Photochemistry of IUPAC to discuss ongoing projects and consider the possibility of new ones.

Since 1988, the Porter Medal[16] has been formally presented at the IUPAC Photochemistry Symposia, followed by a lecture of the medallist. The medal arose from a valedictory symposium held in London in 1986 following the retirement of George Porter as Director of the Royal Institution in London upon his election as President of the Royal Society. The choice of Porter medallist is

made by the EPA, IAPS, and Asia and Oceania Photochemistry Associations/Societies, the first medal being presented to George Porter himself in Bologna, 1988.

Several additional awards are presented during the Symposium by IUPAC and by various Journals to posters and oral contributions by young photochemists. Since 2008, the EPA presents the Prize for the best PhD Thesis in Photochemistry[17] and since 2010, the EPA-PPS Prize for the most cited paper of an EPA member in *Photochemical & Photobiological Sciences*, the society-owned journal, is awarded; the award of each prize is accompanied by a lecture of the prize winner.

Most of the Plenary and Invited Lectures of the Symposia are published in the Journal *Pure and Applied Chemistry*.[1]

An International Foundation of Photochemistry (IFP) with seat in Germany[18] was created in 1974 with the main purpose of helping financing the preparation steps of the Symposia. Its funds come from the accumulated revenues obtained during the Symposia. The Foundation board has also a regular meeting during the Symposia.

The history of the IUPAC Symposia on Photochemistry is a successful story with a promising future. In the recent Symposium in July 2012 in Coimbra[19] there were 640 participants from 53 Countries and many young colleagues presented interesting novel results in the form of talks and posters. The next Symposium is planned for 2014 in Bordeaux, France, and the Scientific Chairman is Dario Bassani. The following Symposium is planned for 2016 in Osaka, Japan and the Scientific Chairman is Tetsuro Majima.

November 2012

Compiled by *Silvia E. Braslavsky*

With contributions and very valuable comments and suggestions, i.e., "with a little help from my friends" *Dario Bassani, Hugh Burrows, Dietrich Döpp, Devens Gust, Frans De Schryver, Angelo Lamola, Fred Lewis, Ugo Mazzucato, Josef Michl, Sandra Monti, Werner Nau, David Phillips, Heinz Roth, Franco Scandola, Kurt Schaffner, and Anthony Trozzolo.*

Year	Site	Scientific Chairman	Local Organizer	Symposium Number
1964	Strasbourg, France	G. S. Hammond, US	J. Levisalles	Organic Photochemistry, Part of a NATO series
1967	Enschede, The Netherlands	W. G. Dauben, US	E. Havinga and M. Kronenberg	II
1970	St Moritz, Switzerland	D. Bryce-Smith, UK	K. Schaffner	III
1972	Baden-Baden, Germany	H. E. Zimmerman, US	D. Döpp	IV
1974	Enschede, The Netherlands	O. L. Chapman, US	J. J. C. Mulder	V
1976	Aix-en-Provence, France	K. Schaffner, Switzerland	J. Kossanyi and M. Julliard	VI
1978	Leuven, Belgium	N. J. Turro, US	F. de Schryver	VII
1980	Seefeld, Austria	H. Dürr, Germany	J. G. Schantl	VIII
1982	Pau, France	J. Joussot-Dubien, France	E. Poquet and H. Bouas-Laurent	IX
1984	Interlaken, Switzerland	D. J. Whitten, US	A. M. Braun	X
1986	Lisbon, Portugal	F. Wilkinson, UK	S. M. B. Costa	XI
1988	Bologna, Italy	V. Balzani, Italy	F. Bolletta	XII
1990	Warwick, UK	F. D. Lewis, US	R. S. Davidson	XIII
1992	Leuven, Belgium	F. De Schryver, Belgium	D. De Keukeleire	XIV
1994	Prague, Czech	J. Michl, US	I. Stibor	XV

	Republic			
1996	Helsinki, Finnland	J. Wirz, Switzerland	H. Lemmetyinen	XVI
1998	Sitges, Spain	R. A. Caldwell, US	J. Font	XVII
2000	Dresden, Germany	S. E. Braslavsky, Germany	T. Wolff	XVIII
2002	Budapest, Hungary	H. D. Roth, US	J. Nyitrai	XIX
2004	Granada, Spain	M. A. Miranda, Spain	B. Quintero	XX
2006	Kyoto, Japan	M. Irie, Japan	A. Osuka	XXI
2008	Gothenburg, Sweden	D. Gust, US	B. Albinsson	XXII
2010	Ferrara, Italy	F. Scandola, Italy	C. Chiorboli	XXIII
2012	Coimbra, Portugal	H. D. Burrows, Portugal	A. J. M. Valente	XXIV
2014	Bordeaux, France	D. M. Bassani, France		XXV
2016	Osaka, Japan	T. Majima, Japan		XXVI

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http://www.iupac.org/publications/pac/conferences/family/PHOTO/
2.
http://pac.iupac.org/publications/pac/pdf/1964/pdf/0904x_vii.pdf
3. http://iupac.org/publications/pac/conferences/Enschede_1967-07-16s/
4. G. Wyman, *Inter-American Photochemical Society Newsletter*, Vol. 22(2), November 1999.

5. F. C. Blacet, *Photochem Photobiol.* (1974) **19**, 384

6. https://www.jiscmail.ac.uk/cgi-bin/webadmin?A2=MOLECULAR-DYNAMICS-NEWS;df37611a.99

7.http://www.kuleuven.be/communicatie/congresbureau/congres/icp2013

8. http://www.i-aps.org/

9. S. E. Braslavsky, J. Simon, *Photochem Photobiol.* (2005) **81**, 768-70.

10. http://www.fotoqca-riocuarto.com.ar/website/

11. http://www.asianphotochem.com/

12. http://photochemistry.jp/apc2012/

13. http://photochemistry.eu

14. U. Mazzucato, The History of the European Photochemical Association, in "Photochemistry"**,** Royal Society of Chemistry, Ed.: Angelo Albini (2012) pp 195-229.

15. http://www.cecp.at/

16. http://www.portermedal.com/index.html

17. http://photochemistry.eu/phd_price.php

18. http://www.mik.nrw.de/nc/stiftungsverzeichnis-fuer-das-land-nrw/alle-stiftungen.html?tx_szstiftungsvz_pi1%5Bpage%5D=91&tx_szstiftungsvz_pi1%5Buid%5D=3709&tx_szstiftungsvz_pi1%5BsortDir%5D=DESC&tx_szstiftungsvz_pi1%5BsortBy%5D=name&tx_szstiftungsvz_pi1%5Bsingle%5D=1

19. http://www.photoiupac2012.com

# Photocatalytic reactions with organometallic and coordination compounds applied to organic synthesis

Norbert Hoffmann
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Photochemical excitation of molecules changes their electronic configuration and thus their chemical reactivity.[1] Applying photochemical reaction conditions largely broaden the reaction spectrum of a chemical compound. New product families or libraries become available or they can be more easily prepared. For these reasons, photochemical reactions are of particular interest for being applied to organic synthesis.[2,3,4]

In the same way, the reactivity of coordination or organometallic compounds is modified when they are electronically excited by light absorption.[5,6] Thus their catalytic properties are influenced and new catalytic reactions can be carried out or existing reactions are improved. When applications of photochemical reactions to organic synthesis are reviewed, reactions of with organometallic or coordination compounds are generally not discussed although in the past as well in the present they play an important role in this field. Thus the Cu(I) catalysed [2+2] photocycloaddition of alkenes was frequently applied to organic synthesis.[7]

In particular, when applied in catalytic reactions, electron transfer and ligand exchange play a central role. Among the reactions of organometallic and coordination compounds, these two processes are efficiently affected by electronic excitation. Therefore a lot of applications to organic synthesis have now been reported. During recent years, a lot of reactions photocatalyzed by $[Ru(bpy)_3]^{2+}$ have been carried out.[8] One typical example is shown in Figure 1. The halogenated indol derivative **1** was transformed efficiently and in a stereoselctive way with **2** into the adduct **3**.[9] This product is a synthesis intermediate for the production of (+)-gliocladin C. After photochemical excitation, $[Ru(bpy)_3]^{2+}$ is easily reduced by the tertiary amines such as Bu_3N. The resulting Ru(I) species is a potent reductant capable of transferring an electron to **1**. Thus, the catalyst is regenerated. After release of bromide, the radical intermediate **4** adds

to **2**.
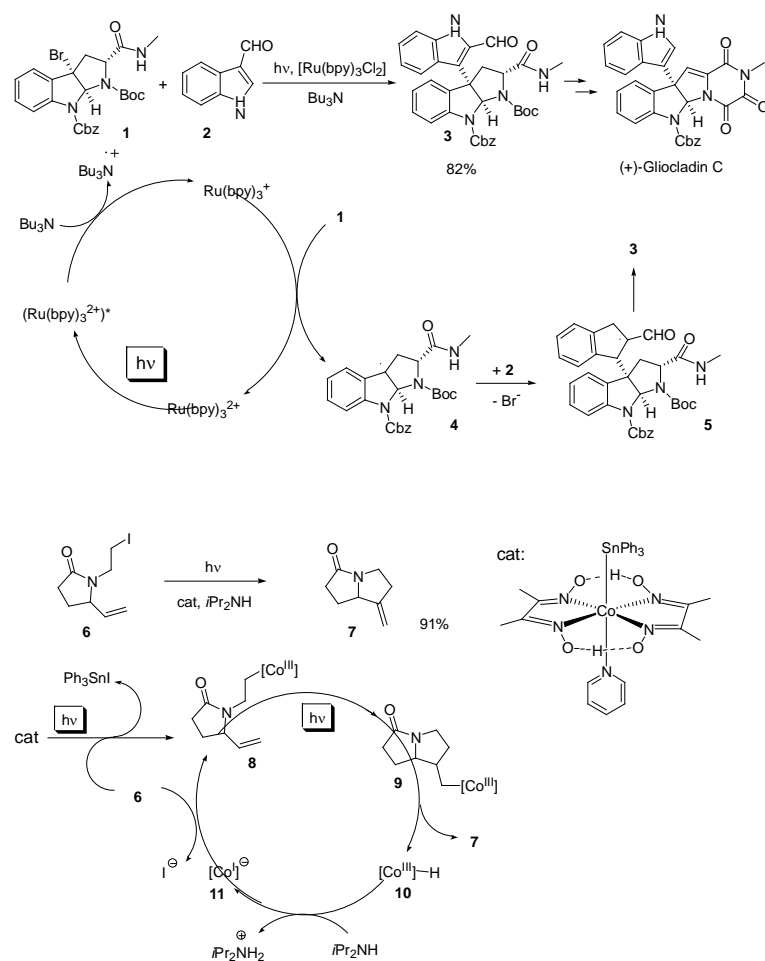
Figure 1. Photoredox catalysis applied to the natural product synthesis and photochemically supported radical cyclisation reaction (Heck reaction).

The final product **3** is formed by oxidation of the intermediate **5**.

This photocatalysis may be carried out with visible light. Many of these reactions need a sacrificial electron donor as in the case of the transformation of **1** or a sacrificial electron acceptor. Processes have been developed in which no such compounds are needed. For example, when photoredox catalysis with $[Ru(bpy)_3]^{2+}$ is combined with organocatalysis, both the reduction and the oxidation of the ruthenium complex are involved in the product formation.[10]

Radical reactions with organometal compounds can also be improved when photochemical reaction conditions are applied. A cobalt catalyst was used to perform a radical cyclization of compound **6** (Figure 1).[11] The photochemical reaction of the catalyst with the substrate **6** generates intermediate **8**. The C-Co bond undergoes homolytic fragmentation[12] and intramolecular radical addition with the olefinic double bond takes place. After combination with the cobalt fragment, intermediate **9** is formed. Elimination of the cobalt hydride species **10** yields the final product **7**. Deprotonation regenerate the nucleophilic and catalytically active species **11**. The overall transformation is a alkyl Heck type reaction. Normally, such reactions are performed with palladium catalysts. Applying photochemical reaction conditions, such transformations can be performed efficiently with much less expensive cobalt catalysts. Photochemical reaction conditions also significantly influence palladium catalysis.[13] In this context unusual oxidation states such as Pd(I) have been discussed.

As indicated above, elimination or exchange of ligands in coordination compounds are accelerated when the products are electronically excited. Often, Fischer type carbenes are involved.[14] Recently, a variety of tungstenhexacarbonyl catalysed reactions were applied to organic synthesis. Thus the alkyne derivative **12** was successfully transformed into the cyclic enolether **13** (Figure 2).[15] In a photochemical reaction step, one carbonyl ligand is exchanged by a triethylamine molecule leading to the catalytically active species **14**. The reaction with the substrate **12** yields the Fischer type complex **15**. Base catalysed cyclization leads to anionic intermediate **16**. Protonation with he ammonium ion yields the final product **13** and regenerate the catalytically active species **14**. In a second example, the chromium containing Fischer type complex **17** was transformed into the tricyclic indole derivative **18** which is a key synthesis intermediate in the total synthesis of carbazoquinocin-C (Figure 2).[16] In the photochemical step, in the carbene complex **17**, a ligand

rearrangement takes place (**19**) and the cyclohexadienone species **20** is formed in a pericyclic reaction. Tautomerization yields the final product **18**.
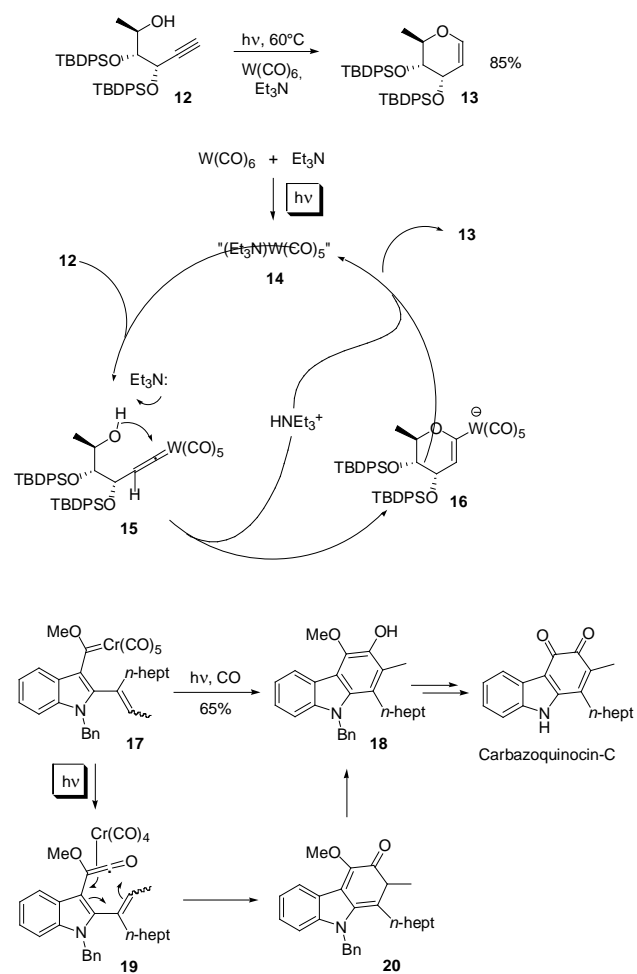
Figure 2. Photochemical reactions involving Fischer type carbenes.

Many other reactions of this type are affected by electronic excitation. For example, the Vollhardt and related reactions with catalysed by inexpensive cobalt complexes are inherently photochemical reactions.[17] It is highly advised to check systematically photochemical reaction conditions either with visible or UV light when reactions of organometallic or coordination compounds are studied.

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SPECIAL REPORTS ON PHOTOCHEMICAL ORGANIC SYNTHESIS

Introduction

Dear EPA members,

This issue of the EPA Newsletter (December 2012) is dedicated to "Synthetic Photochemistry", since we believe that experts in this area of research should demonstrate to the photochemical community that synthetic photochemistry is currently a vital research area. Significant reports on a great variety of research topics, summarizing recent contributions to the field of synthetic organic chemistry using light as an innocuous reagent, are presented in this issue. Both *Thorsten Bach* and *Paul Margaretha* contribute very interesting reports on [2+2]-photocycloadditions*, the former author focusing on enantioselective and catalytic reactions involving coumarins, and the latter on regio- and stereoselective reactions to give rise to cyclobutylalkynones. *Olivier Piva's* results are related to the combination of organic strategies (metathesis and organocatalysis) with [2+2]-photocycloaddition, as well as photodeconjugation reactions leading to β,γ-unsaturated esters which are precursors of interesting targets. The photogeneration of triplet phenyl cations and alkyl radicals reported by *Angelo Albini et al.* as well as that of phenyl radicals by *Burkhard König et al.* are valuable contributions to organic synthesis. *Petr Klán et. al.* made use of the rational design aided by DFT calculations to synthesize pharmaceutically-promising compounds. *Gerald Pattenden et al.* report on the potential connection between photoinitiated contractions of 14-membered cembranoids to 12-membered diterpenes and the biosynthesis of metabolites of coral reefs. A variety of photochemical electron- and hydrogen-transfer mediated reactions involving furanones are presented in the contribution by *Norbert Hoffmann* to demonstrate how photochemistry enriches the methodology of organic synthesis. Finally, *Pedro Campos et al.* report on the importance of the iminic compounds for the synthesis of biologically active aromatic compounds and biomimetic molecular switches.

The EPA Newsletter Board greatly appreciates these experts' contributions and also wholeheartedly thanks *Thorsten Bach's* for his assistance in expediting this endeavour.

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Electron and hydrogen transfer organic photochemcial reactions

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Photochemical excitation of molecules changes their electronic configuration and thus their chemical reactivity.[1] Applying photochemical reaction conditions largely broaden the reaction spectrum of a chemical compound. New product families or libraries become available or they can be more easily prepared. For these reasons, photochemical reactions are of particular interest for being applied to organic synthesis.[2,3,4] For example, electron transfer is favoured under photochemical conditions. Thus, photochemical electron transfer considerably enriches redox chemistry of organic compounds. Such processes as well as photoinduced hydrogen transfer are frequently applied to organic synthesis. Contributions radical chemistry are often reported.

The first example describes a reaction which is induced by a photochemical electron transfer (Figure 1).[5] The reaction between the naphthylamine derivative **1** and the furanone **2** leads in high yields to the adducts **3a,b**. A C-C σ-bond is formed in the α-position of the α,β-unsaturated lactone **2**. When compared to typical ground state reactions of such compounds, e.g. the Michael reaction, the regio chemistry is reversed. At the ground state, an electron transfer between compounds **1** and **2** would be endothermic. However, when the naphthylamine derivative is electronically exited, such a redox process becomes exothermic and a radical ion pair **4** and **5** is formed. Most of these intermediates undergo back electron transfer and the starting products are regenerated. In the presence of a proton donor such as water, the radical anion is protonated in the β position leading to the electrophilic radical **6**. From this observation and based on previous photochemical reactions of furanones,[6] it has been concluded that **4** and **5** most probably constitute a contact ion pair. Intermediate **6** is added to **1** leading to the final products.

From the sustainable chemistry point of view, this reaction is particular interesting because no chemical activation (no acids, no bases, no metals, no sensitizer) is necessary to establish a C-C bond.

Figure 1. Photochemical electron transfer mediated reaction of the npahthylamine derivative **1** with furanone **2**.

Thus, in this case, the concept of the photon as traceless reagent was applied.[7] Furthermore, no leaving group is necessary and the reaction may be discussed in the context of C-H activation. Such transformations are frequently performed in organic photochemistry in a highly selective way.

The second topic deals with hydrogen transfer. Two mechanisms of this process are often encountered in organic photochemical reactions. Either, the two particles, the electron and the proton, are transferred almost simultaneously or the electron is transferred first leading to the a radical ion pair and the proton follows. The second process occurs when the electron transfer involving a photochemical excited species as well as the proton transfer are both exothermic. The first process occurs when the electron transfer is endothermic, nevertheless the formation of the resulting products is exothermic. Both reaction mechanisms have each a significant impact on the outcome of the reaction.

In the reaction of electronically excited α,β-unsaturated carbonyl compounds with tertiary amines, the two step mechanism takes place favouring the formation of a C-C bond in the β position the enone. Thus, the excited enone **7** undergo electron transfer leading to the radical ion pair **8** and **9**.[8] A proton is transferred from the radical cation **9** to the enolate moiety of **8** and the neutral intermediates **10** and **11** are formed. Radical combination leads the final product **12**. Similar reactions have also been carried out in intramolecular versions. When the amine moiety in similar substrates is replaced by an acetal function as hydrogen donor (**13**), a photochemical electron transfer would be endothermic. In this case, the electron and the proton are almost simultaneously transferred from the acetal function to the $^3\pi\pi^*$ excited furanone moiety (**14**).[9] Under the applied conditions, this excited state is generated by triplet energy transfer from acetone. In the $^3\pi\pi^*$ excited and vibrationally relaxed state, furanones possess a high spin density in the β position and the hydrogen abstraction therefore takes place there leading to the biradical **15**.[10] Radical combination than yields the final products **16a,b** in which a C-C bond was formed in the α-position of the α,β-unsaturated lactone. Due to the change of the mechanism, the regioselectivity has been inversed. It must be pointed out that in contrast to the two step process, in the case of the one step mechanism (hydrogen abstraction) stereochemical requirements are very high. In compound **13**, two diastereoisomers exist. Furthermore, to conformers of the tetrahydropyranyl moiety play an
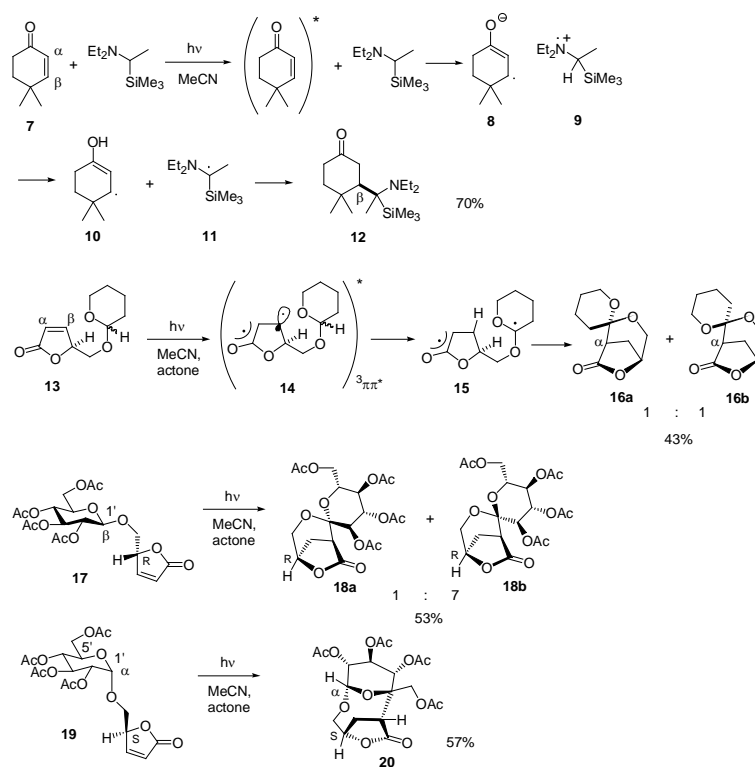
Figure 2. Two mechanisms of hydrogen transfer in photochemical reaction and the influence on the regioselectivity

important role. Thus the substituent at the acetalic function may be orientated in the axial position (α-anomer) or in the equatorial position (β-anomer). In order to determine the influence of each of the two stereochemical elements on the reaction outcome, the transformation was performed with glucosyl derivatives in which these conformations are locked. Thus during the transformation of compound **17**, hydrogen abstraction occurs at the anomeric centre 1' which leads to the formation of the spirocyclic compounds **18a,b**. In the case of compound **19** which is a α-anomer possessing the same relative configuration at the anomeric centre and the furanone moiety, hydrogen abstraction occurs in the 5' position leading to the formation of macrocyclic compound **20**.

Photochemical excitation facilitate electron transfer and thus enriches redox chemistry of organic compounds. Photochemically induced hydrogen transfer mainly involve two different mechanisms leading to different regioisomers. The processes depicted in figures 1 and 2 illustrate well two ways how photochemical reactions enriches the methodology of organic synthesis.

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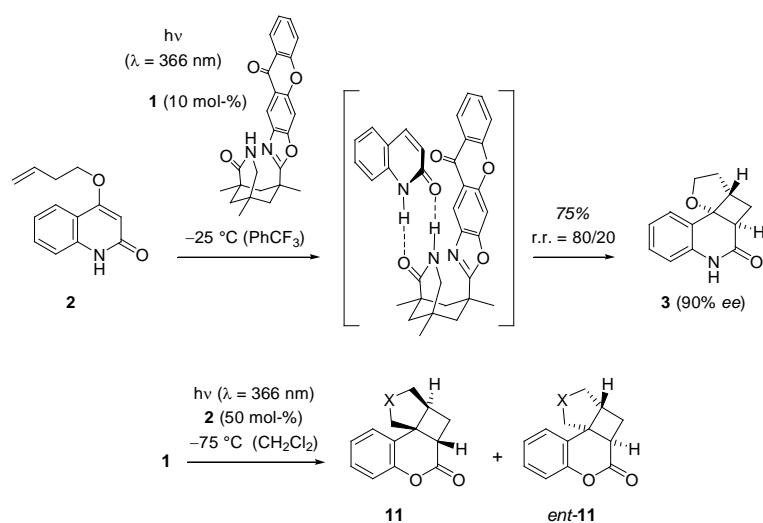
Enantioselective catalysis of [2+2] photocyclo-addition reactions in solution

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Among all photochemical reactions, the [2+2] cycloaddition of two olefins has shown to be the synthetically most useful and generally applicable reaction.[1] Typically, an α,β-unsaturated carbonyl compound is employed as the photoactive component, which upon excitation reacts – frequently via the respective $\pi\pi^*$ triplet state – inter- or intramolecularly with another alkene to generate cyclobutane products. Intrinsically, it is impossible to catalyze this reaction in the classical sense, i.e. by lowering the activation barriers of the individual reaction steps, because the reaction proceeds very rapidly, once the photoactive compound has been excited. A conventional development of chiral catalysts is consequently not feasible for enantioselective [2+2] photocycloaddition reactions. Other modes of action must be found to ensure that chiral information is transmitted from a chiral compound to the substrate in a catalytic fashion.[2] One possible way to achieve this goal is to employ a chiral sensitizer, which acts either by energy transfer or by electron transfer. The key idea in enantioselective sensitization relies on a selective excitation of substrates in the chiral environment of the sensitizer. For [2+2] photocycloaddition reactions of α,β-unsaturated carbonyl compounds, triplet sensitization appears to be best suited provided that sensitizers can be found, which exhibit a long wavelength absorption relative to λ_{max} of the substrate and which have a higher triplet energy than the substrate. In addition, and these requirements are even more difficult to meet, it must be ensured that the substrate is spatially fixed to the sensitizer and that its subsequent [2+2] cycloaddition is faster than dissociation of the substrate-sensitizer complex. With xanthone **1**, we have devised a chiral sensitizer, which fulfills nicely the requirement of substrate coordination because it binds other lactams and amides very efficiently by two point hydrogen bonding.[3,4] As exemplified by the reaction of 4-(but-3-enyl)oxyquinolone (**2**), an intramolecular [2+2] photocycloaddition can be nicely performed in good yields and with high

enantioselectivity (Fig. 1). The selective formation of enantiomer **3** can be explained by assuming a 1:1 complex between sensitizer **1** and substrate **2**. Energy transfer and photocycloaddition are likely to proceed within this complex explaining the observed enantioface differentiation.

Figure 1. Enantioselective formation of tetracyclic product **3** from quinolone **2** employing chiral sensitizer **1** (r.r. = regioisomeric ratio)

A second approach towards enantioselective catalysis in [2+2] photo-cycloaddition reactions relies on a bathochromic shift achieved by complexation of the substrate to a Lewis acid. The shift allows for selective excitation of the chiral complex at long wavelength, which may lead within the complex to a chirality transfer from the chiral Lewis acid to the α,β-unsaturated carbonyl compound. Given the relatively minor change of the chromophore upon Lewis acid complexation, bathochromic shifts are small and it is thus desirable that the complexation also leads to a change in the photophysical properties of the chromophore. For coumarin, it has been observed

that BF_3 or $EtAlCl_2$ induce not only a bathochromic shift but also significantly extend the lifetime of the excited state making the otherwise sluggish intermolecular [2+2] photocycloaddition to alkenes an efficient reaction.[5] Recently, chiral Lewis acids have been identified which enable an enantioselective intramolecular [2+2] photocycloaddition of certain coumarins.[6,7] Oxazaborolidine-based Lewis acid **4** for example allows for an effective conversion of coumarin **5** into the respective product **6** in 90% *ee* (Fig. 2).
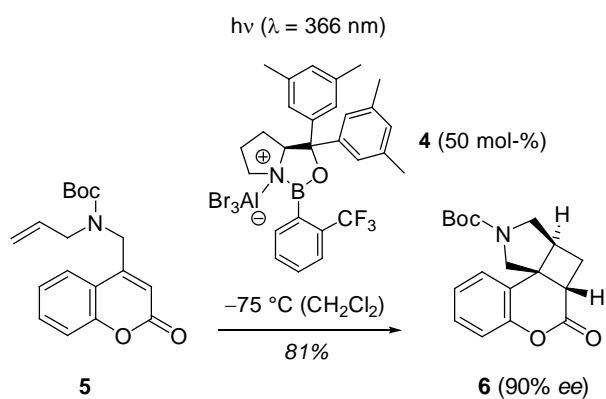
Figure 2. Enantioselective [2+2] photocycloaddition of coumarin **5** mediated by chiral oxazaborolidine-based Lewis acid **4**

Although the catalyst loading could be lowered by appropriate tuning of the reaction conditions for a single case to 20 mol-% without a significant loss of enantioselectivity,[6] the turnover is apparently not very high in the Lewis acid-catalyzed process. Indeed, the observed absorption shift due to Lewis acid complexation is not very extensive.[7]

Despite the fact that the results obtained so far in catalytic enantioselective [2+2] photocycloaddition reactions are preliminary and not general, the concepts presented above have been nicely validated. Research in this direction continues and will hopefully lead to many applications of this exciting reaction class in organic synthesis.

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Photochemical synthesis of four-membered ring amino acids

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In the early 2000s, we initiated a research project aimed at investigating the ability of small-ring β-amino acids to induce particular conformational preferences in peptides. Six- and five-membered carbocyclic β-amino acids were already attracting considerable interest, yet the four-membered ring equivalents – derivatives of 2-aminocyclobutane-1-carboxylic acid (ACBC) – had not received the same attention, mainly due to the lack of convenient synthetic methods for the preparation of these molecular building blocks. Photochemical [2+2] cycloadditions involving nucleic bases were well known to biochemists, notably due to the deleterious effects that such reactions can have on DNA. However, organic chemists had not up to that point considered pyrimidinediones as photochemically-active enones having significant applications in preparative synthetic procedures. We therefore included as part of our research plan the elaboration of a photochemical strategy for the synthesis of the ACBC core structure, based on the [2+2] cycloaddition reaction of a pyrimidinedione and a simple alkene (Fig. 1).
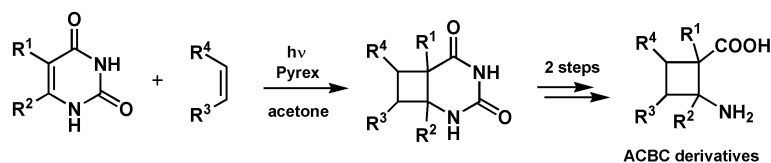
Figure 1. The general strategy for synthesis of ACBC derivatives, using a photochemical [2+2] cycloaddition reaction for the construction of the 4-membered ring.

So it was that, a decade ago, we described the first simple synthetic entry to the parent (unsubstituted) ACBC in high chemical yield via the photochemical [2+2] cycloaddition between uracil and ethene.[1]

This reaction is conveniently carried out in acetone, which serves as both solvent and photosensitizer. With only three steps in total and requiring almost no purification procedures, it was surprising that this synthesis had not been considered before – it is now routinely performed by undergraduates in the teaching lab. One of the attractive features of this entry to the ACBC core is that it provides the thermodynamically less stable *cis*-isomer, which can subsequently be transformed, as required, into the *trans*-isomer using a base-mediated epimerization protocol. The same photochemical reaction was applied to chirally-functionalized derivatives of uracil, including uridines, in order to develop a stereoselective version of the reaction and obtain single enantiomers of the ACBC target.[2] The procedure has undergone several refinements[3] and is today the synthesis of choice for this interesting building block, which serves as an integral feature of peptide-based mimetics of biologically systems including 12-helix foldamers[4] and sequence-selective PNA.[5]

An important aspect in synthetic methodology is the scope of its application. From the outset, we had anticipated that the photochemical [2+2] approach to the ACBC core should have a general character (Fig. 1), and this turned out to be the case, within the limits of the intrinsic stability of target ACBC derivatives. When a substituted uracil is employed, various substituents can be accommodated at the C1 or C2 positions on the β-amino acid backbone; about a dozen such examples have been prepared.[6] Indeed, the uracil–ethene strategy was sufficiently versatile to allow the preparation of a stable analogue of the antifungal rhodopeptin cyclotetrapeptide family which incorporated a C2-alkyl ACBC which does not exist in the free state![7] Selectivity is more of a challenge when C3 or C4 substituted ACBCs are targeted, but we demonstrated that an intramolecular version of the alkene-uracil combination could provide complete regio- and stereo-chemical control, and thus furnish a single 3-hydroxymethyl-ACBC stereoisomer.[8]

The [2+2] photocycloaddition strategy has been applied for the synthesis of other homologated amino acids incorporating 4-membered rings. There was very little precedent for such reactivity with aza-analogues of dihydropyrimidinediones, but we found that 6-azauracil behaved in a comparable fashion to uracil and reacted photochemically with ethene to furnish a previously unknown 4-

membered ring hydrazino acid;[9] this material acts as an inducer of hydrazino turns in small peptides.[10] Using an unsaturated γ-lactam as the chromophore instead of uracil, we established the shortest synthetic access to single enantiomers of cyclobutane γ-amino acids, which are conformationally restricted derivatives of the neurotransmitter GABA.[11]

A few illustrative examples are given of the compounds which have already been prepared (Fig. 2). We are pursuing the development of this synthetic strategy, to enlarge the library of novel cyclobutane amino acids and further the study of their ability to dictate conformational preferences in small peptides.
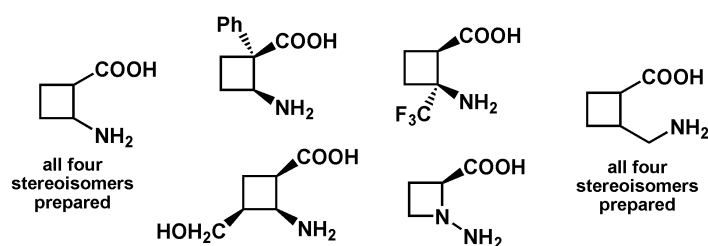
Figure 2. Some examples of four-membered ring amino acids prepared using the photochemical [2+2] cycloaddition strategy.

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Regio- and stereoselective processes in the photochemistry of heterocyclic compounds

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Photochemical reactions can be important methodologies with a lot of practical applications if they will be able in the future to give the corresponding products with high regio- and stereoselectivity.[1] Most of our work has been devoted to find stereoselective reactions on heterocyclic pentaatomic compounds.[2]
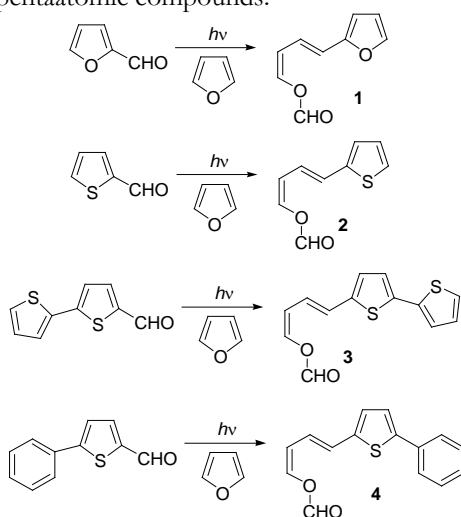
Scheme 1. *Z,E*-butadienyl formate derivatives from the photochemical reaction between 2-substituted heterocyclic aldehydes and furan.
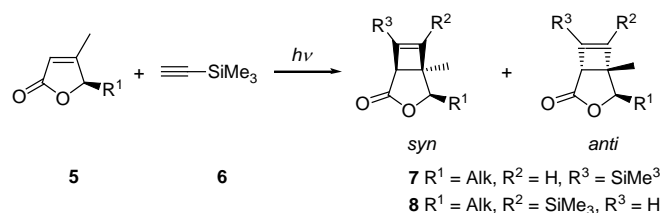
The irradiation of 2-furancarboxaldehyde in furan gave only the 4-substituted butadienyl formate **1** (Scheme 1). The compound **1** was obtained as the only product, while the presence of the oxetane derivative was not detected. The compound **1** showed a *Z,E* stereochemistry at the double bonds.

The presence of a double bond with *E* stereochemistry at C-4 is in agreement with the formation of *exo* stereoisomer of the oxetane.

The same behaviour was observed when thiophene-2-carboxaldehyde was used as a reagent (Scheme 1). Also in this case, the only product we were able to characterize was the butadienyl formate derivative **2**. The corresponding butadienyl formate derivatives were obtained when 5-(2-thienyl)-2-thiophenecarboxaldehyde and 5-phenyl-2-thiophene-carboxaldehyde were used as substrates (Scheme 1). In all the cases the *E* stereochemistry of the double bonds at C-4 was in agreement with an *exo* stereochemistry in the oxetane adducts.

On the contrary, the reaction between pyridine-2-carboxaldehyde with furan gave only the corresponding oxetane derivative.[3]

Furyl derivatives can undergo some other cycloaddition reactions. We investigated the reactivity of lactones **5** toward trimethylsilylacetylene as reaction partner. In principle, from such photochemical cycloaddition we could afford both the diastereomeric *syn/anti* couples of the regioisomeric products **7** and **8**, arising from head-to-head (HH) and head-to-tail (HT) cycloaddition mode, respectively (see Scheme 2).

$$R^1 = \text{Alk}, R^2 = H, R^3 = \text{SiMe}_3$$

7 R^1 = Alk, R^2 = H, R^3 = SiMe$_3$
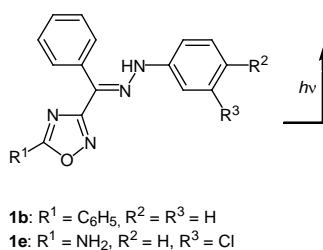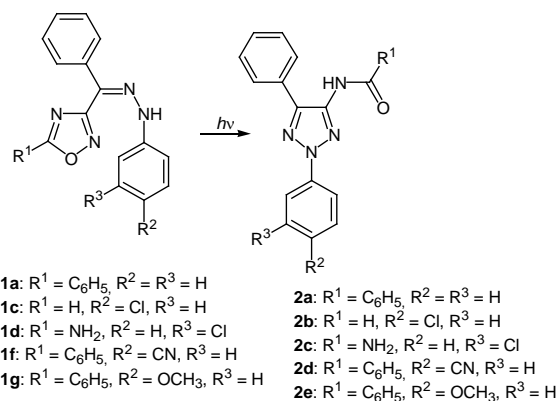**8** R^1 = Alk, R^2 = SiMe$_3$, R^3 = H

Scheme 2. Possible regiochemical outcome and products of [2+2] cycloaddition of lactones **5** with **6**.

Very importantly, as regards the regioselectivity of cycloaddition, the reaction showed to afford selectively only head-to-head products **7** as *syn/anti* mixture.[4]

Finally, we tested the photochemical behavior of the 1,2,4-oxadiazoles **9** (Scheme 3). The solvents used in these experiments were selected after an experiment in the dark, to avoid an uncatalyzed thermal reaction. The *Z* isomer **9a** gave the triazole **10a** with 50%

yield. It is noteworthy that the *E*-isomer **9b** gave the relevant triazole **10a** in 72% yield.

1a: $R^1 = C_6H_5$, $R^2 = R^3 = H$
1c: $R^1 = H$, $R^2 = Cl$, $R^3 = H$
1d: $R^1 = NH_2$, $R^2 = H$, $R^3 = Cl$
1f: $R^1 = C_6H_5$, $R^2 = CN$, $R^3 = H$
1g: $R^1 = C_6H_5$, $R^2 = OCH_3$, $R^3 = H$

2a: $R^1 = C_6H_5$, $R^2 = R^3 = H$
2b: $R^1 = H$, $R^2 = Cl$, $R^3 = H$
2c: $R^1 = NH_2$, $R^2 = H$, $R^3 = Cl$
2d: $R^1 = C_6H_5$, $R^2 = CN$, $R^3 = H$
2e: $R^1 = C_6H_5$, $R^2 = OCH_3$, $R^3 = H$

1b: $R^1 = C_6H_5$, $R^2 = R^3 = H$
1e: $R^1 = NH_2$, $R^2 = H$, $R^3 = Cl$

Scheme 3. Photochemical rearrangement of 1,2,4-oxadiazoles.

On the contrary, the oxadiazole **1c**, where the phenyl substituent at C-5 of the oxadiazole ring is absent, while a chlorine substituent is present on the *Z*-hydrazonic part of the molecule, did not give any rearrangement product.[5]

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Photochemical preparation of naphthalenophanes

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Naphthalenophanes are molecules consisting of a naphthalene unit and a chain forming a bridge between two nonadjacent positions of this unit.[1] Although naphthalenophanes are known since more than 75 years[2] the number of methods for the preparation is rather limited. Especially if the mentioned chain is relatively short, the corresponding naphthalenophanes are considerably strained and the synthesis of such compounds starting with an already existing naphthalene unit is a formidable challenge. Bearing in mind that photochemical reactions has proven as particularly suitable for the preparation of highly strained compounds, we hypothesized that the *Photo-Dehydro-Diels-Alder* (PDDA) reaction as an efficient method for the construction of naphthalenes should be also suitable for the preparation of naphthalenophanes. The PDDA reaction is a special case of the *Dehydro-Diels-Alder* reaction[3] and in recent years we demonstrated on the basis of numerous examples its worth for the preparation of biaryls.[4-8]
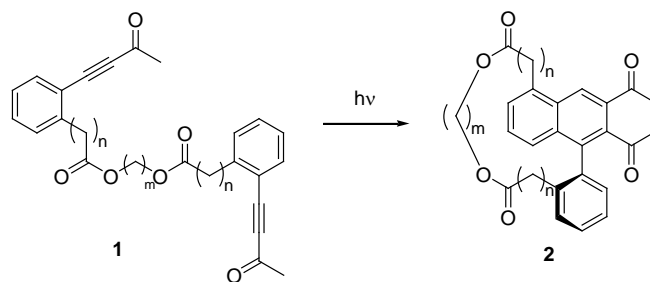
Figure 1. Preparation of (1,5)Naphthalenophanes **2** by PDDA reaction.

As suitable precursors for the synthesis of naphthalenophanes by PDDA reaction we identified diesters **1** with variable chain length (n

= 0-2, m = 2-6) bearing photochemically reactive 3-oxo-but-1-yn-1-yl groups in each *ortho* position. Upon irradiation (λ_{IRR} > 300 nm) in *tert*-butanol these compounds undergo smooth PDDA cyclization to (1,5)naphtha-lenophanes **2** (Fig. 1).[11] As expected, the yields depend on the length of chain bridging positions 1 a 5 of the naphthalene unit. The most highly strained compound of type **2** (n = 0, m = 2) was still obtained with 6% yield. The strain energy of this compound (obtained from DFT calculations) amounts to 31 kcal/mol and hence exceeds the value for cyclopropane (ca. 28 kcal/mol). Furthermore, we could demonstrate that the deformation of the naphthalene unit is a sensitive indicator for the estimation of strain in naphthalenophanes.

Very recently we extended this approach on the synthesis of (1,6) and (1,8)naphthalenophanes.[12]

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Photocycloaddition reactions of - further functionalized - enones
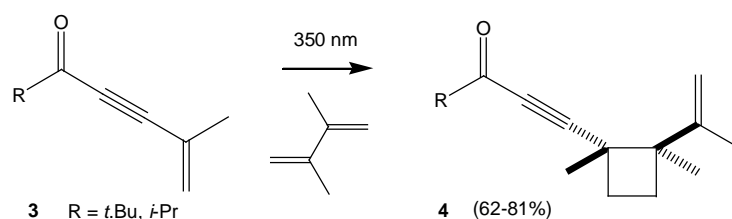
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Preparative organic photochemistry has been highlighted and reviewed routinely over the last fifty years.[1-4] Since then, synthetic applications of (cyclic) enone photocycloadditions to alkenes have been thoroughly investigated.[5,6] One recent example stemming from our group represents a simple multistep conversion of 1,2-dihydro-1,1-dimethoxynaphthalen-2-ones **1** into (3,4-dihydro-3,4-dioxonaphthalen-2-yl)acetates **2** and is depicted in Scheme 1.[7]

X = H, 7-MeO, 6-Br   **2**   (40-45%)
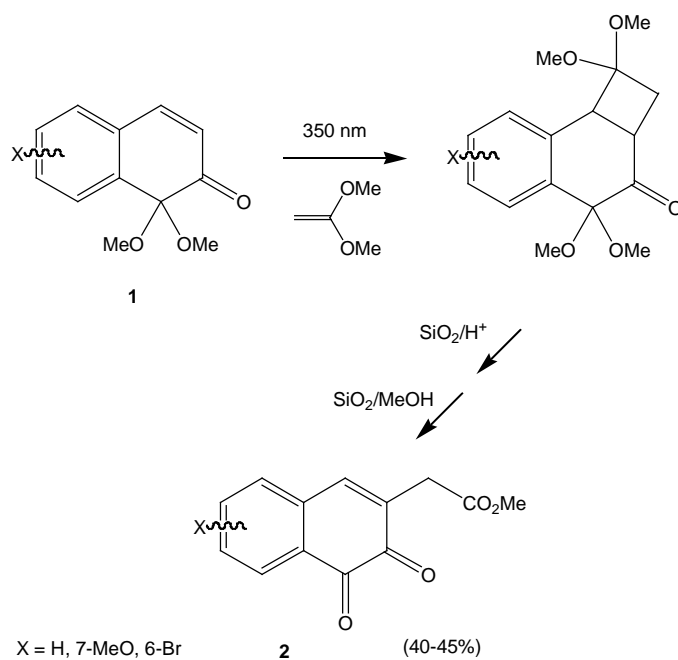
(Scheme 1)

In contrast, irradiation of such compounds in the presence of 1,3-dienes has been regarded as of low synthetic utility, as energy transfer from the excited triplet (cyclic) enone to the diene becomes predominant. Acyclic enones on the other hand deactivate *via E/Z*-isomerization, and therefore also were considered as unsuitable substrates for bimolecular reactions. We have recently shown that 4-acylbut-1-en-3-ynes **3** undergo regio- and diastereoselective [2+2]-cycloaddition at the olefinic C-C bond on irradiation in the presence of 2,3-dimethylbuta-1,3-diene to afford hitherto unknown 1-cyclobutylalk-1-yn-3-ones **4** (Scheme 2).[8]

(Scheme 2)

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Photochemistry of iminic compounds

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The Photochemistry of compounds with C=N bond has been one of the research topics of the Photochemistry Group at the University of La Rioja for many years. Here we discuss some recent research.

The photolysis of oxime esters (acyloximes) generates nitrogen radicals (iminyl) that can be utilized for the photopolymerization (UV cure) or for the synthesis of heterocyclic rings in intra- or intermolecular processes.[1] These reactions represent a new approach to the preparation of nitrogen heterocycles, including the synthesis of compounds with biological activity as trisphaeridine and other alcaloids (Figure 1).[2]
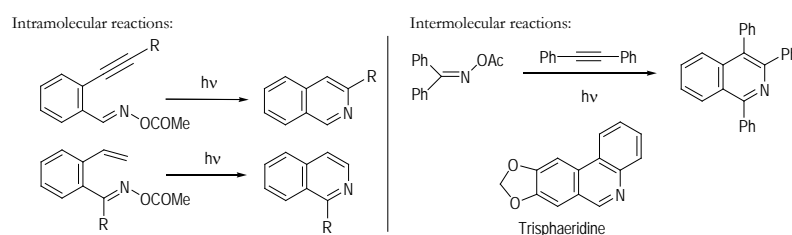

Figure 1

We have prepared a series of trisphaeridine derivatives and studied their photophysical and electrochemical properties. The 7,11-diaryltrisphaeridines have proven to be excellent sensors of protons and some metals (Cu, Pb).[3]

We have also begun to study other photochemical radical cyclization processes. Thus, the direct irradiation of iodoalkenes leads to the formation of carbon-centered radical by homolysis of the C–I bond. The photoreaction is used in cyclizations with formation of six-membered rings.[4]

In collaboration with the group of Professor Olivucci, we have proceeded to lay the foundations of the first logical design, using computational tools, of a biomimetic motor inspired by the process of vision, in which the basic chemical step is a photoinduced *cis-trans* isomerization of a conjugated iminium salt.[5] In this sense, some

fluorenylidene-pyrroline structures have been synthesized and their potential use as biomimetic light driven molecular switches has been analysed (Figure 2 shows an example).[6]
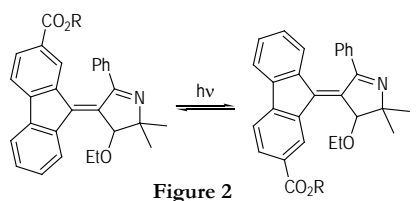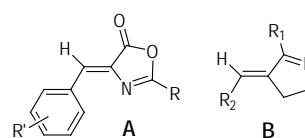

Figure 2

Figure 3

More recently, it has been prepared two other families of biomimetic molecular switches and studied their phophysical and photochemical properties. Compounds with structure based on the green fluorescent protein (GFP) chromophore (**A**)[7] and based on the Schiff base of the retinal chromophore (**B**)[8] (Figure 3).

Once performed the photochemical study of the photoswitches with structure based on the retinal chromophore, these units have been included in peptides. The efficient behaviour of these photoswitches has been kept when bound to the peptide. The reversible isomerization of the obtained cross-linked peptide has been possible by alternating violet (400 nm) and blue (446 nm) light (Figure 4).[9]
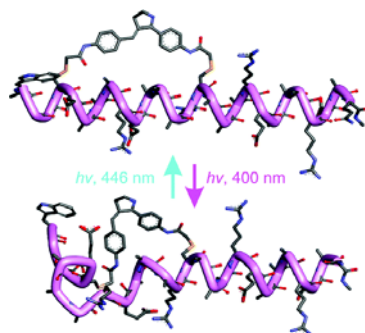

Figure 4

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# Visible light mediated arylation of unsaturated compounds with diazonium salts

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Light is an abundant and powerful reagent in organic synthesis. Chemical transformations by means of light benefit from mild conditions required for substrate activation.[1] Photocatalysts excited by visible light can relax to the ground state not only by energy transfer, but also by electron transfer initiating redox reactions (PET, photo induced electron transfer). Well-known metal-organic photocatalysts like $[Ru(bpy)_3]^{2+}$ as well as organic dyes like eosin Y are able to induce one-electron-transfer steps generating radicals. Depending on the nature of the substrate, the photocatalyst acts either as electron donor or –acceptor. In case of aryl diazonium salts, an electron is transferred from the catalyst to the substrate due to the low reduction potential of diazonium salts. Both, the oxidized form of the catalyst and the reduced substrate, which immediately liberates dinitrogen, are generated. This provides a convenient photochemical access to aryl radicals, which can subsequently react with alkenes, alkynes or heterocycles.

A major drawback in many photocatalytic systems is the need of sacrificial electron donors or –acceptors in order to regenerate the photocatalyst. As a consequence, a stoichiometric amount of waste is produced. In our system the back electron transfer from the intermediary formed radical regenerates the photocatalyst and produces a carbenium ion, which is converted into the final product by deprotonation. Overall, an unsaturated compound is photochemically arylated using $[Ru(bpy)_3]^{2+}$ or eosin Y as photocatalysts and a new sp^2-sp^2-carbon-carbon bond is formed (Fig. 1).

The procedure is experimentally simple and characterized by high yields, low catalyst loadings and mild conditions using visible light LED irradiation or sunlight and ambient temperature. Remarkably, the reaction tolerates a variety of functional groups. Carbon-halide bonds, for example, remain untouched and can be used for

subsequent synthetic transformations employing transition metal catalysis or organometallic reagents.
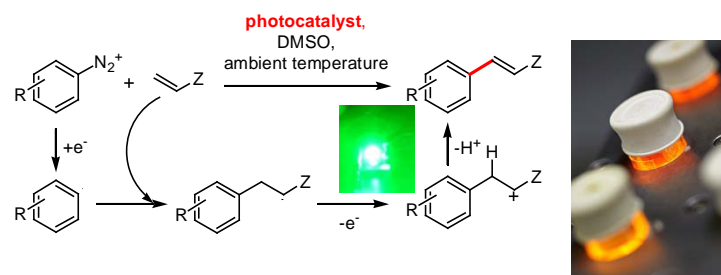
Figure 1. Photocatalytic arylation of unsaturated compounds: reaction sequence (left) and experimental procedure using high power LEDs as source of irradiation (right).

A variety of substituted olefins, acetylenes or enones[2] can be arylated in this process in good to moderate yields. Enol esters are converted to α-arylated ketones upon loss of the acyl group.[3] Particularly interesting is the arylation of five-membered heteroarenes, such as furan, thiophene or N-protected pyrrole. No prior functionalization is required and the reaction can therefore be considered as direct C-H bond activation.[4] The mild reaction conditions avoiding transition metals make this process a useful tool in organic synthesis. The synthetic applicability of this new method has been shown in the synthesis of raloxifene, a selective estrogen receptor modulator. The key step is the photocatalytic formation of a benzothiophene core by the reaction of 2-(methylthio)-benzenediazonium salt with phenylacetylene.[5]

In conclusion, an efficient visible light mediated arylation of alkenes, five-membered heteroarenes, alkynes, enones and enol acetates with diazonium salts by photoredox catalysis has been developed. The easy applicability, often good product yields and high tolerance of functional groups make the process a valuable addition to the repertoire of organic synthesis.

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How to control the photoenolization reaction for synthetic applications

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During the past hundred years, many photochemical procedures have been developed to provide a great variety of products which often possess structures that can be obtained only with difficulty by conventional (dark) methods.[1] Here we present one example in which computational chemistry successfully assists a synthetic organic chemist to control the course of a photoenolization reaction.

2-Alkylphenyl ketones are known to produce the corresponding enols (photoenols; *o*-xylylenols) upon photochemical excitation.[2] 2-Methylacetophenone as a model structure undergoes intramolecular 1,5-hydrogen abstraction via the triplet state to form two isomeric, (*E*)- and (*Z*)-, photoenols.[1] When a leaving group (X) is present in the α-position, a longer-lived (*E*)-photoenol liberates X to give the corresponding cyclization (indanone) products (Scheme 1). Indanone derivatives are key intermediates in the synthesis of some pharmaceutically significant compounds, such as the reversible acetylcholinesterase inhibitor donepezil hydrochloride, and we have recently demonstrated that it can be synthesized using a photochemical step.[3]
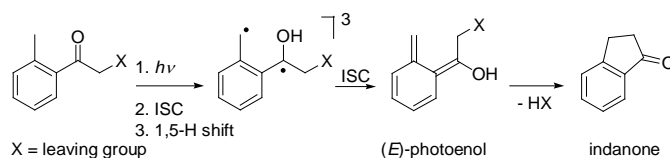
Scheme 1. Photochemistry of *o*-Alkylphenacyl Derivatives

A novel cyclization reaction based on the photoenolization of *o*-methylphenacyl epoxides (**1**) via the ³n, π* excited state has recently been introduced by us (Scheme 2).[4] This reaction gives β-hydroxy functionalized indanones (**2**) that structurally resemble biologically active pterosines in high chemical yields. However, when two electron-donating methoxy groups are attached to the phenyl ring in

3, the selectivity of the photoreaction is altered by inverting the triplet-state energies of the parent phenyl ketone.[4] Consequently, 3-hydroxypropenone derivative **4** is formed by a photochemically driven homolytic C–O cleavage, because the reaction originates from the excited $^3\pi$, π^* state which is unable to undergo efficient hydrogen-atom transfer to give the desired product **5**.
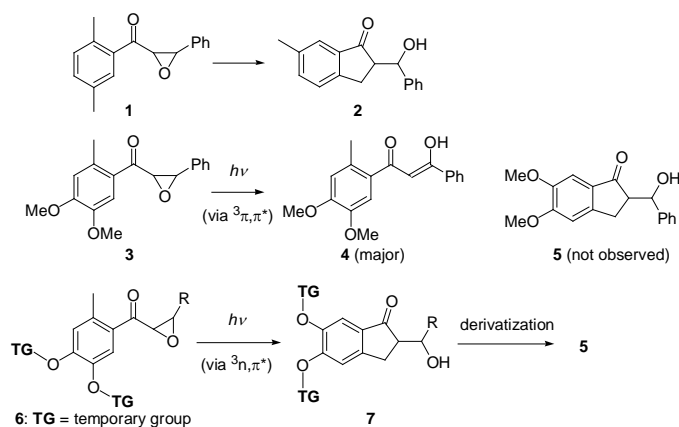
Scheme 2. Synthesis of β-Hydroxy Functionalized Indanones

We proposed to control the reaction selectivity by replacing the two methoxy substituents by a temporary group (TG in **6**, Scheme 2) which would alter the energy order of the $^3\pi$, π^* and ^3n, π^* states.[5] TG would then be easily removed from the product **7**, and the alkyl substituents could be installed. To avoid excessive synthesis, we constructed a library of the candidates **6** *in silico*, and evaluated their lowest energy triplet configurations using *ab initio* calculations. We profited from the fact that the solution of SCF equations converges to the lowest energy state in a given irreducible representation, and used simple and fast DFT calculations based on UB3LYP/6-31+G(d) level of theory mimicking the solvation effects with polarized continuum model (PCM) to calculate the wavefunctions. As a result, a desired TG was selected by the inspection of the calculated triplet wavefunctions. The best candidate (**6**, TG = pivaloyl group) was synthesized in several simple and high-yielding steps.[5] Subsequent irradiation of this compound in hexane or

acetonitrile gave **7** as a sole photoproduct which was subsequently converted to **5** in 39% isolated overall yield.

In conclusion, we have demonstrated that a rational strategy and computational aid can be effectively used in the synthesis of pharmaceutically promising compounds, such as indanorine,[6] an antiproliferative agent, which involves a photochemical step.

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Photon-initiated biomimetic ring contractions of 14-membered cembranoids to 12-membered diterpenes implicating a 1,3-sigmatropic rearrangement process

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The photon has been an important 'reagent' in synthesis since the very early beginnings of organic chemistry. Indeed, many of the earliest photochemical experiments used ordinary sunlight as the source of radiant energy, and there is compelling evidence that sunlight is implicated in the biosynthesis of many secondary metabolites, particularly those found in the marine milieu. Prominent amongst the plethora of marine metabolites are Z-furanobutenolide–based cembranoids, *eg.* rubifolide (**1a**), bipinnatin J (**1b**), and deoxypukalide (**1c**) found in
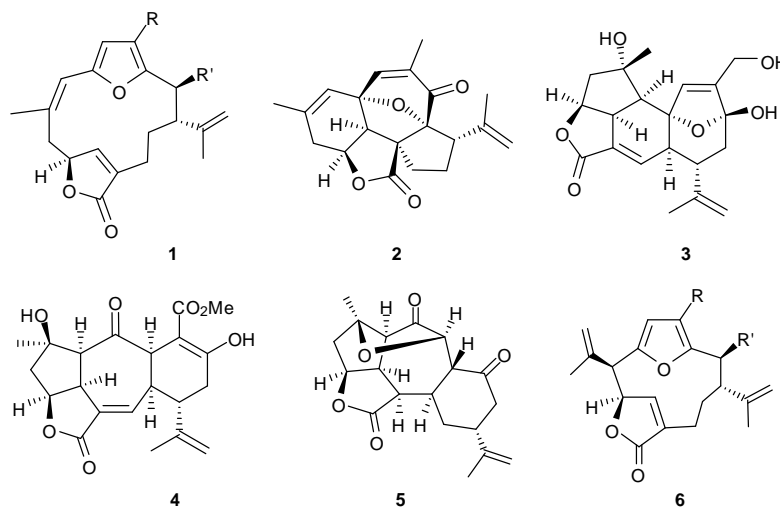
a, R = Me, R' = H; **b**, R = Me, R' = OH; **c**, R = CO$_2$Me, R' = H;

corals.[1] These 14-membered macrocyclic structures frequently co-occur with complex fused-ring compounds, *eg.* intricarene (**2**), plumarellide (**3**), rameswaralide (**4**), ineleganolide (**5**), and also with 12-membered ring diterpenes, *eg.* kallolide B (**6a**) kallolide A (**6b**) deoxypseudopterolide (**6c**). Following a detailed examination of the structural and possible biosynthetic interrelationships between the 14-membered furanobutenolide-based cembranoids **1** and their polycyclic congeners **2-5** [1] we recently developed biomimetic syntheses of the ring systems in these unique polycycles. These biomimetic syntheses featured combinations of [5+2], [4+2] and [4+3] cycloaddition reactions[2] and also successive transannular Michael reactions.[3]

The 14-membered macrocycles **1a-c** are isomeric with the 12-membered ring diterpenes **6a-c** and the two families are almost certainly related biosynthetically.[1] To examine aspects of these relationships we first developed syntheses of the three *Z*-furanobutenolide-based cembranoids **1a-1c**, and then investigated their fundamental photochemistry. Thus, when separate solutions of **1a**, **1b** and **1c** in acetonitrile were irradiated through Pyrex using light from a 400W sun lamp, each of them was found to undergo *Z/E* photoequilibration leading to the relatively unstable *E*-isomers **7a, 7b** and **7c** respectively in approx. 60% yields (Scheme 1).[4] We then found that on further irradiation all of the *E*-

**a**, R = Me, R' = H; **b**, R = Me, R' = OH; **c**, R = CO$_2$Me, R' = H;
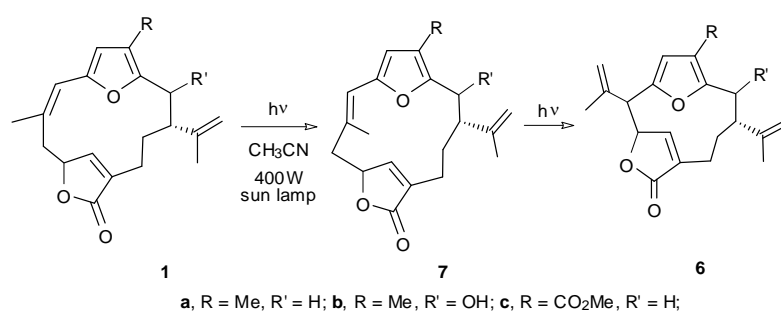
Scheme 1. Photochemical *Z→E* isomerisations of 14-membered ring cembranoids, and their biomimetic photon-induced ring contractions to 12-membered ring diterpenes **6**.

isomers **7a, 7b** and **7c** underwent facile rearrangement and ring contraction producing the corresponding 12-membered ring isomers **6a, 6b** and **6c** respectively in 70-90% yield.[4]

The photochemical conversion of natural *Z*-bipinnatin J (**1b**) to kallolide A (**6b**) was observed earlier, in 1998, by Rodriguez *et al.*[5] who were the first to establish the biogenetic relationship between 14- and 12 – membered cembranoids in corals. Our own studies not only showed the generality of these photon-induced ring contractions, *i.e.* with the synthesis of kallolide B (**6a**) and deoxypseudopterolide (**6c**),[4] but they also established, for the first time, that the relatively unstable *E*-furanobutenolide cembranoid isomers **7a**, **7b** and **7c** were probably natural products and also key intermediates in the ring contractions of **1** leading to **6** in corals. Subsequent to our studies, Mulzer *et al.* described a further example of the aforementioned photon-induced ring contraction process in their synthesis of the 12-membered ring diterpene 11-gorgiacerol.[6]

The isomerisations of the *Z*-cembranoids **1** to their *E*-isomers **7** are triggered by π-π* photochemical excitations of the alkene bonds in **1**, implicating the bi-radical intermediate **8** (Scheme 2). The ring contractions **7→6** are stereospecific with the centres at C10 in **7** migrating across their C7-C8 alkene bonds with retention of configuration. These conversions might proceed by a radical pathway, involving cleavage of the C9-C10 σ- bond in **8** leading to the allylic bi-radical species **9** whose centres then recombine at C7 and C10 producing the 12-membered ring in **6**. However, we have suggested that the ring contractions **7→6** most likely occur *via* [1, 3] sigmatropic processes.[1,4] These processes are allowed photochemically and are represented as [$\sigma_2+\pi_2$] cycloadditions (Scheme 2). Whatever the precise mechanisms however, the ease with which the photon-induced isomerisations **1→7→6** take place indicate that they mimic the likely biosynthesis of the 12-membered ring metabolites **6** in coral reefs, *i.e.* from **1/7** using ordinary sunlight.
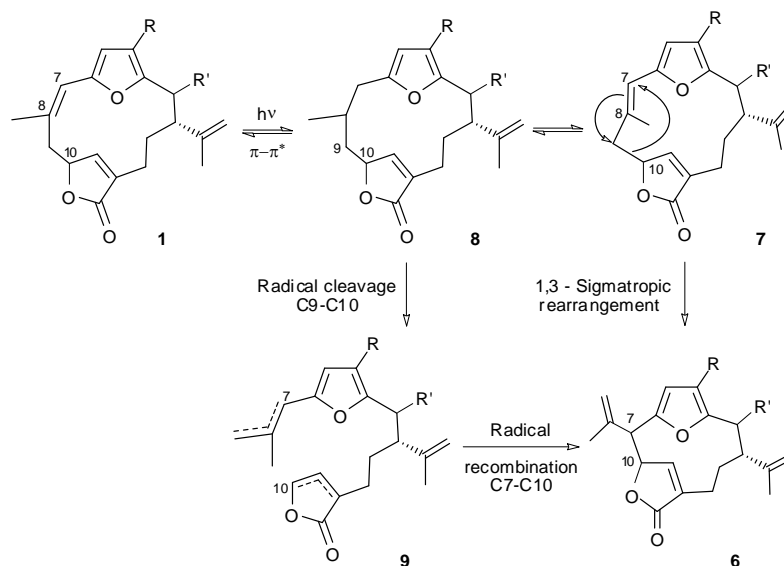
Scheme 2. Mechanisms for the photochemical ring contractions of the 14-membered cembranoids **1/7** to their 12- membered ring isomers **6**.

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Mild photoactivation of strong chemical bonds

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Photons are traceless reagents that promote thermally inaccessible processes.[1] Thus, transition metal catalysis is required for the activation of aryl-X bonds. A recent photochemical alternative that avoids the use of such toxic and delicate compounds is the ArS_N1 reaction. This involves the heterolytic photocleavage of aryl-halogen or aryl-oxygen bond in triplet aromatic chlorides, fluorides or esters (sulfonates and phosphates).
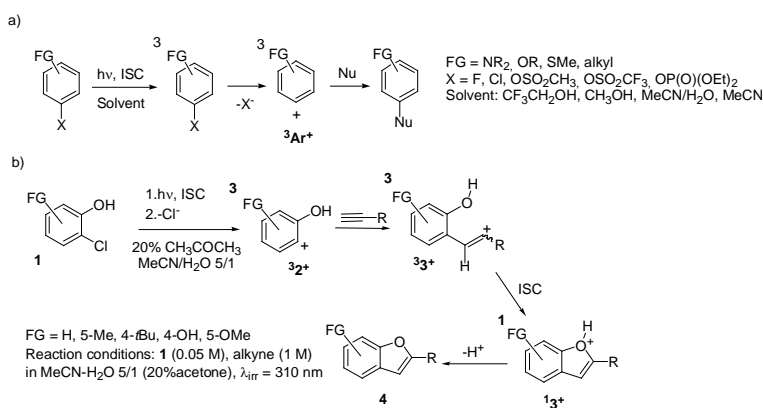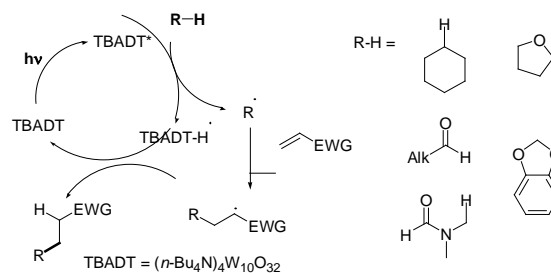

Scheme 1

Triplet phenyl cation ($^3\mathbf{Ar^+}$, Scheme 1a) reacts with π bond (alkenes, alkynes or (hetero)aromatics) or σ (cyanide ion) nucleophiles and allows for a mild arylation procedure.[2] The scope extends to electron-rich aromatic derivatives, or to electron-poor derivatives such as chloro-benzaldehydes, acetophenones or benzoate ester after conversion to the corresponding 1,3-dioxolanes (orthoester).[3] Arylations via $^3\mathbf{Ar^+}$ are advantageous for tandem carbon-carbon and carbon-oxygen bond formation, as in the synthesis of 2-substituted benzo[*b*]furans by irradiation of 2-chlorophenols (**1**, Scheme 1b) in water/acetonitrile in the presence of 1-alkynes. The photogenerated triplet cation $^3\mathbf{2^+}$ adds to the alkyne and gives β-aryl vinyl cation ($^3\mathbf{3^+}$)

that then intersystem crosses to singlet $^1\mathbf{3^+}$ and forms the C−O bond and the end product (**4**).[4]

     On the other hand aliphatic C-H bonds have been activated by using a photocatalyst that absorbs light and activates one of the reagents by means of a chemical step (but is regenerated at the end of the process).[5] TBADT (TetraButylAmmonium DecaTungstate) activates homolytically C-H bonds in simple aliphatic derivatives, such as alkanes, aldehydes, amides, alcohols, ethers and acetals (R-H in Scheme 2). This mild approach allows to generate chemo-selectively carbon-centered radicals (**R˙**) that are conveniently employed in conjugate radical addition reactions to electron-poor olefins (α,β-unsaturated esters, ketones, nitriles and sulfones).[6]

Scheme 2

A combined application of the two above strategies is offered by the one-pot synthesis of a safrole derivative from 5-chloro-1,3-benzodioxole in Scheme 3. [7]
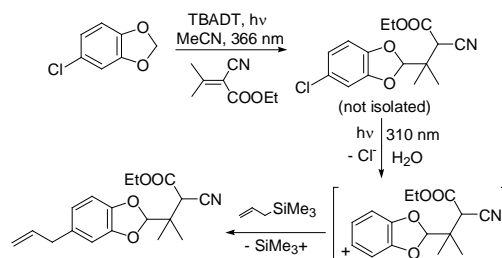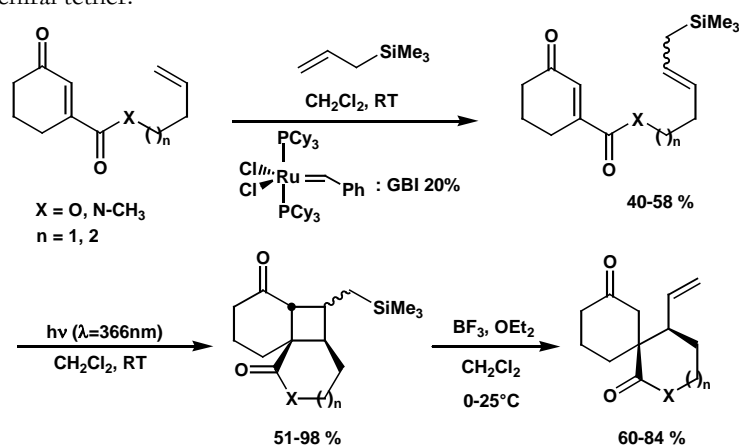

Scheme 3

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# Merging metathesis and organocatalysis with photochemistry

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Since the discovery of powerful catalysts, metathesis is nowadays considered as one of the most suitable method to directly functionnalize alkenes.[1] On the other hand, olefins play a central role in synthetic organic photochemistry.[2] In order to have an efficient and rapid access to complex structures especially cyclobutane derivatives, we have studied the combination of cross or ring-closing metatheses with a further [2+2] photocycloaddition. Thus, unsaturated oxoesters and oxoamides has been transformed into silyl derivatives in the presence of Grubbs type I catalyst. After irradiation, the resulting cyclobutanes underwent in presence of a strong Lewis acid a selective ring-opening to furnish the corresponding spiroderivatives (Scheme 1).[3] To achieve an enantioselective access to these frameworks, a stereofacial cycloaddition was also performed using lactic acid as a temporary chiral tether.[4]


Scheme 1. Combination of a cross-metathesis and [2+2] cycloaddition

Unsaturated ethers of ascorbic acid have been also submitted to ring-closing metathesis. Under UV irradiation, the resulting macrocyclic structures underwent a transannular cycloaddition leading to tetracyclic compounds.[5] Despite a poor diasteroselectivity, the two cycloadducts obtained were easily separated by chromatography (Scheme 2). Work is underway to transform these compounds into new organocatalysts.

1) GBI (5 mol%)
CH_2Cl_2, Δ

2) hυ, CH_3CN, 5°C

55-60% (2 steps) - d.r. = 6/4
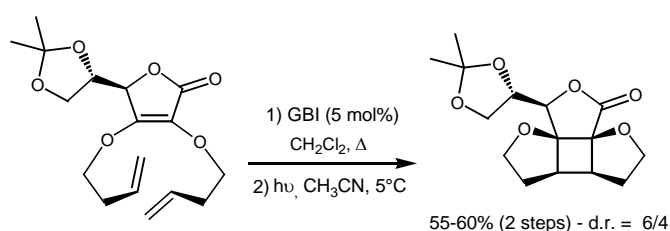
Scheme 2. Access to fused tetracyclic derivatives by RCM and transannular photocycloaddition.

As part of our interest to prepare β,γ-unsaturated esters possessing a stereocontrolled allylic centre, we have investigated for a long time the asymmetric photodeconjugation of α,β-unsaturated esters. This process requires two different photochemical steps. At first, a photoisomerization furnishes the Z isomer which is solely able to undergo a 1,5-sigmatropic reaction leading to a prochiral photodienol. In the presence of an organocatalyst (typically an aminoalcohol), this intermediate can be stereoselectively protonated to deliver the corresponding β,γ-unsaturated esters. Two different approaches have been studied. The enantioselective photodeconjugation requires the use of a chiral aminoalcohol (typically derived from camphor) introduced only in catalytic amounts. Otherwise, the diastereoselective approach which is more general has been conducted with esters possessing a chiral alkoxy group, the cheap diacetone D-glucose delivering the highest de (Scheme 3). These two processes have been advantageously used to prepare α-fluorolactones[7] and different natural products: arundic acid,[8] amphiasterin B4,[9] and gymnastatine H[10].
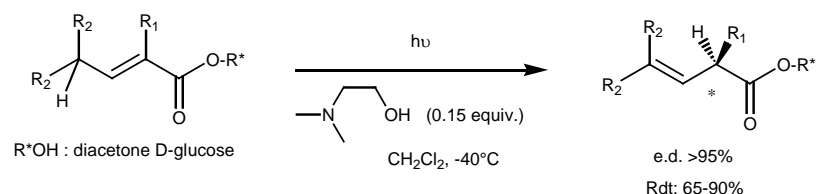
Scheme 3. Diastereoselective photodeconjugation
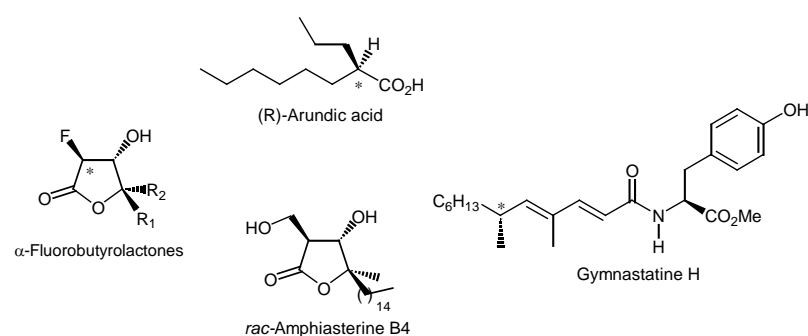
Figure 1. Targets recently obtained by photodeconjugation.

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Microflow photochemistry – an advantageous combination of synthetic photochemistry and microreactor technology

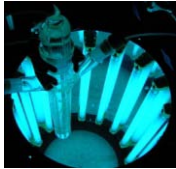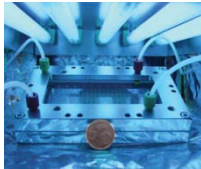*Oksana Shvydkiv,[1] Alexander Yavorskyy,[1] Kieran Nolan,[1] Michael Oelgemöller[2]**
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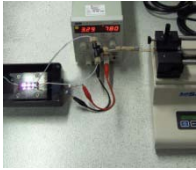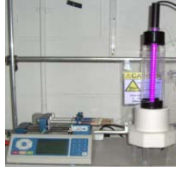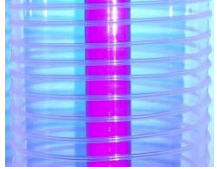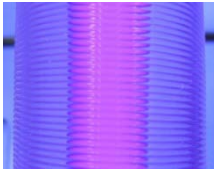
Introduction – The development of continuous microflow reactors for chemical production processes has found considerable attention over the last years. These micro-structured devices offer many elementary and practical advantages. In contrast to conventional batch vessels, microflow reactors use micro-structured channels or chambers as reaction room. At least one of the inner dimensions of these microstructures (typically depth or diameter) is below 1 mm in size. This unique geometry is particularly beneficial for photo-chemical transformations.[1-3] In particular, the narrow micro-structures enable the generation of thin solution layers that are highly transparent for light. This feature results in improved energy and light efficiencies. The continuous flow operation of microreactors additionally ensures constant removal of photoproducts from the irradiated area, thus preventing or minimizing photodecomposition and other secondary photoprocesses. The improved mass and heat transfers within the micro-structured systems also enable higher regio- and stereoselectivity of reactions. These advantages have led to the emergence of a new R&D tool for chemical industry, i.e. micro-flow photochemistry.[3]

Microphotoreactors - The initial focus of our research work was to demonstrate the feasibility of microflow reactors for photochemical synthesis on small scales. To achieve this aim we assembled two experimental setups using commercially available microreactors (Table 1): (1) a Dwell device under a UV-panel and (2) a Micronit microchip in combination with an array of UV-LEDs. The results obtained in these microreactors were compared with those from batch reactions using a conventional Rayonet chamber reactor.[4-7]

Table 1. Experimental setups and reactor parameters

Rayonet chamber[4-9]		
		a: 3.2 × 8.5; ID × H [cm] **b:** 85.41 cm²/50 cm³ **c:** 171 m²/m⁻³
Dwell device[4,5,7]		
		a: 0.2 × 0.05 × 115; W × D × L [cm] **b:** 23.0 cm²/1.68 cm³ **c:** 1369 m²/m⁻³
Microchip[6,7]		
		a: 0.015 × 0.015 × 75.7; W × D × L [cm] **b:** 1.14 cm²/0.013 cm³ **c:** 8735 m²/m⁻³
Dual-capillary[7,8]		
		a: 0.056 × 460; ID × L [cm] **b:** 80.6 cm²/2.24 cm³ **c:** 7169 m²/m⁻³
Multi-capillary reactor[9]		
		a: 0.08 × 1000; ID × L [cm] **b:** 1256.0 cm²/50 cm³ **c:** 5000 m²/m⁻³

a: Width, depth or internal diameter and length of the reaction vessel; **b:** irradiated area/irradiated volume; **c:** irradiated area to volume ratio

<u>Microflow photoreations</u> - Photodecarboxylation reactions involving phthalimides (**1**) and photoaddition reactions to furanones (**3**) were used as model transformations (Scheme 1). In all cases examined, higher conversions and/or isolated product yields were obtained in the microreactor systems. For example, the furanone (**3**) photo-addition reactions performed in the LED-microchip reached completion after just 2.5-5 min, while the batch reactor showed incomplete conversion rates of 87-90% for the same time period despite much larger light power.[6]

A:

B:
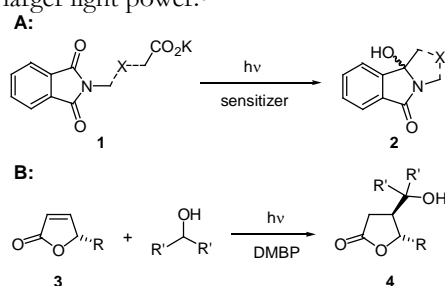
Scheme 1. (a)Photodecarboxylation reactions involving phthalimides and (b) DMBP-sensitized isopropanol addition to furanones

Commercially available, 'closed' microreactor systems have fixed dimensions of their reaction channels which subsequently restrict their irradiated volume and ultimately productivity. They nevertheless represent valuable R&D tools in early drug development processes, where only small amounts of materials are required. To overcome this limitation, we have investigated flexible polymer-based tubing as an alternative reaction vessel for photochemical reactions (Table 1). This approach was originally developed for analytical applications and later adopted for continuous flow processes.[10-13] Transparent PTFE or FEP capillaries are available in many different diameters and wall thicknesses. They can be almost any length, are chemically inert, UV-transparent and inexpensive. Based on this design concept we have initially constructed a dual-microcapillary reactor and have applied it successfully to the photosensitized addition of isopropanol to furanones (**3**).[8] The reactor utilized two FEP capillaries that were wrapped loosely around a glass cylinder with a single UVA fluores-cent tube in its centre.

The remarkable performance of this simplified microcapillary proto-type encouraged us to apply this reactor concept to parallel synthesis.

This approach offers a cost- and space-efficient alternative to micro-reactor "clusters" and can be implemented into typical R&D scenarios. An advance multi-microcapillary flow reactor (MμCFR) comprising 10 parallel FEP capillaries was subsequently constructed.[9] Each capillary had a length of 11.5 m, an inner diameter of 800 μm and an internal (irradiated) volume of 5 ml. Using the alcohol-addition to furanones (**3**) as a model reaction, this novel reactor was subsequently employed successfully for parallel reaction optimization, scale-up and library synthesis. In addition, the multi-capillary reactor did not require any cooling water and consumed ~30% less energy if compared to the batch Rayonet system.

The microreactor systems utilized in our studies varied in size and dimensions (Table 1). The Micronit microchip had the smallest volume of just 13 μL but showed the largest irradiated area to volume ratio of 8735 m^2/m^{-3}. Its combination with miniaturized UV-LEDs resulted in a very energy efficient setup. Despite its naturally low productivity, the microchip represents an advantageous R&D tool in early lead finding processes, for example, when only trace amounts of products are required for biological screening. The bigger Dwell device system (1.68 ml volume) allows for the generation of larger amounts of products, whereas capillary reactors have been used for parallel operations,[9] low-temperature irradiations[13] and multi-gram synthesis.[11]

Conclusion – Microflow photochemistry combines successfully the benefits of microscopic dimensions and flow operation. The results from our studies show clearly the superiority of this novel technology over conventional reactor systems. In contrast to commercially available 'closed' microreactors with fixed inner dimension, flexible 'open' microcapillaries allow for task specific applications. Advanced multi-capillary flow reactors furthermore enable parallel operations. It is hoped that this technology will find future applications in chemical R&D processes.[1-3,14]

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Synthesis of macrocyclic lactams and lactones using photochemical dimerization reaction

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Macrocyclic compounds are very attractive target molecules in organic synthesis.[1] For example, crown ethers and aza analogues have been known for several decades and their host-guest chemistry with a large variety of metal ions has been thoroughly investigated so far. Since macrolactones and –lactams possess biological activities, many synthetic methodologies of lactonization and lactamization have been reported. Yamaguchi's lactonization,[2] tin-catalyzed trans-esterification,[3] and ring-closing methathesis (RCM) reaction[4] are the most well known methods among the synthetic procedures.

Recently, Booker-Milburn[5] and this laboratory[6] independently reported the synthesis of macrolactones and –lactams using [2+2] photochemical dimerization reactions. Booker-Milburn and coworkers reported the intramolecular [2+2] photochemical cycloaddition reaction of N-alkynyl-substituted maleimide **1** was not observed to give the dimerization products **MLA1** and **MLA2** in a ratio of 4 to 1 in total 71% yield (eq. 1). The stepwise procedure was found to allow the efficient photochemical macrocyclization to produce asymmetric macrocyclic rings. Furthermore, the size of the macrocycles and their shape was found to be controlled through the intramolecular photochemical [2+2] cycloaddition reaction of compound **2** (eq. 2).

The formation of macrocyclic lactones **MLOa,b** was found in the Paternò-Büchi dimerization reaction of furan-2-ylmethyl-2-oxoacetates **3** in ca. 25% yields (eq. 3). The structure of **MLOa** was confirmed by the X-ray crystallographic analysis. The dimerization reaction was size-sensitive, because the starting compound **3c** did not produce the corresponding macrocyclic lactone. The one-step preparation of the highly functionalized twelve-membered ring system would be synthetically attractive. The scope and limitation for the synthesis of macrocyclic rings using the photochemical dimerization reaction are now investigated in this laboratory.
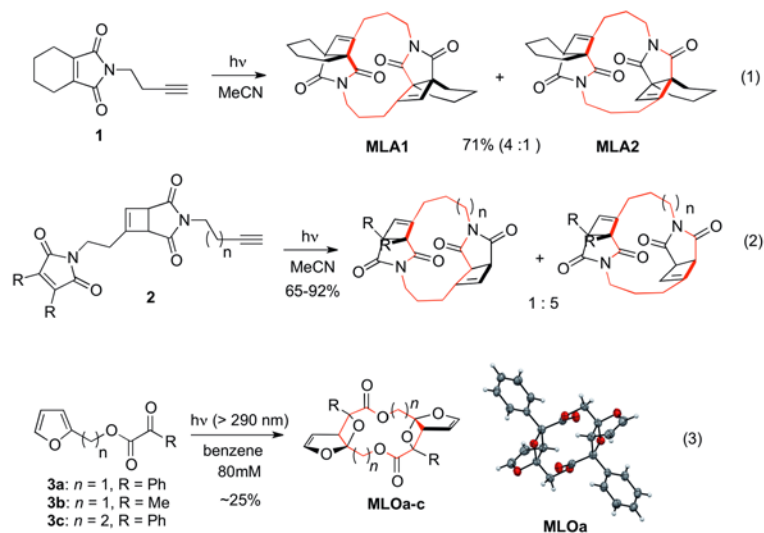
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PILLS OF HISTORY

In this section we reproduce part of an interesting paper published by Emanuele Paternò in 1909 on Rev. Gen. Chim. Pure Appl.*, 12, 299-302. This article can be relevant in order to clarify some items of the controversy occurred between Paternò and Ciamician. On this argument a contribution will appear in the next issue.*

Maurizio D'Auria

Les nouveaux horizons de la synthèse en chimie organique[1]

E. Paternò
Professeur à l'Université de Rome, Vice-président du Sénat.

Le développement rapide et merveilleux de la chimie organique, dans la deuxième moitié du siècle passé, s'est fait en parcourant simultanément duex voies, différentes par la nature des obstacles, mais convergeant vers un même but. Un travail tenace nous a permis de sonder la structure intime des composés organiques naturels, d'une part; nous avons cherché, d'autre part, à les reproduire artificiellment dans nos laboratoires, en prenant pour guides des hypothèses hardies et ingènieuses, qui se sont développées et se sont adaptées aux résultats de l'expérience.

Le travail accompli a été colossal; les difficultés, vaincues avec une trés grande opiniâtreté; les résultats, dignes des hommes de génie qui y avaient collaboré. Il en sorti un corps de doctrine qui, tout en n'étant pas parfait, est sans doute admirable par la soldiité de ses bases, par la largeur de ses vues, par les innombrables applications scientifiques et industrielles qui en sont dérivées. Mais, pendant que l'on découvre des réactions nuovelles, qui ajoutent de nouveaux succès à ceux déjà obtenus par la synthèse de l'alizarine et de l'indigo, des corps gras et des alcaloïdes, des sucres et des substances protéiques; pendant que l'on est en train d'abattre les derniers obstacles par la synthèse asymétrique, de nouvelles régions à explorer, de nouveaux horizons lointains, plein de promesses et d'espoir, s'offrent à l'activité des hommes d'étude. Les procédés classique de la

synthèse sont désormais insuffisants. L'homme cherche dans son œuvre à s'approcher toujours plus de la nature. S'il a eu des succès, c'est dans les laboratoires et par des moyens complexes, par des voies indirectes et des chemins tortueux, petit à petit, péniblement, tandis que la nature procède avec une simplicité d'autant plus grande qu'elle nous paraîtmystérieuse. C'est ainsi que la ciguë pousse et se développe en sortant d'une toute petite graine, que, par une simple distillation en présence de l'eau, on en retire la coniine; tandis que l'homme, fier de ce qu'il a pu la préparer artificiellement, ne peut oublier la nombreuse série de transformations par lesquelles il a dû passer et la nombre de composés dont il a dû se servir.

C'est pourquoi si, dans les premiers temps, sans se soucier des movens, les chimistes ont visé seulement au but, maintenant que le but est atteint, ils se retournent vers l'étude des moyens, pour tâcher d'arriver aux mêmes résultats, et même à des résultats meilleurs, par un chemin plus bref, avec des difficultés moindres et une plus grande économie. C'est l'histoire constante des progrès humains dans toutes ses manifestations.

Pour que la synthèse des substances organiques puisse être réalisé d'une façon plus directe, plus rapide, plus proche des conditions naturelles, il est nécessaire que l'on connaise complètement les transformations qui sont dues à l'action de la lumière, aux microorganismes, aux enzymes et aux catalyseurs. Le travail a été brillamment entrepris, et l'on peut dire que, jusqu'à un certain point, il est en bonne vie. La synthèse organique peut et doit obtenir, sans doute, un grand secours de l'emploi des catalyseurs; mais il est peut-être nécessaire d'abord que les réactions dites de contact, catalytiques ou d'induction, deviennent plus claires. Et, surtout, il faut que l'on fasse disparaître toute confusion et toute incertitude. Sous le nom d'actions catalytiques, on a tour à tour désigné des réactions essentiellement différentes. Le sujet ne peut pas être traité ici incidemment. Mais, bien plus que par les faits de la synthèse organique observés avec l'intervention d'un catalyseur et qui sont du reste assez rares, le plus grand espoir nous vient de quelques observations d'apres lesquelles certaines réactions chimiques varient avec la nature du catalyseurs. (...)

Il n'y a plus de doute à l'heure actuelle sur l'importance de la lumière solaire comme agent de la synthèse chimique. L'étude de l'action de la lumière sur les corps organiques remonte aux origines de la chimie; mais, dans ces dernières années, on a étudié d'une façon toute

spéciale les procédés d'oxydation et de réduction réciproque déterminée par la lumière sur un mélange de duex substances et même plus. De remarquables cas de synthèse ont été étudiés.

J'ai eu l'occasion récemment d'en observer quelques-uns d'ordre général, et ils me semblement susceptibles de subir un développement encore plus grand.

Les hydrocarbures éthyléniques, et surtout le triméthylene, s'additionnent directement aux aldèhydes et aux cétones, pour donner naissance à des composés intéressants, parmi lesquels ceux obtenus avec le benzaldéhyde et la benzophénone, peuvent avec grande probabilité être représentés par les formules schématiques suivantes:

$$C^6H^5.HC\!-\!CH\!-\!C\overset{\displaystyle O}{\diagup}\!\!\overset{CH^3}{\underset{CH^3}{\diagdown}} \qquad C^6H^5\!\!\underset{C^6H^5}{\diagup}\!\!C\!-\!CH\!-\!C\overset{\displaystyle O}{\diagup}\!\!\overset{CH^3}{\underset{CH^3}{\diagdown}}$$
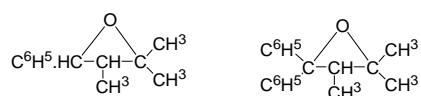
D'autres réactions, aussi remarquables, peuvent se produire les cétones et les hydrocarbures saturés. Le toluène et les autres homologues de la benzine nous donnent des alcools tertiaires du type:

$$C^6H^5.H^2C\!-\!\underset{C^6H^5}{\overset{C^6H^5}{C}}\!-\!OH$$
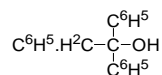
mais, en même temps, une partie de la cétone a été, aux dépens de l'hydrogène de l'hydrocarbure, transformée dans la pinacone correspondante, pendant que l'on obtient le radical de l'hydrocarbure. On obtient ainsi, avec le p-xylène, le dixylilyle, et, avec l'ethylbenzène, le diphénylbutane:

$$\begin{array}{cc} H^2C\!-\!\!-\!CH^2 & \\ & CH^2.CH^2.C^6H^5 \\ & CH^2.CH^2.C^6H^5 \\ CH^3 \quad CH^3 & \end{array}$$
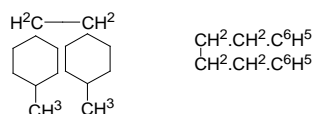
Toutes le fois que la complexité de la chaîne latérale le permet, on voit, en outre, se former la pinacone aux dépens de deux atomes d'hydrogène de la même chaîne; il y a alors un double lien, et l'hydrocarbure non saturé ainsi obtenu se combine presque

complètement à la cétone. Cette réaction se fait encore plus facilement avec les hydrocarbures de la série grasse.

Et ces réactions ne sont pas restreintes aux seuls hydrocarbures; mais elles se font avec les substances les plus diverses. Il suffit de signaler, à titre d'exemple, que la benzophénone et l'acétate de benzyle donnent le composé:

$$
\begin{array}{ccc}
C^6H^5 & C^6H^5 & \\
CH\!-\!\!-\!\!-\!C\!-\!\!-\!\!-\!OH \\
OC^2H^3O & C^6H^5 &
\end{array}
$$
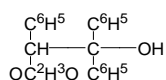
Les recherches et les travaux que je poursuis permettront de mieux comprendre la nature et la constitution de ce que nous appelons les résines. A chaque pas, dans les réactions de la chimie organique, nous rencontrons del substances résineuses. On a pu en étudier plusieurs qui ont une composition définie; mais ces produits se forment par des réactions assez profondes, qui rendent difficile la connaissance de leur structure chimique. Dans mes recherches, par l'action douce de la lumière, j'ai obtenu une série de résines à composition définie, n'ayant pas un pois moléculaire trop élevé, et qui constituent de vrais corps chimiques, ayant une structure bien déterminée; leur molécule est relativement simple, puisqu'il s'agit de produits d'addition sans polymérisation.

Ces résultats m'ont poussé à étudier les poids moléculaires de quelques-unes des plus communes parmi les résines naturelles, et j'ai trouvé qu'elles ont aussi des molécules assez simples, qui ne sont pas comparables, par exemple, à celles de l'acide tannique, de la gomme, de la gélatine, et qui ne sont pas des substances polymérisées. En comparant ensuite les transformations de ces résines à constitution commune avec celles que l'on peut produire dans le résines naturelles, on peut avoir des indications pour remonter à leur constitution. Les recherches dans cette voie doivent être intéressantes.

J'ai obtenu des résultats qui me paraissent remarquables dans la formation des produits azotés par l'action de la lumière: l'acétone avec l'ammoniaque m'a donné un alcaloïde complexe. (...)

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TECHNICAL NOTES

Optical spectroscopy methods

This technical note is the first in a continuing series that will discuss key optical spectroscopic techniques as well as the instrumentation required to allow sample measurements. As the series develops we hope it will be come a useful guide to the techniques, the equipment needed, and also how they will be used together to make measurements. The goal is to demystify the instrumentation and to allow a more open understanding of instrumentation artifacts and effects that might influence or become important to successful measurements.

Optical spectroscopy is the science of the interaction of optical radiation with matter. In many cases this involves specific transitions between the energy levels (states) of a sample and is monitored experimentally by the absorption or emission of electromagnetic radiation. In these types of interaction the radiation is considered to comprise of packets of energy called photons and they have a dual character in that they have both particle and wave like properties. Thus the photon energy is related to its wavelength and frequency by:

$$E = h\nu = \frac{hc}{\lambda}$$

where E is the photon energy, h is Planck's constant, ν is the frequency, c is the speed of light and ν is the wavelength.

There are many types of radiation/matter interactions, such as diffraction, refraction, reflection, and scattering that do not involve transitions between energy levels. However, these interactions may cause changes in the measured optical radiation due to direction or polarisation and are often the result of bulk material properties rather than specific chemical species.

In the ultraviolet to infrared spectral regions the instrumental needs are similar in terms of the optical materials required for focusing, steering and dispersing light. "Spectrometry" is defined as the

quantitative measurement of the intensity of an optical signal at one or more wavelengths using a photo-detector.

Method	Measured Quantity	Examples
Absorption	Absorbance or the ratio of transmitted to incident radiant power, $A = -\log(P/P_O)$	Atomic absorption, UV-VIS molecular absorption, IR absorption
Emission	Radiant power of emission, P_E	ICP and DCP emission, spark emission, laser-induced breakdown emission, flame emission, DC arc emission
Luminescence	Radiant power of luminescence, P_L	Molecular fluorescence and phosphorescence, chemi- and bio-luminescence, atomic fluorescence
Scattering	Radiant power of scattering, P_S	Raman scattering, Mie scattering, turbidity

Table1: Methods of optical spectroscopy and the measured quantity

Spectroscopic information about a species and its micro-environment is usually obtained by stimulating the sample with some energy source such as electrical energy, radiation, particles, or heat. Before the stimulation is applied the sample normally is residing in its lowest energy level, or ground state. After the stimulation the samples is momentarily induced to a higher energy level or excited state. Spectroscopic measurements are made from either the radiative emission from the excited species as it return to the ground state or

by the amount of absorbed excitation radiation. The magnitude to of the optical signal as a function of wavelength describes the chemical information about the sample. The signal intensity can be described in radiometric terms, now exclusively used in optical spectroscopy, or in photometric terms that have been based upon the human eye response. In the radiometric system, the basic quantity measured is the actual amount of radiative energy in joules (J) either being emitted by a source or incident upon a detector.

The four main methods of optical spectroscopy are absorption, emission, luminescence and scattering, table 1.

Although this chapter will specifically concentrate on luminescence spectroscopy it is helpful for completeness to consider the other three main methods in optical spectroscopy in the context of the instrumentation and measurement requirements.

Absorption

The absorption method involves measuring the ratio of two radiant powers, calculating the absorbance, and relating the absorbance to concentration. For absorption to occur, the frequency of the incident light must correspond to the energy difference between two states, which allows the species to be excited from the ground state to some higher energy state. The energy absorbed is dissipated as luminescence (radiant energy), photochemical reaction (chemical energy) or thermal energy. For many experiments, the absorption of light follows Beer's law:

$$A = -\log(T) = -\log\left[\frac{P}{P_0}\right] = \varepsilon c l$$

where A is the absorbance, T is the sample transmittance, ε is the extinction coefficient of the sample, c is the concentration of the absorbing species and l is the optical path length through the sample.

The absorption method is based on the following assumptions:

• The absorbers act independently of each other.

• The incident light intensity is not so high as to cause saturation or

bleaching effects.

• The incident light beam is perpendicular to the absorbing surface.

• The path length is uniform, and the sample is homogeneous and does not scatter the light.
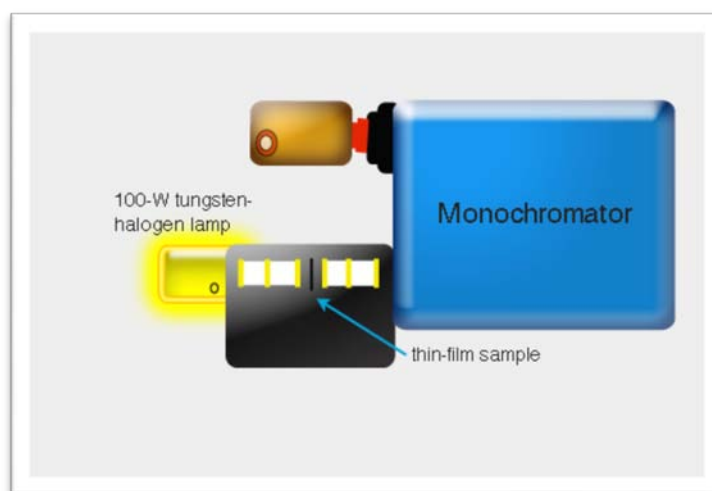
Figure2: Single channel absorption spectrophotometer

Emission

Emission spectroscopy relies upon a radiative emission from the sample following excitation by a non-radiational source, such as a flame, DC current, high-voltage spark or pulsed laser heating. Figure 3 demonstrates a typical arrangement of instrument.
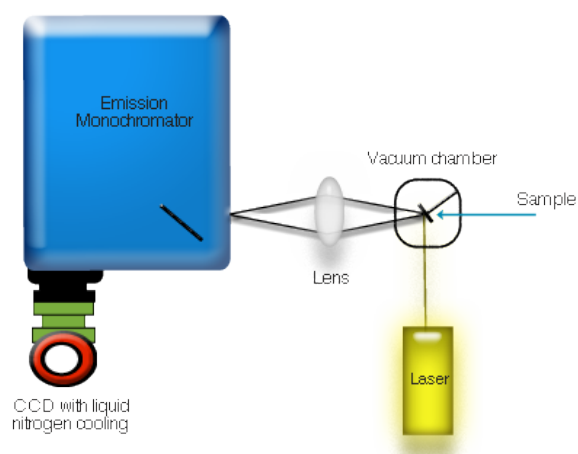
Figure 3: Emission spectrometer.

As an example: sodium atoms emit a characteristic emission when excited in a flame by a collisional process. When it produces a thermal equilibrium, it generates a statistical distribution of excited states. Once generated, the number of atoms, n , at a particular energy level, i, is given by the Boltzmann distribution:

$$n_i = \frac{n_t g_i e^{-E_i/kT}}{\sum_{i=0}^{\infty} g_i e^{-E_i/kT}}$$

where n_i is the total atom density, k the Boltzmann's constant, T the absolute temperature and g the statistical weight for state i. The frequency of the radiative emission corresponds to the difference in energy levels of the excited analyte.

Alkali metals such as sodium and potassium have excited levels close to their ground states and, as such, are relatively easy to excite using flames. Such atoms have resonance lines generally in the visible and near-IR regions of the spectrum. However, many other elements

have energy levels significantly farther from their ground states, and they require considerably more intense excitation from sources such as plasmas to generate a suitable emission signal. Because of the high energy difference between the higher and lower states, these elements generally exhibit emission spectra in the UV.

The radiant emissive power, P_E, from state j to i is given by:

$$P_E = A_{ji} h \nu_{ji} n_{ji}$$

where A_{ji} is the transitions probability, $h\nu_{ji}$ the energy of the emitted photon and n_j the number density of the higher energy state j.

The radiant power of the emission is directly related to the population densities of the excited states and hence to the analyte concentration through the Boltzmann distribution. Thus by measuring the emission spectrum from a sample, one can apply known spectra from a library to identify and quantify the concentration of species in the sample.

Scattering

Radiation incident upon an analyte may be scattered as well as absorbed by the sample. The intensity, angular distribution and radiation frequency of the scattered light can be used as a means of analysis. Several classes of scattering are possible (Table 2).

The most widely used class in scattering type spectroscopy is Raman scattering. Incident photons scattered inelastically from an analyte may either gain or lose energy. The amount of the difference typically corresponds to one quantum of vibrational energy of the species. The wavelength of the scattered light shifts accordingly. The most common form of Raman, called Stokes scattering, involves a loss of energy causing a red shift in the scattered photon. A gain in energy is called anti-Stokes scattering.

Class	Scatter Method
Rayleigh	Elastic scattering from small particle such as atoms or molecules, resulting in scattered radiation that occurs in all directions uniformly
Debye or Mie	Elastic scattering from large particle with dimensions comparable to the incident radiation wavelength (Debye) or much larger than the incident wavelength, where the result from scattering is non-uniform
Brillion	Inelastic scattering where the frequency of the reflected radiation is changed by thermal sound waves
Raman	Inelastic scattering where the frequency of the reflected radiation is changed by the gain or loss of vibrational quantum of energy by the analyte molecule

Table 2: Classes of Scattering Phenomena

Raman spectroscopy, much like infrared absorption spectroscopy, provides a method of determining the unique "fingerprint" of a species. Unlike IR absorption spectroscopy, however, there is no need to detect the incident light. In most cases, light scatters in all directions, making Raman spectroscopy especially useful for analysis of opaque solids. In a Raman microscope, one may analyse the properties of a material at various points along its surface.

In Raman spectroscopy, there are several important factors to consider when designing an experimental system. Because the analyte

scatters light with a frequency shifted with respect to the input light, the excitation source is almost always a monochromatic laser. Also because Raman scattering is a relatively weak phenomenon, it is necessary to avoid simultaneous detection of the scattered light and of the input laser, which would dwarf the desired signal. Figure 4 demonstrates a typical configuration of Raman spectrometer.
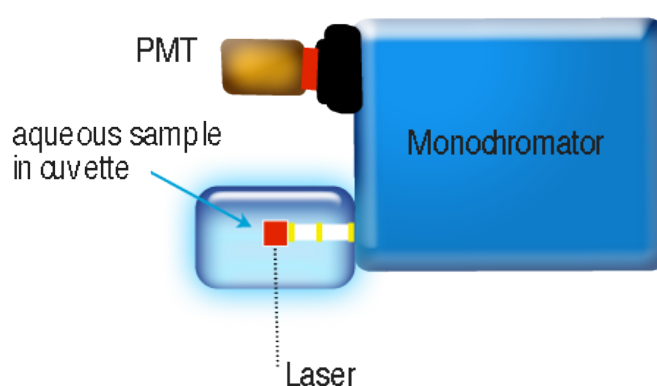
Figure 4. Basic Raman spectrometer

Also competing with Raman scattering is the much more intense Rayleigh scattering. Because the Raman and Rayleigh are of different wavelengths, Rayleigh light can be filtered at relatively little expense to the Raman signal using a notch filter or a double or triple monochromator. For some materials, an excitation source too high in energy will give rise to strong fluorescence, which may dominate the Raman scattering. Increasingly, longer wavelength lasers and time-resolved techniques are eliminating this problem. Techniques such as surface-enhanced Raman scattering, resonance Raman scattering and coherent anti-Stokes Raman scattering greatly enhance the signal with respect to spontaneous Raman scattering.

One area where Raman spectroscopy is particularly useful is in the determination of species in aqueous media. In these solutions, water is the dominant species with a lower concentration of the molecules

of interest. Infrared absorption may be ineffective because water absorption may dominate the spectrum and obscure the desired results. Because water has a weak Raman signal, however, Raman spectroscopy is typically a useful tool for solute determination.

Luminescence

Luminescence is optical radiation emitted from relatively cool bodies and can be generated from a variety of processes, including chemical reaction, and electronic or optical interaction. The types of luminescence emission can be defined from the mechanism of excitation (Table 3).

Type	Scatter Method
Bio-	Biochemical reaction
Chemi-	Chemical Reaction
Electro-	Electrical discharge, recombination of ions and electrons at an electrode
Cathodo-	Interaction with accelerated electrons
Thermo-	Enhancement of other luminescence types by the application of heat
Photo-	External radiation (as in absorption)

Table 3: Luminescence Mechanisms

Molecular and atomic fluorescence are examples of widely accepted photoluminescent phenomena that are used to characterise analytes that encompass an extremely wide and diverse range of applications. Fluorescence and phosphorescence spectrometry are examples of photoluminescence where the quantity of interest in the

measurement is the radiant power luminesced from the sample following absorption of a monochromatic incident light. Fluorescence involves the emission from singlet to singlet states; i.e., of the same multiplicity. Phosphorescence, however, involves a radiative transition from triplet to singlet states; i.e., of different multiplicity.

The probability that a fluorophore will emit a photon is a combination of the absorption probability the probability that the excited state will decay by radiative emission. This is related to the quantum yield of the sample. The probability of absorption is expressed by the molar extinction $\varepsilon(\lambda)$, m^2/mol. The important property is that there will be a wavelength(s) of maximum absorption and the spectral shape. The extinction coefficient is sensitive to the microenvironment of the fluorophore, thus solvent, impurities, concentration, and temperature will all play a role in the absorption and emission properties of the fluorophore.

For many situations, the emitted radiant power, P_l, proportional to the absorbed radiant power. Thus,

$$P_l = 2.303 k P_0 \varepsilon c l = k' P_0 c$$

where k is dependent upon the species, its environment, and the efficiency with which the excited molecule or atom returns to its ground state by emission of a photon. For low absorbances (εcl < 0.01), the luminescence radiant power is directly proportional to the absorbed power and the sample concentration.
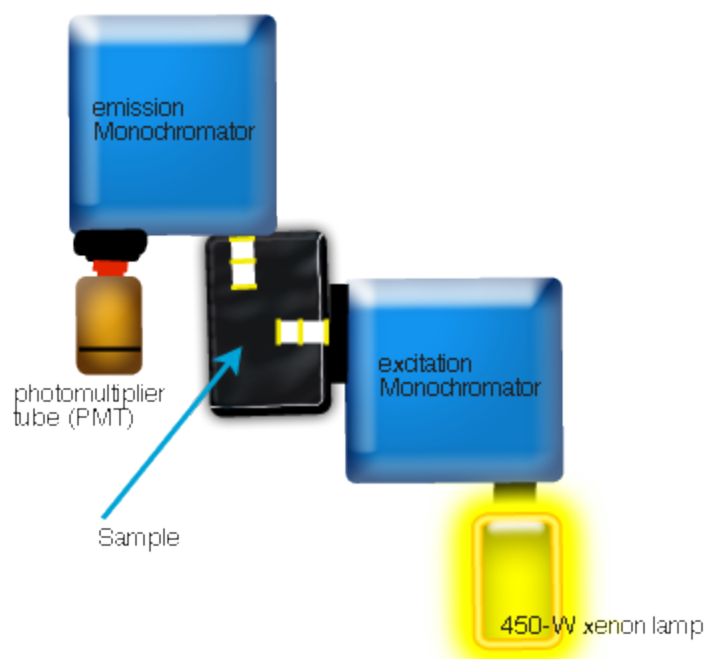
Figure 5: Basic fluorimeter arrangement

In the experimental diagram of a fluorimeter (Figure 5), the lamp provides broadband light to the excitation monochromator, which selects the excitation wavelength. Subsequent fluorescence is resolved and detected through the emission monochromator and photomultiplier tube detector.

The emission intensity of luminescent materials can strongly depend upon a range of materials parameters, for example:

Fixed Parameters	ϕ, Quantum Yield
	I, Fluorescence Intensity
	P, fluorescence polarisation
	r, fluorescence anisotropy
Dependence on 1	I(λ), spectra: excitation, emission,

parameter	synchronous
	I(c), concentration or titration
	I(T), temperature
	$r(\lambda)$, spectrally resolved anisotropy
	I(t), time-resolved
Dependence on 2 parameters	$I(\lambda,t)$, time-resolved emission spectra
	$I(\lambda_{exc}, \lambda_{em})$, excitation-emission spectral maps (EEM)
	$I(\lambda, T)$, temperature resolved spectra
	$R(\lambda, t)$, time and spectrally resolved anisotropy

Table 4: Luminescence dependence

It is the measurement of fluorescence emission that is the fundamental quantity in all fluorescence studies. Not only is this quantity affected by the dependence on other sample related parameters but also but a series of instrument specific effects that can have significant bearings upon the results, not only from day-to-day, but also instrument-to-instrument and laboratory-to-laboratory. It is these drawbacks, such as: intensity, wavelength, polarisation and time-resolved behaviours of all fluorescence based detection methods and their proper removal that make accurate measurement of the absolute fluorescence intensities extremely difficult. At the same time there are still relatively few fluorescence standards readily available that can be used to demonstrate the instrument performance validation through rigorous characterisation of the instrument.

In order to understand how to calibrate the instrument a detailed understanding of its operation is needed.

In the following series of related articles we will introduce the components that are used to make such instruments that cover these applications and discuss the operational characteristics of the components used.

The following articles will include:

- Light sources
- Wavelength selection devices
- Sample Chamber configurations and Optical Connections
- Measurement systems for Signal Acquisition.
- Calibration and Correction

Dr. John R Gilchrist,
Gilden Photonics Ltd

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PHOTOCHEMICAL AND PHOTOBIOLOGICAL SCIENCES

CONFERENCE REPORTS

Report on the XXIV IUPAC Symposium on Photochemistry
Coimbra, July 15-20, 2012
http://www.photoiupac2012.com/

The Symposium took place in the wonderful City of Coimbra, in the historical buildings of the University, overviewing the City. The subjects treated during the Symposium showed how photochemistry is nowadays employed in very different areas, running from new materials for medical applications, solar cells, photoremediation of contaminated water, photodynamic therapy, manipulation of nanostructures, mimicking of biofunctionality, restoration and conservation of art objects and others. For all these applications, basic research and theoretical understanding is a prerequisite and that was also demonstrated in some of the lectures, such as the plenary by G. Scholes on "Quantum mechanisms for light harvesting in photosynthesis". Other plenary lectures were by A. Harriman on "Artificial light harvesting antennae", by B. L. Feringa on "Controlling assembly and motion by light", by F. Scandola on "Supramolecular strategies towards functional units of artificial photosynthesis", by G. Bazan on "Conjugated polyelectrolytes and oligoelectrolytes for emerging optoelectronics", by T. Majima on "Charge transfer in DNA", by S. J. Formosinho and L. Arnaut (a joint lecture) on "From elementary reactions to chemical relevance in photodynamic therapy", and by V. W. W. Yam on "Photofunctional organometallics". One of the highlights of these meetings is the award of the Porter medal, which was given this year to Tom J. Meyer from the Univ. of North Carolina who gave an account on "$Ru(bipy)_3^{2+}$ and other remarkable MLCT states".

Among the 640 participants from 53 Countries there were many young fellows who either contributed short communications organized in three parallel sessions, or presented more than 400 posters. A remarkable session was that on solar energy conversion, which included contributions on material science and engineering for solar energy conversion. Many contributions on nanoparticles,

nanocrystallites and nanocomposites were presented. The novel techniques used to monitor the photochemical reactions in complex materials and in nanoparticles were also subject of many contributions.

Several awards were given to young colleagues (for details click on Awards in the Symposium webpage: http://www.photoiupac2012.com/). The European Photochemical Association (EPA) prize for the best thesis in photochemistry 2011-2012 was awarded to Karl Börjesson form Chalmers University, Sweden. The Langmuir award for best presentation in the Young Photochemists' session was presented to Danielle Wilson, Victoria University, Canada, and a special commendations was given to Laurence Pessoni, Université de Pau et des pays de l'Ardour, France and to Marina Blanco-Lomas, Universidad de La Rioja, Spain.

IUPAC Poster Prizes were awarded to Waheed Saban, University of Western Cape, South Africa, and to Joanna M. Malicka, University of Namur, Belgium. The Springer Editors awarded a PhD student poster prize to Karel Goossens, KU Leuven, Belgium, and to Giorgio Pariani, Osservatorio Astronomico di Brera, Italy.

A special XXIV IUPAC Photochemistry Symposium Young-at-Heart Poster Prize was awarded to Devens Gust from Arizona State University, USA, for the presentation: "Bio-inspired solar energy conversion".

Several Companies generously sponsored the Symposium (see Sponsors in the webpage), some of them located in Portugal and some being a spin-of of research groups at the University. This represented an important novelty.

A special impact on the audience was made by Franco Scandola, who showed, during his lecture, a sequence from the famous 1938 movie from Frank Capra "You can't take it with you" demonstrating Capra's vision on the future of solar energy.

The Symposium was inaugurated by fados beautifully sung by a Tuna from Coimbra and closed by a banquet in a refined venue with a gracious landscape (Quinta do Sobreiro), an impressive setting. Also fados were sung by a very wonderful group at the end of dinner.

The General Assembly of the European Photochemical Association (EPA) was held in one of the evenings and the IUPAC Sub-Committee on Photochemistry held its meeting during one of the lunch breaks.

We thank Hugh Burrows, the Portuguese photochemical community and the organizing Committee for the organization of the Symposium, which showed again that photochemistry is a lively interdisciplinary area, which can fascinate many young fellows and can greatly contribute to solve many technical and scientific questions.

Pictures from the Symposium can be seen at http://www.photoiupac2012.com/ (click photo gallery).

The next IUPAC Symposium on Photochemistry is planned to be in Bordeaux (France) in July 2014; Scientific chairman is Dario Bassani.

Silvia E. Braslavsky
Max Planck Institute for Chemical Energy Conversion
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Figure 1: Karl Borjesson (Chalmers University, Sweden) winner the EPA PhD Prize

Figure 2: Mike Heilemann (Julius-Maximilians University Wurzburg, Germany) gave the EPA-PPS Prize Lecture

Figure 3: Tom Meyer (University of North Carolina) winner of the Porter Medal.

International Symposium
"The Photochemistry of the Future – 100 Years Later"

> *The photochemistry of the future should not [...] be postponed to distant times*
>
> *The true solution consists in utilizing the radiations that [...] reach the surface of the earth in large amounts*
>
> *The fundamental problem [...] is how to fix the solar energy through suitable photochemical reactions*
>
> *Photochemical reactions often furnish surprises and proceed along quite different lines*
>
> *If our black and nervous civilization [...] shall be followed by a quieter civilization based on the utilization of solar energy, that will not be harmful to progress and to human happiness*
>
> Giacomo Ciamician,
> The Photochemistry of the Future (some topical sentences)
> *Science,* **1912***, 36*, 385-394

On Saturday 13 October 2012 the one-day international symposium *"The Photochemistry of the Future –100 Years Later"* was held in Bologna in the Aula Magna of the Chemistry Department named after Giacomo Ciamician. The symposium was organized by the Photochemical Nanosciences Laboratory of the University of Bologna to celebrate the 100th anniversary of the famous talk "The Photochemistry of the future" that Giacomo Ciamician delivered at the 8th International Congress of Applied Chemistry in New York in 1912.

The event was supported by the University of Bologna, the Italian Group of Photochemistry (GIF), the Interuniversity Research Center for the Chemical Conversion of Solar Energy (SolarChem), and the Italian Chemical Society (SCI) through its Interdivisional Group of Photochemistry (GIdF) and its Emilia-Romagna regional section; it also received the patronage of the European Association for Chemical and Molecular Sciences (EuCheMS) and financial support from Casa Editrice Zanichelli and Gruppo Tozzi.

The program was comprised of seven plenary lectures presented by Vincenzo Balzani (University of Bologna, Italy), Ben Feringa (University of Groningen, The Netherlands), Luisa De Cola (University of Strasbourg/ISIS, France), Franco Scandola (University of Ferrara, Italy), René Janssen (Eindhoven University of Technology, The Netherlands), Giulio Jori (University of Padova, Italy), and Devens Gust (Arizona State University, USA).

Figure 1. Lecture speakers: from left to right Balzani, Gust, Scandola, Janssen (first row), Feringa, De Cola, and Jori (second row).

The speakers focused their lectures on various aspects and applications of photochemistry that are highly topical in our days pointing out that some of them – e.g. solar energy conversion, photoresponsive materials – had already been forecast by Giacomo Ciamician in the talk celebrated by the Symposium.

Vincenzo Balzani, in his lecture "Giacomo Ciamician: a man ahead of his time", after a brief description of the scientific interests and social commitment of this great scientist, focused on the problem of energy and in particular on the possibility to produce fuels by non-biological photochemical reactions (artificial photosynthesis), an idea clearly present in Ciamician's talk. He pointed out that, after one century, the energy transition from fossils to renewable energy is no longer an option, but a must.

Artificial photosynthesis was the topic dealt with also by Denvens Gust and Franco Scandola with lectures entitled "Artificial Photosynthesis – Pursuing Ciamician's Dream", and "Self-Assembling Molecular Devices for Light Energy Conversion", respectively. Starting from Ciamician's vision of the future, predicting that polluting coal-fired factories and power plants would have been replaced with installations producing clean, renewable energy from sunlight, Devens Gust described several examples of current progress towards practical artificial photosynthesis, such as the development of artificial antennae that efficiently harvest light, artificial reaction centers that use excitation energy from the antennae to carry out photoinduced electron transfer reactions, and catalysts for large-scale solar fuel production. Franco Scandola focused on the interesting possibility to exploit non-covalent synthetic routes for artificial light energy conversion, as it happens in nature where the active molecular components involved in photosynthesis are assembled by means of weak intermolecular interactions. He described some of the "soft" strategies used and discussed the non-trivial problem of self-assembling intrinsically asymmetric systems, such as triads for photoinduced charge separation or photocatalytic hydrogen evolution.

Organic solar cells offer an opportunity for low-cost, large area renewable energy production and this task was addressed by René Janssen in his lecture "Converting solar energy with organic materials". After a brief introduction on operational principles and future applications of polymer solar cells, he discussed the effects of disorder and the role of the morphology on the generation, separation, and collection of photogenerated charge carriers and showed design strategies and synthesis of new conjugated polymers for the development of more efficient solar cells.

Ben Feringa in his lecture "Controlling Dynamic Functions in Molecular Systems" faced one of the more exciting and challenging

topics of the recent research, that is the integration of structures and functions in the design and synthesis of synthetic systems. In particular the speaker described switches and motors in which light-controlled molecular dynamics is coupled to specific functions, like light-sensitive biohybrid membrane transport systems, control of optical and electronic communication and self-assembly of nanostructures with responsive functions.

Biological aspects of suitable photosensitized processes were presented in the lectures of Luisa De Cola and Giulio Jori. Luisa De Cola in her talk "From solution to in vivo photophysics" showed that the self-assembly process can be studied in living cells and that the use of the dynamics behavior of selected luminescent complexes can be exploited for new type of imaging labels. Then she described nanometer-sized containers and nanoparticles useful as efficient multimodal labels and/or for the delivery of molecules inside the nucleus of cells also evidencing that these materials can be employed to construct porous patterned substrates, which can be made biocompatible upon functionalization with suitable biomolecules. Giulio Jori, in his lecture "Photosensitised processes promoted by visible light: their application in medicine and environment", focused on porphyrin compounds because of their peculiar properties that can be modulated to endow them with a predetermined behavior even in complex systems. He also showed that a careful exploitation of such features paves the way to promising and steadily expanding applications in the fields of medicine, including the early diagnosis and palliative or curative treatment for diseases, and the environment, including the definition of protocols toward an environmentally friendly methodology for the disinfection of water and the development of sunlight-activated insecticides with a low impact on ecosystems.

The lectures were of an excellent level and the atmosphere of the Liberty-style Aula Magna was an ideal place to celebrate Ciamician who had closely followed the work of the famous architect Edoardo Collamarini in the design of the Aula Magna and the library of the Chemistry Department where the symposium was held. Unfortunately, however, Ciamician dead before the building was completed.

Figure 2. The Liberty-style Aula Magna of the Chemistry
Department "Giacomo Ciamician".

Figure 3. Left: Sebastiano Campagna presents to the attending people the activities of the Interuniversity Research Center for the Chemical Conversion of Solar Energy (SolarChem); right: a view of the participants.

The international symposium *"The Photochemistry of the Future –100 Years Later"* was really an unforgettable day for the numerous attending photochemists.

Margherita Venturi
Chairperson of the Organizing Committee

4th Summer School Photochemistry 2012 "Photochemistry, Fundamentals, and Applications", September 15-19, Hotel Het Hoge Duin, WijK aan Zee, The Netherlands, organized by Holland Research School of Molecular Chemistry under the auspices of the European Photochemistry Association.

A formidable army of scientific prowess consisting of 39 PhD students and post-doc, 6 invited lectures and 5 members of the organizing committee had swept down on the little town of Wijk aan Zee, the Netherlands. The five generals of the organizing committee, Fred Brouwer (UvA), Gert van der Zwan (VU), Francesco Buda (Leiden), and René Janssen (TU Eindhoven) led by field marshal Ineke Weijer (HRSMC) had strategically chosen one of the highest dunes of the Netherlands as the excellent training site for the "4th Photochemistry summer school" regiment. Setting up camp in the barracks on top of the dune, aptly called hotel "Het Hoge Duin", quickly revealed the excellent quality of the lodging provided for even the lowest ranking of recruits, complemented by the great food and stimulating beverages available throughout the week.

Even before the official start of the 2012 summer school on Saturday evening, most of the recruits has already found their way into the main lecture room of the hotel to listen to two inspiring talks by generals Fred Brouwer and René Janssen, demonstrating a tremendous motivation and eagerness to learn. Fred and Rene reminded everybody of the basics of photochemistry with the objective of providing a smooth start into the school. Also, Fred presented the participants with a riddle that would keep the minds occupied and discussion flowing for days to come. The questions was which white powdery substance, available from any local supermarket, quenched the blue fluorescence emitted from a glass of tonic water when illuminated by a UV lamp, and by what mechanism; taking into account the clearly observable gas evolution when said powdery substance was deposited in the tonic water.

Every recruit had been encouraged to bring a poster about his or her work which had to be presented and hold up to the scrutiny of other recruits, the organizing committee and the lecturers during the three planned poster sessions, the first one of which was already scheduled on Saturday, directly after the first feast. And starting the meeting with a poster session turned out to be an ideal occasion to get to know the other participants in a nice and relaxed atmosphere. Also the two poster sessions that followed the next two evenings gave plenty of room for fruitful discussions amongst participants and stimulated further exchange of (more or less scientific) ideas, which often continued until late at night.

The scientific program extended over six half-days and included well-prepared lectures by invited lecturers as well as three short talks by PhD students, selected beforehand by the organizing committee based on the submitted poster abstracts. Every invited lecturer was given 45 minutes slots distributed over different half-days to give an easily accessible introduction to his or her area of expertise. A short impression of the various lectures:

Céline Frochot (Nancy, France) did an excellent job familiarizing us with the concepts of photodynamic therapy (PDT) and shared with us some of the latest incredible achievements in her filed.

Rienk van Grondelle (Amsterdam, The Netherlands) illustrated in his inspiring lectures the importance and complexity of photosynthesis and demonstrated how to use the knowledge available so far fo use in other applications.

Adalgisa Sinicropi (Siena, Italy) had the challenging task of explaining the details of computational photochemistry and answering various questions on conical intersections, which she managed quite well.

Sander Woutersen (Amsterdam, The Netherlands) took it upon himself to illustrate in a series of extraordinarily clear lectures the concepts of femtosecond 2D-IR spectroscopy and explained how this could be used to detect molecular motions of complex biomolecules on a ps timescale and extract information on fast structural changes.

Manifesting his almost contagious passion for science, **A. P. de Silva** (Belfast, Ireland) explained how to apply basic knowledge of physics and chemistry to understand the principles and applications of photo-induced electron transfer and luminescent molecular switches.

Finally, **Michel Orrit** (Leiden, the Netherlands) took us on a journey into the world of single molecules and impressed with unexpected results obtained from sophisticated single particle experiments.

Part of what made the lectures so successful were the 45 minutes slots reserved for discussion of the presented content after each half-day of lectures. After the session of lectures the students were asked to prepare and discuss questions that come up during the lectures, first in small groups amongst themselves, and then to select some could be posed to the respective lecturers of that session. This procedure worked surprisingly well, because it allowed for an informal setting amongst peers to first filter the questions using the combined knowledge of the group, which not only left the questions really worth asking but also took away the barrier that is normally present when asking questions to more senior scientists in a large group setting.

After every series of morning lectures, a generous lunch break allowed us to digest the diverse scientific input, and get some rest from the extensive discussions the night before, or to explore the beautiful Dutch beach right next to our hotel, so that we had no problem following also the afternoon session attentively.

On Tuesday, the afternoon session was replaced by the (in)famous HRSMC group excursion where the destination is traditionally kept a secret and so we were all very surprised when we finally arrived to an old fortress on "forteiland" a few km south of our accommodation in the middle of the north sea channel. Armed with nothing but a sharp mind and a lust of exploration we set foot on the artificial island. After receiving some initial explanations, we were divided into four subgroups that had to accomplish various tasks which all demanded a combination of team spirit and physical and psychological skills. Although, of course, in the end only one of the teams could win the competition, everybody seemed to enjoy the afternoon in the old fortress, as could be judged from the discussions that extended from the evening dinner at a nearby beach restaurant until late at night. An if the experience on forteiland had not brought us close together, then for some of us the walk back from the restaurant to the hotel, in the middle of a blistering autumn storm certainly did the trick.

All in all the summer school was an unforgettable experience for all of us in terms of scientific input as well as social aspects and it is presumably not exaggerated to state that everyone of us would really recommend the school to those lucky people who are given the possibility to take part in the next edition in four or five years in some other beautiful place somewhere in the Netherlands.

On behalf of all participants

Sabine Richert (University of Geneva) *and Joris Snellenburg* (Vrije Universiteit Amsterdam)

Follow us ...

The next issue will be dedicated to the preparation of new materials for optoelectronic and photovoltaic applications.

John Gilchrist will continue the series of technical notes on optical spectroscopy.

A brief description of the controversy between Paternò and Ciamician will appear.

Do not miss the opportunity to follow us ...

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