Photochemical Key Steps in Organic Synthesis

An Experimental Course Book

Edited by
Jochen Mattay and Axel G. Griesbeck

in cooperation with
Christian Stammel, Joachim Hirt
and Thomas Rumbach

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Preface

Synthetic organic photochemistry constitutes a research area with exceptional importance for the development of efficient and selective transformations for the preparation of natural products as well as unnatural and complicated molecules. However, a remarkably high level of resistance still exists towards integrating this type of reactions in experimental courses for students, and thus presenting this important area of chemistry at an early stage of the training of chemists. A reason for this resistance could be the lack of appropriate experimental procedures in textbooks and manuscripts for experimental courses. Another reason should be sought in the lack of the necessary photochemical equipment in many laboratories - basically trivial reasons having a great effect on the training of young chemists.

Some time ago we developed the idea of combining a number of experimental procedures for multistep synthesis with one or two *photochemical key steps*. We tried to collect these procedures directly from the respective researchers. Who else could tell us more about all the tricks and requirements than the photochemist himself who developed the synthesis? Therefore we asked leading chemists active in the field of organic photochemistry to kindly support us with their "*showpieces*". The very positive response allows us now to present a collection of experimental procedures from nearly every area.

An important task was to define the requirements for useful and widely applicable photochemical procedures. Nor only should the light induced reaction be efficient and show high chemo-, regio-, and (if possible) stereoselectivity but also be an integral ingredient of an interesting multistep synthesis. The starting materials, solvents, and reagents for these syntheses should be cheap and readily available, the necessary photochemical equipment available in most institutes, and the products well characterized and not synthesized for the sake of example. Additionally, we tried to include other modern techniques and reactions such as the preparation of organometallic compounds as well as catalytic or stoichiometric stereoselective transformations. This book should therefore give supervisors of lab courses the opportunity to take over new experiments and students to learn more about modern techniques and especially about the importance of photochemistry.

We would like to express our thanks to all colleagues who have contributed experimental procedures of a high quality. The help of Christian Stammel, Joachim Hirt and at an early stage of Thomas Rumbach is gratefully acknowledged. Their effort was substantial as well as the help of Dr. Ute Anton and her coworkers at the VCH.

Jochen Mattay, Axel G. Griesbeck

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How To Use This Book

Many syntheses in this collection represent multistep procedures starting with readily available compounds which are transformed using non-photochemical methods into the necessary substrates for the photochemical "*key-step*". A number of sequences, however, already require substrates which must be prepared using procedures from the literature. In each case, you should consult the literature which is given by the authors and find out about a) the source for all substrates and reagents used in the synthesis, b) the photochemical set-up which was used by the authors, c) the purification of starting materials and solvents as well as the characterization of the products, d) the mechanism of the reaction.

Never avoid a walk to the library before you run a reaction!

Always recalculate the reaction stoichiometry. Many problems and also hazards can originate in wrong reaction stoichiometry. Never take numbers just as they are written in a textbook or a publication. Always confirm for yourself that these numbers make sense!

Photochemical reactions sometimes are capricious (*vide infra*). Many parameters can influence the outcome of such a reaction. Always run a UV spectrum of your photoactive compound and compare it with the data given in literature. Sometimes it is useful to check the quality of the radiation source by running a standard photochemical reaction where the quantum yield is known and the products are easy to characterize.

GENERAL FEATURES

a) Further reading: from introductory to sophisticated photochemistry

You will find at least two dozen textbooks on photochemistry in a well equipped library and many more on special aspects covering all possible areas of inorganic, organic and physical photochemistry. Some of these books combine mechanistic with synthetic aspects, whilst some of them concentrate on one of these aspects. Finding the right text is therefore a question of how deep you want to go into a specific problem. In 1978 N. J. Turro set a landmark with his "*Modern Molecular Photochemistry*" which still is one of the best books combining mechanistic with synthetic aspects[1]. A modern variation is "*Essentials of Molecular Photochemistry*" by Gilbert and Baggott (1991)[2]. Sometimes it is worthwhile to go deeper into mechanistic thinking especially concerning the application of modern quantum theory. R. P. Wayne published "*Principles and Applications of Photochemistry*" in 1988[3] and for all who want read the *non plus ultra* we recommend "*Electronic Aspects of Organic Photochemistry*" by J. Michl and V. Bonacic-Koutecky (1990)[4]. You won't find a word about synthetic photochemistry in this impressive work. In order to understand the more basic aspects one should read "*Excited States and Photochemistry of Organic Molecules*" by M. Klessinger and J. Michl (1994)[5].

Half a dozen books concentrate on synthetic aspects of organic photochemistry and should be consulted in order to obtain more information about specific photoreactions. Everything from brief summaries[6],[7] up to elaborate descriptions is available[8-10]. J. Kopecky published "*Organic Photochemistry: A Visual Approach*" in 1992[11] as an interesting experiment to present photochemistry in a different way. It is up to the reader which text he wants to choose.

Sometimes you will have to look up data, e.g. the triplet energy of a sensitizer, the transmission of a certain filter, the emission of a lamp, etc. In this case consult the "*Handbook of Photochemistry*"[12] or the "*CRC Handbook of Organic Photochemistry*"[13]. If you become interested in inorganic or organometallic photochemistry, look for the books by Ferraudi[14] and Geoffroy and Wrighton[15]. A. M. Braun et al. published an interesting book on "*Photochemical Technology*" in 1991[16]. The increasing importance of electron transfer processes in photochemistry is reflected in "*Photoinduced Electron Transfer*", edited by M. A. Fox and M. Chandon[17].

Besides the different journals on photochemistry[18] there are two important series: "*Organic Photochemistry*" (now edited by A. Padwa)[19] and "*Advances in Photochemistry*" (now edited by D. H. Volman, G. S. Hammond and K. Gollnick)[20]. In these periodically published books special areas of photochemistry are reviewed. A specialist periodical report about photochemistry reviews the literature published over a period of twelve months[21] and is essential for all researchers active in this area. Among all important photochemical meetings only the IUPAC Conferences on Photochemistry (every two years) should be mentioned. Abstracts of all lectures appear in Pure & Applied Chemistry. Also in this journal a collection of experiments for teaching photochemistry appeared in 1992[22].

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b) Purity of the starting materials: a problem of reactivity and absorption

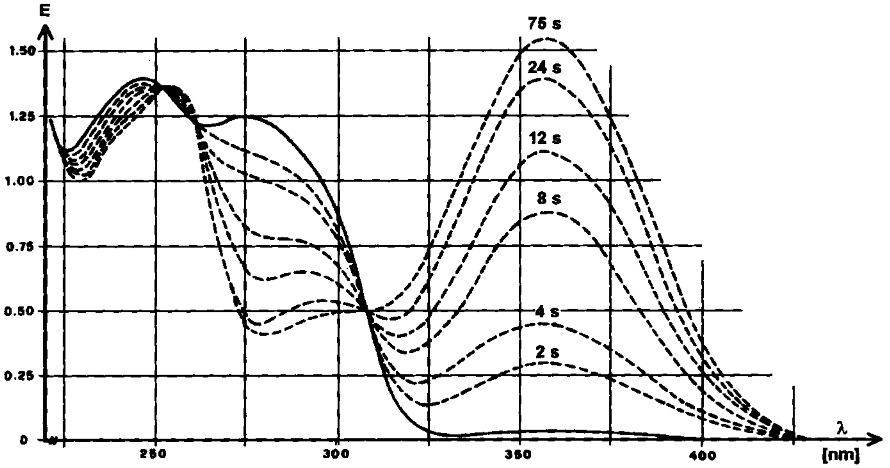
Every technique in synthetic organic chemistry has its prerequisites. When working with organometallic substrates for example one usually has to exclude oxygen and water or other protic substrates. If, however, the substrates, the reagents, the intermediates, or byproducts are highly colored the reaction could proceed exactly as described in the literature. The appearance of a colored species is often useful in organometallic chemistry to follow the progress of certain reaction steps. Quite the contrary holds for most photochemical processes. In many cases the use of substrates which are contaminated with colored material or the occurrence of colored byproducts inhibits the reaction progress. Obviously, photons have to be absorbed by substrate molecules and not by contaminants or byproducts. The design of a photochemical reaction is essentially linked to the absorption properties of all components in a specific reaction mixture. Therefore, careful purification of the starting materials has a similar status in photochemistry as in organometallic chemistry.

c) UV spectra of substrates: a first hint

Before starting a photochemical reaction the absorption spectrum of the "*photoactive*" compound(s) should be recorded. The "*photoactive*" compound is the material which should be electronically excited either to a singlet or a triplet state. This compound could further undergo (i) unimolecular transformations, (ii) bimolecular reactions with a ground-state substrate molecule, (iii) bimolecular reactions with another electronically excited molecule (a rare case), (iv) serve as a photosensitizer, i.e. activate another substrate molecule by energy or electron transfer, or (v) serve as a photoinitiator, e.g. in photochemical induced radical chain reactions.

It makes sense to record several spectra using different substrate concentrations, so that the extinction coefficients for all absorption bands can be calculated. In many cases the weakest bands in the long-wavelength region are the important ones. Of course, the absorption spectra should also be recorded from the reagents which are applied in the reaction. It is advised to record as well an absorption spectra from the reaction mixture to look for additional bands in the UV-spectra which could indicate ground-state interactions such as the formation of CT-complexes.

These photophysical data, however, does not say anything about the success of the reaction. If the desired product is already available one should also record an absorption spectra of it. Finally a set of several spectra (Figure 1) is available which should be carefully studied to decide on the right irradiation conditions.



——— spectrum of substrate; -------- after different irradiation times

Figure 1: UV-spectra during irradiation of a tetrazole (compound analogous to **2.7d**, see page 142, 1.02 x 10^{-4} M in ethanol, mercury high-pressure lamp, pyrex lamp); from H. Meier, H. Heimgartner, *Helv. Chim. Acta* **1985**, *68*, 1287.

d) Solvents: finding the best medium for the desired transformation

In principle photoreactions can be performed in the gas phase, in the liquid phase, and in the solid phase. In contrast to many other techniques in chemistry all of these possibilities can lead to a successful conversion of the substrate. The majority of the reactions, however, are still performed in the liquid phase. Using normal concentrations of photoactive substrates and reagents, the concentration ratio solvent to substrate is around 100 - 1000! An extinction coefficient of the photoactive compound only ten times higher than that of the solvent (in the wavelength region used for irradiation) corresponds to a pronounced filter effect of the reaction medium. Before starting a photoreaction one should therefore consult a table with the transmission data for the solvent used (see Table 1).

Table 1: Solvents used for photoreactions[1]

Solvent	Cut-off wavelength[2]	ε_r[3]	ET(30)[4]
water	185	78.30	63.1
acetonitrile	190	35.94	45.6
n-hexane	195	1.88	31.0
ethanol	204	24.5	51.9
methanol	205	32.66	55.4
cyclohexane	215	2.02	30.9
diethyl ether	215	4.20	34.5
1,4-dioxane	230	2.21	36.0
methylene chloride	230	8.93	40.7
chloroform	245	4.81	39.1
tetrahydrofuran	245	7.58	37.5
ethyl acetate	255	6.02	38.1
acetic acid	250	6.17	51.7
carbon tetrachloride	265	2.23	32.4
dimethylsulfoxide	277	46.45	45.1
benzene	280	2.27	34.3
toluene	285	2.38	33.9
pyridine	305	12.91	40.5
acetone	330	20.56	42.2

[1] taken from C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry* **1988**, VCH, Weinheim.

[2] wavelength (nm) at which E is approximately 1.0 in a 10 mm cell.

[3] dielectric constant.

[4] Dimroth-Reichardt values (kcal/mol) for the longest-wavelength solvatochromic absorption based on a pyridinium-*N*-phenoxide betaine dye no. 30.

There is a wide variety of solvents which transmit down to short wavelengths, e.g. hydrocarbons, alcohols, and water. Sometimes it is advisable to use non-transparent solvents, but in these cases the solvents change their role and function as sensitizers. Acetone which absorbs up to 330 nm is often used as a solvent and sensitizer. It is also required that the solvent is free of impurities, especially for those which absorb in the wavelength region used for excitation and for those which could interfere with relatively long lived intermediates formed during the photoreaction. The first prerequisite is easily checked by recording a UV-spectrum. The second problem is often not obvious until a new solvent fraction is used. Sometimes it is useful to treat the solvent with EDTA in order to get rid of metal traces. Certain intermediates in photochemical reactions such as biradicals or zwitterions could be stabilized or destabilized by the surrounding solvent sphere. Therefore new experiments should be prepared by testing a series of solvents with increasing solvent polarity to find the optimal medium.

e) Direct or sensitized photolysis: you have to find out !

The absorption behavior of the photoactive component does not say anything about the behavior of the excited state. Does it deactivate rapidly in the singlet channel with fluorescence or radiationless ? Does it undergo fast intersystem crossing into the triplet manifold ? What is the chemistry of all these excited states ? If we have the opportunity to measure them, fluorescence and phosphorescence spectra will supply us with lifetime and quantum yield data. A comprehensive up-to-date collection of photophysical data can be found in Murov's *Handbook of Photochemistry* (see Table 2).

Table 2: Sensitizers and quenchers in non-polar solvents[1]

compound	E_T[2]	E_S[3]	Φ_{ISC}[4]
benzene	353	459	0.25
toluene	346	445	0.53
methyl benzoate	326	428[7]	
acetone	332[5]	372[6]	0.90[6]/1.00[5]
acetophenone	310	330	1.00
xanthone	310	324	
benzaldehyde	301	323	1.00
triphenylamine	291[5]	362	0.88[6]
benzophenone	287	316	1.00
fluorene	282	397	0.22
triphenylene	280[5]	349	0.86
biphenyl	274	418	0.84
phenanthrene	260	346	0.73
styrene	258	415	0.40
naphthalene	253	385	0.75
2-acetylnaphthalene	249	325[5]	0.84[5]
biacetyl	236[5]	267[5]	1.00
benzil	223	247	0.92
anthracene	178	318	0.71
eosine	177	209	0.33
rose bengale	164	213	0.61
methylene blue	138	180	0.52

[1] taken from ref. [12] (chapter *General Features, a*).

[2] triplet energies in kJ/mol.

[3] first excited singlet state energies in kJ/mol.

[4] quantum yields for singlet-triplet intersystem crossing.

[5] in polar solvents.

[6] taken from H. G. O. Becker, *Einführung in die Photochemie*, **1991**, Deutscher Verlag der Wissenschaften Berlin.

[7] benzoic acid.

From this data we can learn if it is necessary to sensitize the formation of the triplet excited state, or if the triplet state is rapidly formed by intersystem crossing without our help. Without this luminescence data the reaction efficiency and product composition has to be investigated in the presence and absence of a triplet sensitizer. If a specific reaction does proceed in the presence of a triplet sensitizer, variation of the triplet energy of this catalyst (when not incorporated in the photoproduct) can serve as a method for determining the triplet energy of the photoactive molecule. Typical triplet sensitizers and their corresponding energies are given in Table 2. On the other hand, the application of triplet quenchers serves as a method for the determination of triplet versus singlet reactivity. There are several possible reactivity patterns and methods to determine their existence:

(i) pure singlet reactivity: no reaction in the presence of (appropriate) triplet sensitizders.
(ii) pure triplet reactivity: enhanced product formation in the presence of (appropriate) sensitizers, no reaction in the presence of triplet quenchers.
(iii) triplet as well as singlet reactivity: combination of methods (i) and (ii) gives a product pattern corresponding to the specifically activated states.

f) Reaction control: spectroscopy and chromatography

As the product is formed in solution, it will compete more and more with the photoactive compound for absorption of the incident wavelength which may lie within the region of overlap of their absorption spectra. If the product is known, a UV spectra should be recorded before the photoreaction is started to avoid these problems. With increasing absorption of light by the products the reaction efficiency is reduced and, if all the incident radiation lies within the region of overlap, this may lead to a premature end of the reaction. Therefore, reaction control using absorption spectroscopy often is an important method to study the progress of a reaction (see Figure 1). Analogously, byproducts could be formed which also may absorb in the wavelength region used for excitation. NMR spectroscopy can help to study the quantitative reaction progress and find the optimal point for ceasing the transformation. Thin layer chromatography as well as gas or high performance liquid chromatography also are useful to study the substrate/product composition at certain points of the reaction.

g) Side reactions: can sometimes become the major track !

There are special features in photochemical reactions where side reactions become the major track and make a well planned synthesis unsuccessful. Sometimes the photoactive compound in the reaction mixture which could be applied in stoichiometric or catalytic (photosensitizer) amounts may also be the photoinitiator of a radical chain reaction. Again, the role of the solvent has to be considered carefully. If hydrogen abstraction reactions can be induced (e.g. when reactive free radicals are produced), solvents labile to this process must be excluded. Many saturated hydrocarbons, ethers, and alcohols (which normally are useful solvents because of their optical properties) have to be avoided in these cases. Benzene is a relatively inert solvent, likewise acetonitrile, acetic acid, and *tert*-butanol. The latter three solvents, however, are highly polar and could therefore favor electron transfer steps and the formation of radical ions which also could give rise to side reactions.

Despite its low solubility in most organic solvents, oxygen is a highly efficient quencher of electronically excited triplet states and additionally can react with many radicals. Sometimes these processes are desired (*"photooxygenation"*), however, in most other cases oxygen has to be removed by bubbling nitrogen or argon through the reaction mixture prior to and during the photoreaction. If the essential electronically excited state is not very efficiently quenched by (triplet) oxygen, (which is often the case for short living singlet states), the use of an inert gas may not be necessary. Despite this fact, it is rewarding to exclude oxygen because of possible hazardous effects from peroxides (even in low amounts !) which could be produced in the presence of molecular oxygen. For special precautions see *k)*.

If there are free radicals produced during the reaction, they could undergo side reactions. Consequently radical scavengers such as substituted phenols have to be added. In many cases this has to be found out by trial and error.

h) Quantum yields and chemical yields

There are specific properties of photochemical reactions which do not have to be considered in normal "*ground-state chemistry*". The chemical yield of a reaction, the *non plus ultra* for any reaction of nonexcited molecules, is no longer the only relevant number when excited states are involved. The quantum yield of a photoreaction, defined as the number of events (e.g. a certain photochemical induced transformation) divided by the number of photons absorbed by the specific system, also has to be considered. Quantum yields can range from 0 to 100 and more. A quantum yield of less than 0.01 for a photochemical process gives rise to a very slow conversion of the starting material. Still the chemical yield of the desired product could be satisfactory (90 - 100%), however, long irradiation times have to be used. If such low quantum yields for photochemical processes are observed, the quantum yields for the photophysical (deactivation) pathways are normally high. Some of these are rather easily determined by luminescence spectroscopy (quantum yields for fluorescence, phosphorescence, and radiationless decay), and these data are also useful for the design (and modification) of photoreactions. In cases of photoinitiated radical chain reactions, the quantum yield for chemical processes could reach values as high as 100.000 (for certain industrial processes an exceedingly important number in order to reach low lamp-costs, e.g. for the photochlorination of acyclic alkanes).

There are more complex properties such as differential quantum yields and reaction efficiency which should not be discussed here.

i) Lamps, vessels and filters

Light sources commonly used for preparative photoreactions are a) the sun (covering the visible and IR-A wavelength region of ca. 300 - 1400 nm), b) mercury lamps (low-, medium-, and high-pressure Hg lamps), and c) sodium lamps (low- and high-pressure Na lamps). Of course, one can also use a laser or a xenon high-pressure lamp, however, in most cases these light sources are too expensive for preparative work. The decision to use a certain light source is directly connected to the absorption properties of the substrate which has to be electronically excited (see part c). Figure 2 shows the different emission lines for some of the light sources mentioned.

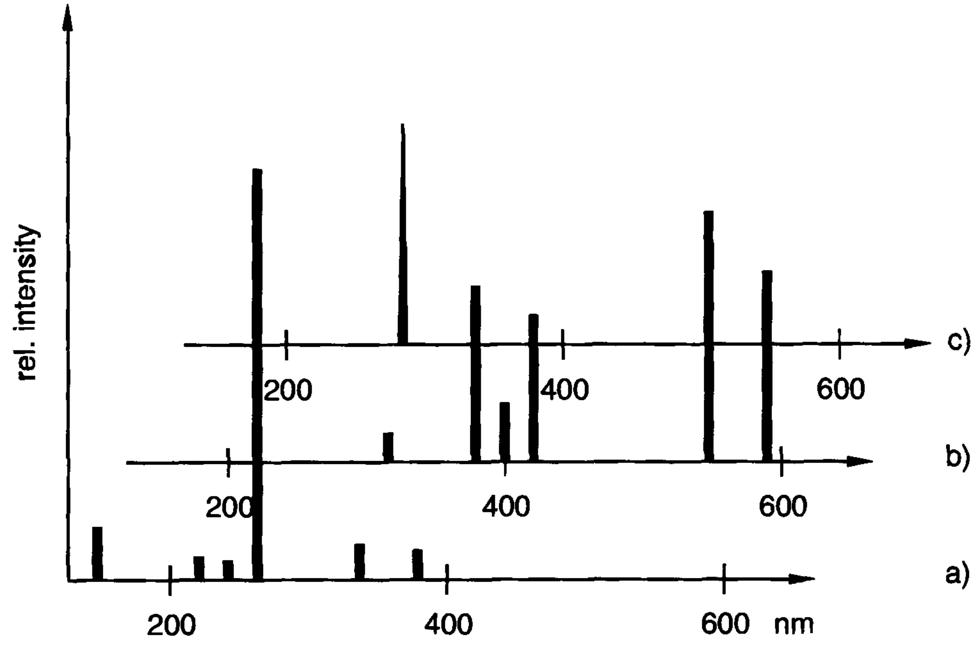


Figure 2: Emission properties of a) mercury low-pressure lamp (strong 254 line), b) mercury high-pressure lamp and c) RPR-3000Å lamp for Rayonet photoreactors (300 nm line).

Low-pressure resonance mercury lamps (mercury vapor pressure ca. 10^{-5} atm) emit at 185 nm (ca. 5% of the energy) and 254 nm (ca. 95% of the energy). Coating the envelope of these lamps with phosphors can lead to a rather broad secondary fluorescence emission at 300 nm or 350 nm. These lamps (RPR-1849/2537, RPR-2537, RPR-3000, RPR-3500 and RPR-4190; the numbers indicate the wavelength of emission in Å) are used in commercially available Rayonet® photochemical reaction chambers. The mercury vapor pressure in medium-pressure Hg lamps varies in the range of 5 atm and the spectral distribution of the emission lines constitutes a number of distinct lines between 250 and 600 nm. A set of much broader lines in the vis-region (360 - 600 nm) characterizes the output of high-pressure Hg lamps (mercury vapor pressure ca. 100 atm). These lamps are more expensive and are easily damaged and therefore have to be kept in a suitable box. Low-pressure as well as high-pressure sodium lamps cover a specific region in the visible region (around 600 nm) and are often used to excite dyestuffs which strongly absorb in this region (e.g. porphyrins or other dyestuffs in photooxygenation reactions).

Preparative photoreactions can be performed in two principal ways: by external irradiation where the lamps are located outside the reaction mixture or in immersion-well reactors where the light source is surrounded by the reaction solution. The latter constructions are more efficient because one can take full advantage of the emitted light. Reactors with external lamps permit the performance of many photoreactions at the same time and work with large volumes of reaction mixtures. Likewise merry-go-round photoreactors are used to perform more than one photoreaction (at smaller scale) at the same time, e.g. for the determination of reaction quantum yields where identical irradiation conditions are necessary for all probes. Falling film photoreactions are often used for the irradiation of concentrated solutions where appreciable amounts of polymeric byproducts normally lead to the formation of deposits at the reaction walls. An additional advantage is the use of thin liquid films which are irradiated in special immersion-well or falling film reactors and lead to a high local concentration of excited states.

The reaction vessels used in the photoreactors mentioned must fit the irradiation conditions, i.e. the wavelength region which is needed for electronic excitation of the substrate. For irradiation at 254 nm vessels made of quartz glass are needed, pyrex and solidex glass is needed for irradiation around 300 nm, and normal lab glass (or window glass) is transparent for wavelengths > 350 nm. In all cases the glass material serves as an solid optical filter. In some cases additional liquid optical filters have to be used in order to avoid undesired short wavelength irradiation.

k) Hazards

The ultraviolet region of the sun emission spectrum (at the earth's surface) consists of ca. 3% UV-A (315 - 380 nm) and ca. 0.5% UV-B (280 - 315 nm). Fortunately essentially no UV-C (100 - 280 nm) is present which constitutes a highly hazardous energy region. This wavelength composition enables us to go into bright sunlight without immediately suffering from severe cell damage. Wavelengths shorter than 300 nm are particularly dangerous to the eye and the skin. Sunburn and snow blindness symptoms could occur a relatively long time after exposure. Special care should be taken when low-pressure mercury lamps are used which have almost all of their output at 254 nm. Reaction vessels and photoreactors must be shielded (e.g. by aluminium foil) and lamps should always be turned off when manipulations (changing of reaction vessels, e.g. in Rayonet reactors, checking the reaction progress, etc.) have to be performed. All photoreactors should operate in fume hoods or in special sufficiently ventilated rooms because of the possible ozone production from molecular oxygen and short wavelength UV light. Most lamps operate at high temperatures (e.g. medium-pressure mercury lamps around 700 °C, which requires efficient cooling) and at high vapor pressures (e.g. mercury vapor pressure in high-pressure lamps around 100 atm). Handling of lamps during operation is therefore strictly forbidden. Do not touch lamps after switching off before they have cooled down sufficiently.

1 Carbonyl Compounds

1.1 Aldehydes and Ketones

Electronically excited carbonyl compounds serve as versatile intermediates in countless reactions. They not only operate as reactive substrates for intra- and intermolecular hydrogen abstraction and cycloaddition reactions as well as C-C cleavage steps, but many of them also are useful sensitizers for the generation of triplet excited compounds. This variety of reaction possibilities makes carbonyl photochemistry sometimes very complex, i.e. it delivers many products and depends quite sensitively on the reaction conditions (temperature, sensitizer, solvent, irradiation wavelength). The absorption properties of these substrates are convenient for irradiation around 300 nm: the characteristic absorption band for the $n\pi^*$ excitation lies in the 330 - 280 nm region. The low lying S_1 states are populated with low probability, i.e. the electronic transitions are symmetry forbidden and the ε-values are around 10 - 30. Because of a rather small triplet-singlet energy gap (20 - 70 kJ/mol, see Table 2) the intersystem crossing rates are high and the intersystem crossing quantum yields near unity. The lifetime of the first excited singlet state is in the nanosecond region for aliphatic aldehydes and ketones and in the subnanosecond region for aromatic aldehydes and ketones. Due to these parameters, singlet photochemistry can be detected with aliphatic carbonyl compounds, however, aromatic substrates such as acetophenone or benzophenone react exclusively from their corresponding triplet states (and represent excellent triplet sensitizers for many compounds with lower lying triplet states).

In general electronically excited carbonyl compounds show five reaction types:

i) Norrish Type I cleavage reaction (intramolecular α-cleavage),
ii) Norrish Type II reaction (cleavage of the β-bond),
iii) Cyclobutanol formation (Yang reaction) or formation of smaller/larger ring cycloalkanols (following β-, γ-, δ-, etc. hydrogen abstraction),
iv) Paternò-Büchi reaction (cycloaddition with alkenes, dienes, alkynes, etc.), and
v) Photoisomerization and photoreduction (intra- or intermolecular).

(i) Norrish Type I cleavage reactions

Norrish Type I cleavage reactions dominate in the gas phase photochemistry of many acyclic aldehydes and ketones, whereas in the liquid phase this process is less common and alternative pathways (ii, iii, v) dominate. When no suitable C-H bonds are present to allow hydrogen abstraction reactions, however, this process will also constitute an important synthetic method for the cleavage of α-C-C bonds in solution. One important subsequent reaction of the resulting acyl and alkyl radicals is carbon monoxide formation and radical combination. Overall CO extrusion results which represents a versatile method for the formation of C-C single bonds from ketones. When cyclic substrates (cycloalkanones but not conjugated cycloalkenones which exhibit a different photochemistry) are used, ring contraction reactions result from a Norrish Type I reaction. An impressive approach to tetra-*tert*-butyltetrahedrane is described by **G. Maier**, where the key step is the photochemical extrusion of carbon monoxide from an appropriate precursor. Another type of photochemical extrusion of a small fragment precedes the decarbonylation step: the extrusion of carbon dioxide from a (photochemically generated!) bicyclic anhydride.

(ii) Norrish Type II reaction

Beside carbon monoxide extrusion acyl radicals formed in a α-cleavage reaction can stabilize by subsequent hydrogen migration. Thus the α-trimethylsilylmethyl substituted cyclopentanone used by **L. F. Tietze** gives in a clean photochemical reaction the corresponding aldehyde with a vinylsilane moiety in its side chain.

(iii) Cyclobutanol formation

The Yang reaction (a name used to honor the exceedingly valuable contributions of N. C. Yang in this field of organic photochemistry) is the most effective method for the synthesis of cyclobutanols provided that the appropriate alignment of C=O and C-H groups is given and no secondary transformations prevent cyclization of the 1,4-biradical. A beautiful example for the Yang reaction is given by **H. M. R. Hoffmann** who uses a rather complex and constrained substrate. There is an impressive number of different γ-hydrogen positions, however, due to the substrate geometry only one of the diastereotopic methyl groups of the isopropyl substituent is active. It is highly recommended to build molecular models in order to learn more about this phototransformation.

Two illustrative examples for "*unusual*" hydrogen abstractions, i.e. not from the normally preferred γ-position, are reported by **H. G. Henning**. In his first synthesis, a bichromophoric substrate (ketone/amide) was chosen. Irradiation at 300 nm solely activates the ketone CO-group which subsequently abstracts a hydrogen atom from the β-position (γ-, δ-positions are blocked). δ-Hydrogen abstraction can become a serious reaction pathway as shown for the second substrate, where the β-amino group is only monoacylated. In this case a highly functionalized pyrrolidine derives from the photochemically induced δ-hydrogen abstraction.

(iv) Paternò-Büchi reaction

Three examples are given for the well-known Paternò-Büchi reaction, two intermolecular and one intramolecular version: in the course of his studies on pharmaceutically active oxetanes, **G. Just** developed the [2+2]-cycloaddition of O-protected α-hydroxy acetic aldehyde to 2-methylfuran and an interesting further functionalization of the resulting oxetane.

The use of cheap and readily available chiral auxiliaries such as menthol, 8-phenylmenthol, and *trans*-2-*tert*-butylcyclohexanol in Paternò-Büchi reactions is described by **H.-D. Scharf**. High diastereoselectivities are obtained in the photocycloaddition of the corresponding pyruvic esters to electron rich cycloalkenes. Both the synthesis of the chiral auxiliary as well as of the cycloalkene are interesting non-photochemical steps.

R. Gleiter submitted an intramolecular version which transforms 5-acetylbicyclo-[2.2.2]oct-2-ene into a complex tetracyclic photoproduct.

(v) Photoisomerization and photoreduction

This part covers the phototransformations initiated by electronic excitation which do not fit in (i) - (iv). The photoisomerization of the amino acid derivative PHT=Val-OMe is one example. In this reaction, described by **A. G. Griesbeck**, the first event is abstraction of a hydrogen from a γ-position. Neither cyclization (Yang reaction) nor fragmentation (Norrish II) follows this step. Another hydrogen (now from the δ-position) migrates and leads to the formation of a photoisomerization product which could be transformed into N,C-protected isodehydrovaline. This reaction indicates that a broad variety of transformations should be possible at the primary 1,4-biradical stage.

From **B. Pandey**'s research group comes a straightforward photochemical method for the synthesis of spirocyclic compounds. An intramolecular hydrogen abstraction by an excited enone group is followed by radical combination. It is remarkable that no product arising from photoenolization and subsequent cyclization was observed. This is usually observed in *ortho*-alkyl substituted benzophenone and acetophenone derivatives.

A strategy developed by **H. R. Sonawane** which is based on a photochemical induced 1,2-aryl shift allows the efficient transformation of 2-chloropropiophenones into 2-arylpropionic acids. This method is a straightforward alternative to the classical umpolung/ Lewis-acid induced 1,2-aryl shift sequence used in ground state chemistry.

Photoreduction of α,β-epoxy ketones is possible in the presence of an external and efficient hydrogen donor such as triethylamine. An application in carbohydrate chemistry is described by **J. Cossy**. In the final step of a 7-step synthesis, a cyclic α,β-epoxy ketone is reduced (with retention of configuration) to a β-hydroxy ketone.

As shown by **J.-P. Pète** the hydroxyalkyl radical formed initially can also be trapped in an intramolecular reaction, for example, by an alkyne moiety. The resulting vinyl radical abstracts another hydrogen from an external source. The starting material for this reaction sequence can be prepared by photochemical Wolff ring contraction reaction (see also Chapter 2).

It is again a photochemical transformation which leads to a structure modification of an unsaturated bicyclo[4.1.0]heptanone as developed by **J. Mattay et al.** The key step starts with a photoinduced electron transfer (PET) from the donor triethylamine to the electronically excited cyclohexanone cleaving the exocyclic C-C bond followed by 5-*exo* cyclization.

Recommended further reading

Hydrogen Abstraction Reactions: P. J. Wagner, *Organic Photochemistry* **1991**, *11*, 227 - 366.

[2+2]-Cycloaddition reactions of carbonyl compounds (Paternò-Büchi reaction): G. Jones II, *Organic Photochemistry* **1981**, *5*, 1 - 122.

Norrish Type I Processes: D. S. Weiss, *Organic Photochemistry* **1981**, *5*, 347 - 420.

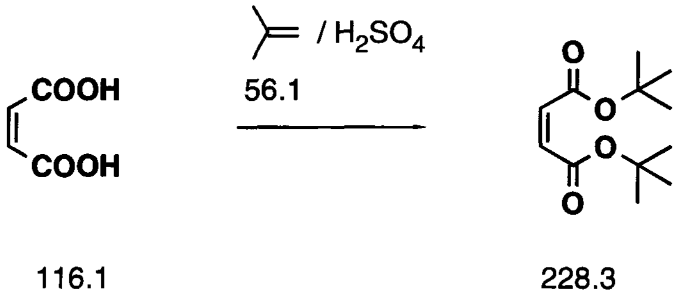
and the corresponding chapters in: *Rearrangements in Ground and Excited States* P. de Mayo (Ed.), **1980**, Vol. 42 - 43 of *Organic Chemistry* H. H. Wassermann (Ed.);

Photochemistry in Organic Synthesis J. D. Coyle (Ed.), **1986**, The Royal Society of Chemistry, London; *Synthetic Organic Photochemistry* W. A. Horspool (Ed.), **1984**, Plenum Press, New York, London; W. A. Horspool, D. Armesto, *Organic Photochemistry: A Comprehensive Approach*, **1992**, Ellis Horwood, PTR Prentice Hall, New York.

1.1.1 Tetra-*tert*-butyltetrahedrane [4] (route I)

submitted by G. Maier and F. Fleischer

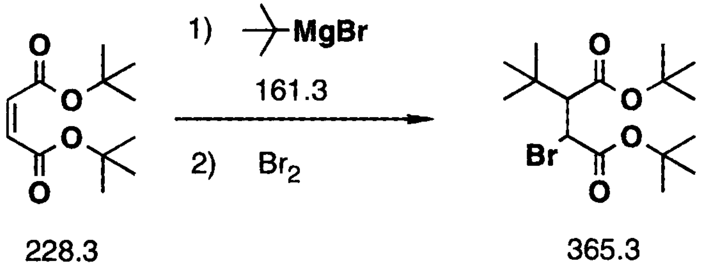
1.1.1a Maleic acid di-*tert*-butylester



120 mL of isobutene were condensed into a pressure vessel (cooling with a methanol/dry ice bath). 100 mL of diethylether and 5 mL of concentrated sulfuric acid were added. After addition of 56 g (0.48 mol) of maleic acid, the vessel was capped and shaken for 15 h. The vessel was opened cautiously (ice-cooling) and the content was poured onto a mixture of 250 g of ice, 70 g of NaOH and 350 mL of water. After separation of the organic layer, the aqueous layer was extracted with two 75 mL portions of diethylether. The combined organic layer was dried over $MgSO_4$, the solvent was removed by distillation and the crude product was recrystallized from pentane, yielding 87 g (80%) of maleic acid di-*tert*-butylester **1.1.1a** as colorless crystals, mp 68 °C.

^{1}H-NMR ($CDCl_3$): $\delta = 6.09$ (s, 2 H, C$\underline{H}$=C), 1.50 (s, 18 H, OC(C$\underline{H}_3$)$_3$).

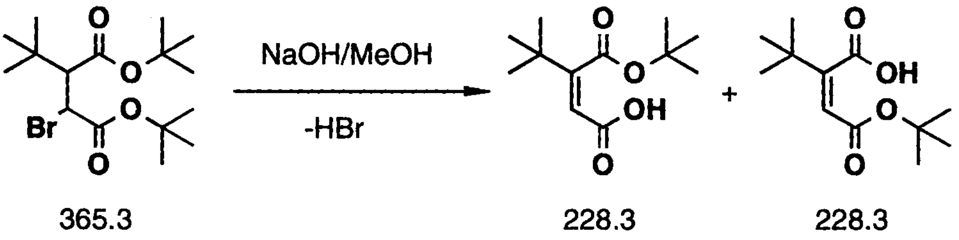
1.1.1b 2-Bromo-3-*tert*-butyl succinic acid di-*tert*-butylester



To 440 mL of a 1,26 M *tert*-butyl magnesium chloride solution were added at -35 °C 122.6 g (0.55 mol) of **1.1.1a** in 550 mL of diethylether over a 30 min period. The mixture was allowed to warm to room temperature and was additionally stirred for 10 min. Beginning at -40 °C 88 g (0.55 mol) of bromine were added over a 4 min period. The temperature was maintained below -20 °C. Excess bromine was destroyed by addition of saturated Na_2SO_3 solution. 2 N HCl was added at room temperature. The separated organic layer was washed with 2 N NaOH and water and dried over $MgSO_4$. Evaporation of the diethylether gave 170 g (85%) of crude **1.1.1b** (mixture of the diastereomers), which was used without further purification.

^{1}H-NMR ($CDCl_3$): δ = 1.05 (s, $C(CH_3)_3$), 1.16 (s, $C(CH_3)_3$), 1.45 - 1.55 (2 pairs of $OC(CH_3)_3$), 2.90 (d, J = 10, CH), 3.02 (d, J = 12, CH), 4.37 (d, J = 10, CHBr), 4.43 (d, J = 12, CHBr).

1.1.1c *tert*-Butyl maleic acid mono-*tert*-butylester



A mixture of 173 g (0.47 mol) of crude **1.1.1b,** 54 g of NaOH and 1400 mL of methanol were refluxed for 2 h. The methanol was evaporated. The residue was dissolved in water and acidified to pH 2. After extraction with diethylether, drying over $MgSO_4$ and evaporation of the solvent, 96.3 g (90%) of the crude product **1.1.1c** were obtained.