1

Photochemical Methods

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1.1

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1.1.1

Photochemistry and Organic Synthesis

A cursory look to the literature shows that only about 1% of the published papers classed as organic syntheses by *Chemical Abstracts* involve a photochemical step. On the other hand, in photochemistry courses it is often stated that excitation by light multiplies by 3 the accessible reaction paths, because the chemistry of the excited singlet and triplet states are added to that of the ground state. It thus appears that photochemical reactions are less used as they may be. As it has been again recently remarked, this limited diffusion may be due to ill-founded prejudices [1].

Two conditions should be verified in order that the potential of photochemical reactions is more extensively exploited. These are:

- That the knowledge of the main classes of such reactions is more largely diffused among synthetic practitioners, so that a photochemical step comes more often into consideration when discussing a synthetic plan.
- That the prejudice that photochemical reactions are mostly unselective, experimentally cumbersome and at any rate difficult to generalize is overcome, so that there is no hesitation in considering the introduction of a photochemical step on the basis of the analogy with known examples, just as one would do with a thermal reaction.

The connection between synthesis and photochemistry is vital. As long as photochemistry is felt as a “sanctuary” of the small group of “professional” photochemists, many synthetic perspectives will be ignored, and this is a negative impact also on mechanistic photochemistry that loses part of its interest. As a matter of fact, this remark is not new. In a talk in Leipzig in 1908, Hans Stobbe, a pioneer of photochemistry (well known for his innovative studies on the photochromism of

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fulgides), stressed the importance of devising new photochemical applications in organic chemistry [2]. “Then probably. . .” he hoped “. . .organic chemists would become interested and take into account the effect of light on their experiments. Known photoreaction would become better known and new photoreactive compounds will be looked for. Final products and intermediates would be isolated, their structure demonstrated and on the basis of the chemical structure the process will be understood. In this way the physical chemist would always have in his hands a wealth of material for his favorite studies of kinetics and for investigating the relation between radiation and chemical energy.”

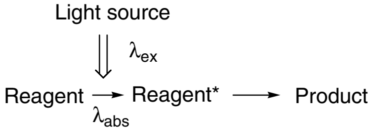
Stobbe’s wish has been only partially fulfilled in the century which has elapsed in the meantime. Whilst many photochemical reactions have been discovered, certainly many more wait to be uncovered, and it still holds true that more photochemistry carried out by synthetic chemists would contribute to the growth of photochemistry as a whole. This Handbook represents a modest attempt to contribute towards this aim and to foster the synthetic use of photochemistry. The presentation is referred to the small-scale laboratory synthesis of fine chemicals. In this aspect, the photochemical literature does not differ from the large majority of published synthetic work, most of which is carried out on the 100 mg scale for exploratory studies. However, there is no reason to think that a photochemical reaction is unfit for scaling up. As will shown below, an increase up to the 100 g scale can be obtained in the laboratory by simple arrangements. Furthermore, while the presently running industrial applications are limited in number, they are nonetheless rather important [3]. Some of these are well established, an example being the synthesis of vitamin D_3 which has been produced at the several tons level each year for several decades, and for which dedicated plants continue to be built. This indeed demonstrates that photochemical syntheses are commercially viable.

1.2
Irradiation Apparatus

1.2.1
General

As the name implies, photochemical reactions result from the absorbance of light by the starting reagent. Conditions for a successful course of the photoreaction are that:

- There is good matching between the emission of the light source and the absorption by the reagent; that is, the wavelength emitted by the lamp falls within the absorption band of the reagent.
- Nothing interferes with the photons before they reach the target molecule; for example, the wall of the vessel and the solvent are transparent to λ_{ex}.
- Nothing interferes with the electronically excited states and quench them before they react (see Scheme 1.1).



Scheme 1.1

In other cases, rather than irradiating the reagent ("direct" excitation), a photosensitizer or photocatalyst is irradiated and activates the reagent by some mechanism (energy transfer, a redox step, hydrogen abstraction). In this case, the above conditions apply to the sensitizer.

Today, there are several companies which supply lamps as well as complete photochemical reactors (lamp + power supply + reaction flask with accessories, e.g. for gas inlet). However, the complete set may be rather expensive and not necessarily provide the most convenient solution. The most widely used light sources are mercury vapor arcs, both in photochemistry and in indoor and outdoor illumination, and which are classed according to the operating pressure. It is important that the wattage on the lamp label is not confused with the amount of light emitted. The efficiency of conversion into light is low, and the lamp output is dispersed over a range of wavelengths and towards all directions; thus, only a part of the light emitted (in turn, a fraction of the electrical power dissipated) is absorbed. Therefore, it is important to take care of the geometry of the lamp/reaction vessel system as well as of the wavelength matching between lamp emission and reagent absorption, because these factors are at least as important as the lamp power in determining how many molecules of the reagent will be excited. The quantum yield then indicates the fraction of excited states that reacts [$\Phi = $ (molecules reacted)/(photons absorbed)], provided that no competitive quenching occurs. The main characteristics of lamps used for photochemical synthesis are presented in the following sections.

1.2.2
Low-Pressure Mercury Arcs

The most widely used lamps are low-pressure (10^{-5} atm under operating conditions) Hg arcs, of 6–16 W, that are often identified as germicidal lamps or mercury resonance lamps. These are supplied as quartz (or rather "fused silica," a synthetic amorphous SiO_2) tubes of various lengths, typically 20–60 cm (although lamps >1 m long are available), and with 1.0–2.4 cm diameter (see Figure 1.1). In these lamps, >80% of the emission occurs at 254 nm (and a fraction at 185 nm, a wavelength to which the common "quartz" is not transparent and thus is available only if a high-purity "UV-grade" quartz is used).

Under these conditions, the excitation of most classes of organic compounds (including many solvents!) is ensured. It must be taken into account that, given the large size of the lamp, the amount of photons emitted per surface unity is low. Therefore, these lamps are most useful for external irradiation by using (quartz!) tubes for the irradiated solutions. The heating under operating conditions is modest.

Figure 1.1 Lamps used for photochemical syntheses. (a) Low-pressure mercury arc; (b, c) phosphor-coated lamps, emission centered at 305 and 370 nm; (d, e) medium- and high-pressure mercury arcs, respectively.

Multilamp apparatus are commercially available where between eight and 12 lamps are arranged in a circular fashion (40–60 cm diameter), with room inside to accommodate the vessel in which the solution to be irradiated is contained. These were initially marketed by the Southern New England Ultraviolet Co. under the name of "Rayonet," now the name is often used for similar devices by other companies. These units are fitted with a fan which maintains the temperature below 40 °C; otherwise, this might increase in such a confined space (see Figure 1.2).

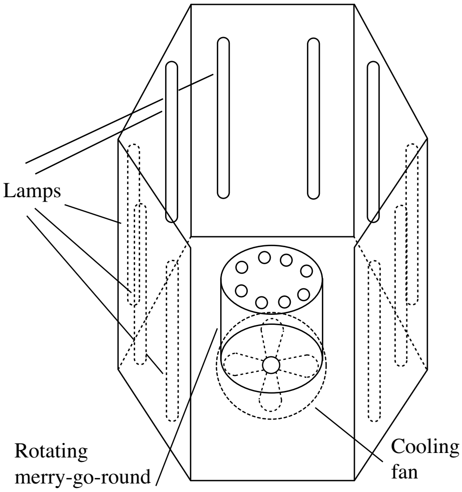


Figure 1.2 Multilamp apparatus fitted with low-pressure mercury lamps and a rotating "merry-go-round" that ensures the uniform illumination of several test tubes. Alternatively, test tubes or other vessel(s) containing the solution to be irradiated can be accommodated.

However, anybody can build an "amateur" version of the irradiation apparatus, simply by placing one to three pairs of lamps (with each pair mounted on a normal lamp holder for household "fluorescent" lamps) around a small space where two to four test tubes or a single cylindrical vessel of larger diameter can be placed. This home-made apparatus can be easily installed (but well separated from the laboratory, in order to maintain appropriate safety precautions, or better still under a ventilated hood to remove ozone; see below and Figure 1.3). In order to maximize the fraction of light absorbed, it is convenient that the tubes are as long as the lamps, or even slightly shorter. The manufacturers can provide lamps of this type in different shapes (U-shaped, coiled) with a more concentrated emission; this makes their use possible in different set-ups, an example being an immersion well apparatus with internal irradiation (see Figure 1.4).

Figure 1.3 Two pairs of lamps used for external irradiation. In the arrangement shown, only a small fraction of the light flux is used.

Low-pressure mercury arcs are manufactured for much more widespread use than preparative photochemistry, and therefore are by far the cheapest light source (particularly if buying them from companies selling optical components can be avoided). Furthermore, these lamps are long-lived (>10 000 h, depending on how they are used), consume less energy, and require only an inexpensive transformer and a starter for operation.

Whilst there is no doubt that these are the most convenient sources, their geometric optimization is difficult and part of the lamp emission may be lost. In the external irradiation set-up, the most convenient choice is to use tubes which are about the same length as the lamps, and contain 20 ml of solution. In fact, this set-up works very well for small-scale photochemical syntheses, with irradiated volumes in the region of 100 ml distributed in a number of quartz test tubes or in a single cylindrical vessel. This set-up is also convenient for optimizing the reactions, since results can easily be compared under different conditions but constant irradiation when placing different solutions in the tubes. One available accessory for these multilamp apparatuses is a "rotating merry-go-round"; this can hold several tubes and ensures equivalent irradiation in all positions (see Figure 1.2).

The lamp emission can be changed by means of a coating made from a phosphor (or a combination of phosphors) that absorbs the almost monochromatic Hg radiation and emits a range of longer wavelengths. Phosphor-coated lamps maintain the same advantages of "quartz" lamps (including price, due to their large-scale manufacture for different uses, including household illumination), and are available in a variety of wavelength ranges. Apart from "fluorescent" lamps for household illumination, which emit over most of the visible (and are useful for dye-photosensitized irradiations), lamps with emission centered at 305, 350 and 370 nm (half-height width 20–40 nm; the last one is known as "Wood" or "black light" lamp) that are most useful for photochemical applications are commercially available (as well as lamps with the emission centered at various wavelengths in the visible). Except for the 305 nm type, Pyrex glassware (transparence limit 300–310 nm, but take into account that the transparency changes somewhat with the use) [4] can be used with phosphor-coated lamps, as there is no emission below that wavelength. The phosphor coating does not alter the electrical characteristics, and these lamps can be interchanged with germicidal lamps in all of the settings mentioned above. Having available three to four pairs each of 254, 305, and 350 (or 370) nm lamps, as well as lamps emitting in the visible range, allows one to carry out any type of small-scale photochemical reaction with negligible financial investment.

One subcategory of low-pressure lamp that might become more important in the future is the electrodeless discharge lamp, which is energized by an external field. These lamps comprise a quartz tube that has been evacuated, leaving behind a small pressure of argon and mercury or other metal or metal halide. Emission is obtained by placing the lamp in a microwave field, for example. Whilst these lamps are available commercially, they may also be built in-house rather easily [5].

1.2.3
Medium- and High-Pressure Mercury Arcs

Medium-pressure (sometimes dubbed “high pressure,” 1–10 atm) mercury arcs are available in different types, ranging from 100 to 1000 W. They are supplied as small ampoules (from 3 to 15 cm in length, depending on the power; see Figure 1.1). The emission consists of a range of lines (the most prominent are those at 313, 366, 405, and 550 nm) over a continuum, while the 254 nm line is strongly diminished. The emission from these lamps is at least 10-fold stronger than that of low-pressure arcs, and occurs over a much smaller surface. In contrast to the previous type, these sources develop a considerable amount of heat, and require several minutes to achieve their optimal temperature, where the emission reaches full intensity. Cooling is required, but running tap water is normally sufficient to maintain the temperature at about 20 °C. Due to these characteristics, these lamps are typically used in an immersion well apparatus with circulating water. If the cooling well is made from Pyrex, the (small) fraction of emission below 300 nm is lost, which may make a difference (see below and Figure 1.4a). The most powerful lamps require a forced circulation for cooling. A suitable power supply is also required for operation, the lifetime is limited, and overall the system is considerably more expensive than the low-pressure lamps. There may also be some concern regarding safety aspects; it is suggested that the reactor is provided with a switch that will cut the power supply in case of an increase in temperature.

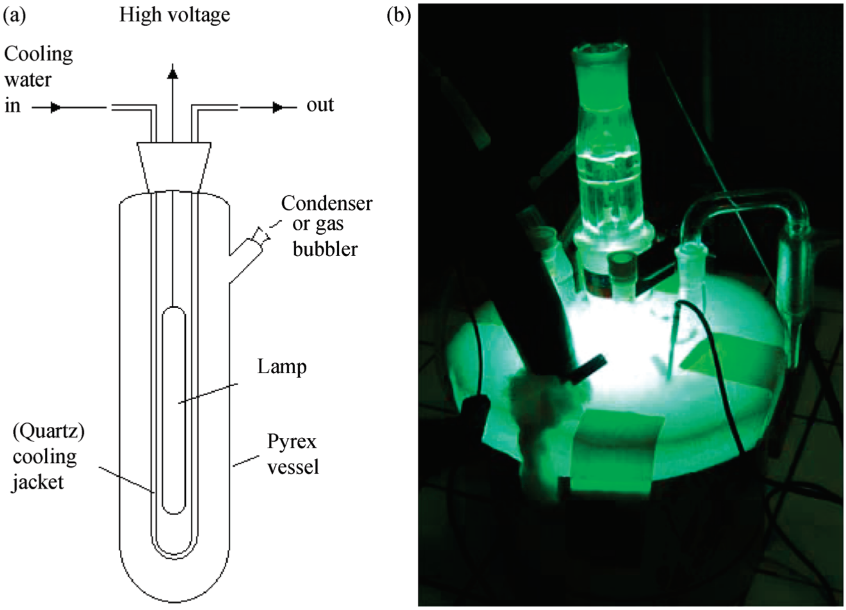


Figure 1.4 (a) Immersion well irradiation apparatus; (b) a refrigerated apparatus for conducting reactions at low temperature.

These compact and rather powerful sources are convenient for internal irradiation of volumes of between 100 and 1000 ml, where the emission in any direction is exploited (obviously within the range of absorbed λ); and are well suited for preparative irradiations up to the gram scale. The apparatus can be easily adapted to low-temperature experiments (e.g., at −80 °C) by circulating a refrigerant liquid through the lamp jacket (in this case, the lamp must be ignited outside and placed in position when lit, otherwise it will not function) and adding an external cooling bath (see Figure 1.4b) [6]. Lamps doped with different metals are also available; these yield an emission which is richer in some regions of spectrum, and may be better suited to particular photoreactions, although they are generally more expensive.

High-pressure (or "very high" pressure, 200 atm; see Figure 1.1) arcs, ranging from 150 to 1000 W and above, operate at higher temperatures. In this case, the contribution of the continuum is much more important than that at a lower pressure, although the maxima may still be distinguished. The optimal temperature requires several minutes before it is reached, and must be maintained by appropriate cooling. These Hg-lamps are the most powerful and the smallest sources, with a distance between the electrodes of only a few millimeters. In view of the severe operating conditions, such lamps are used in explosion-proof cases (finned for cooling, unless forced cooling is required) that are fitted with mirror and lenses. In this way a collimated emission is obtained, typically 5 cm in diameter, and the lamp is mounted on a optical bench where other optical components can be added (see Figure 1.5).

By inserting either an interference filter or a colored filter, it is possible to select a more or less extended region of the spectrum; likewise, by adding an optical fiber it is possible to direct the beam where desired. This set-up best exploits the characteristics of these powerful lamps, and offers an excellent choice for the irradiation of small surfaces. Consequently, spectrophotometric cuvettes or cylindrical cuvettes are used for the irradiation, which involves small volumes. Such restrictions, as well as the high price and short lifetime of the lamp and its accessories, favors the use of these arcs for kinetics studies and quantum yield measurements, rather than for preparative photochemistry.

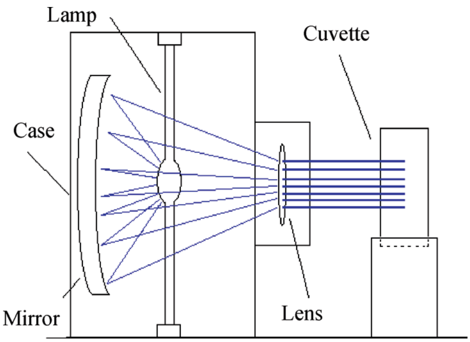


Figure 1.5 High-pressure mercury arc mounted on an optical bench.

1.2.4
Other Light Sources

Several other sources are available commercially, such as high-pressure xenon arcs (that mimic solar emission), mercury–xenon or antimony–xenon arcs (which are richer in the UV) or sodium arcs (dominated by the strong yellow-green emission of sodium metal). The latter type may be useful for dye-sensitized photo-oxidation, but are relatively expensive and short-lived; light-emitting diodes (LEDs) are more convenient in this application (see below). Tungsten (incandescent) and tungsten–halogen lamps evolve large amounts of heat (the former type is quite inefficient, and will likely be banned from commercial application; the latter is more efficient). These lamps may be used for photoinitiated chain reactions (where $\Phi \gg 1$; see Chapter 10), but emit poorly in the UV range and are rarely used for proper photochemical reactions ($\Phi \leq 1$).

Lasers have been shown to serve as an efficient light source for some reactions. In particular, the 308 nm emission of the XeCl "excimer" laser is a convenient source that, unlike arc lamps, is monochromatic and does not emit heat. A commercial 3 kW laser of this type (60 cm long, vertically mounted) has been used to build a falling film reactor capable of converting 10 g or more in 10–20 h [7]. At least at present, however, these light sources are rather expensive and require considerable care for their maintenance; consequently, they cannot be considered for adoption by an organic photochemistry laboratory requiring a versatile tool for preparative applications.

Substitute systems that may in time become a convenient alternative are the rapidly developing LEDs. These are semiconductors that emit an incoherent electroluminescence over a short wavelength range. These small devices are fitted with optics that shape the emission (parallel or with an angle), and are available in a large variety of "monochromatic" emitting types (actually over a narrow range, typically 20 nm) for almost any wavelength. The conversion of absorbed power (which is in the hundred mW range) into light depends on the wavelength, and LEDs that are reasonably effective light sources are available over the whole of the visible spectrum. LEDs emitting in the UV-A, down to 320–310 nm are also available, although their emission is much less intense (one-tenth or less compared to those emitting in the visible), and they are more expensive. The advantages are that such sources are cheap and long-lived ($>10^4$ h), and although a single LED is too weak (more powerful sources are expected in a few years) a set of perhaps 20 LEDs would be adequate. Mounting these light sources on a cylindrical surface, at the center of which test tubes containing the solution can be accommodated, might represent an efficient approach to carrying out photochemical reactions with small volumes (2–30 ml) and will most likely become increasingly common [8].

Having available a certain number of LED sets might also be an alternative to having the above-mentioned sets of phosphor-coated lamps. Whilst the former set-up would be more expensive than the latter, it would be much more versatile, because in the case of LEDs a much wider choice of λ is available (unfortunately, this is not as extensive as might be wished in the UV, which is the most interesting region for synthetic photochemistry). The precise choice of λ_{ex} may be advantageous if a specific class of reactions is under investigation, and where fine-tuning of the wavelength is important (typically, to avoid the primary product undergoing further unwanted photochemical reactions). Another area where LEDs are convenient is that of dye-sensitized reactions (which in practice are oxidations), as lamps emitting in the visible spectrum are already more powerful and are undergoing a more rapid development (in view of their use for illumination purposes). Moreover, further improvements are expected in this area.

Solar light is an obvious and ecologically convenient alternative, its main limitations being a low density and scarce UV component. Nevertheless, placing a solution on the window sill on a sunny day represents a very convenient way of carrying out a photochemical reaction on the 100 mg scale, even with compounds of which the absorption is limited to UV-A (see Figure 1.6a). The obvious lack of reproducibility according to season and weather, may make this not the preferred choice. However, for any compound absorbing at 330 nm or at a longer wavelength, there is no reason why, in an exploratory test, a one- or two-day exposure to the sun should not be substituted for an overnight exposure to a multilamp apparatus, with significant energy savings.

Given the importance of using alternative energy sources, some attention has been paid also to organic syntheses by solar light on a (relatively) large scale. For this, a variety of apparatus have been built, which generally circulate the solution through tubes exposed to the sun by means of a pump, with the addition of a heat exchanger in order to avoid overheating (see Figure 1.6b). Exposure to the sun can be achieved either by using a simple flat-bed arrangement, or concentrating the solar emission by locating the tubes in the axis of parabolic mirrors. Sophisticated versions of this apparatus are equipped with a mechanical system that allows the sun to be tracked during the day. In this way, some reactions have been scaled up to 500 g [9].

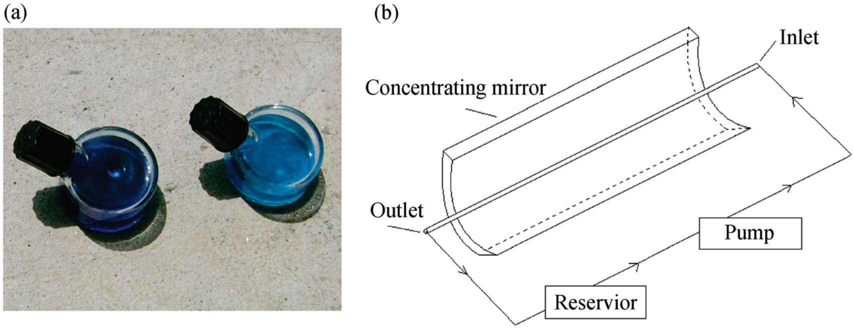


Figure 1.6 (a) Cylindrical vessels exposed to the sun on a window sill; (b) moderately concentrated solar light. The solution is circulated through the tube placed in the axis of a parabolic mirror.

1.3
Further Experimental Parameters

1.3.1
Concentration and Scale

As mentioned above, small-scale photoreactions are quite often carried out in quartz or Pyrex tubes, by external irradiation. However, this is certainly not an optimal solution for maximizing the exploitation of the emitted radiation. Internal irradiation is obviously better from the geometric point of view, but (relatively) large-scale preparations must take into account all of these factors and achieve optimal light and mass transfer. These elements are not taken into account in exploratory studies or small-scale syntheses, just as is the case for thermal reactions, where the optimization is considered at a later stage; the essential requirement is that the explorative study is carried out under conditions where occurrence of the reaction is not prevented. Thus, it is important that the source is matched with the reagent absorption, the vessel is of the correct material, and the solvent does not absorb competitively (unless it acts also as the sensitizer). Figure 1.7 and Table 1.1 may help in this choice, in conjunction with the UV spectra of all of the compounds used (it is recommended that the spectra are measured on the actual samples used, in comparison with those taken from the literature, in order to check for absorption by impurities).

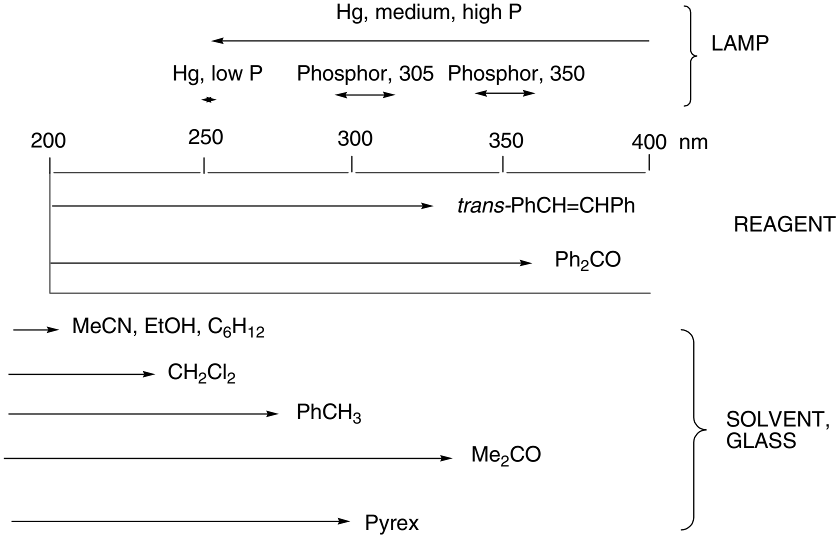


Figure 1.7 Checking that the conditions for a successful photochemical reaction are met. To use this system: (1) Insert into the frame the range of active wavelengths (up to the longest wavelength where the reagent absorbs significantly; two representative examples are shown). (2) Check whether this fits with the lamp chosen, the solvent and the material from which the reaction vessel, cooling well, etc. are constructed.

Table 1.1 Choosing a solvent with reference to the reagent irradiated.

Solvent	λ_{lim}[a]	Reagent	λ[b]
Acetone	329	Aniline	308
Acetonitrile	190	2-Cyclohexenone	310
Benzene	280	Stilbene	333
Cyclohexane	205	Benzophenone	360
Dichloromethane	232	1,4-Naphthoquinone	385
Diethyl ether	215	Uracil	285
N,N-Dimethylformamide	270	Phenanthrene	345
Dimethylsulfoxide	262	Anthracene	378
Ethanol	205	Pyrrole	238
Pyridine	305		
Pyrex, Vicor	λ_{lim}[c] ca. 300		

[a] Limiting wavelength; the wavelength at which a 1 cm layer of the solvent absorbs 90% of the light impinging; use only when the reagent absorbs above this value.
[b] The longest wavelength at which the reagent has absorbance $A = 1$ at a 0.01 M concentration.
[c] Wavelength at which a 1 mm layer of the glass absorbs 90% of the light.

How light is absorbed is also important. Beer's law states that the absorbance of a solution is $A = \varepsilon bc$, where c is the molar concentration and b the optical path. The value of ε_{max} ranges from about 10 for a "forbidden" band (e.g., aliphatic ketones at 280 nm), to 10^4 and more for "allowed" transitions. When considering a solution at a preparatively sensible concentration such as 0.1 M, this means that when using a tube with an internal diameter of 1 cm or an immersion well apparatus with a 1 cm path between the cooling well and the outer wall, $A = 1$ when irradiating on a maximum, and $\varepsilon_{max} = 10$. Since $A = \log(1/T)$, this means that 10% of the light flux is transmitted and 90% is absorbed. On the other hand, when $\varepsilon_{max} = 10^4$ the absorbance $A = 10^3$; that is, 99.9% of the light is absorbed. Thus, there is only a 10% difference in the overall number of photons absorbed in the two cases. However, in the latter case 90% of the photons are absorbed in the first 0.1 mm layer, and a further 9% in the following 0.9 mm, while the remaining part of the solution is excluded from activation. Obviously, when considering irradiation in a part of the spectrum different from the maximum, a more equilibrated absorption results; however, the problem remains that homogeneous activation is difficult to attain at concentrations useful for synthesis.

This has some negative implications. The first implication is that it lengthens the irradiation time; mechanistic studies obviate to this limitation simply by using a low concentration, but this obviously does not apply to a preparative irradiation. A very effective mixing would help, but this is difficult to obtain in a simple laboratory set-up, such as the usual cylindrical immersion well apparatus. On the contrary, attaining a satisfactory mixing is one of the main points of attention for chemical engineers when designing a large-scale reactor (the "mass transfer" problem; see above) [10]. The second implication is that, if the product of the photochemical reaction absorbs in the same wavelength range as the starting material (which is a common

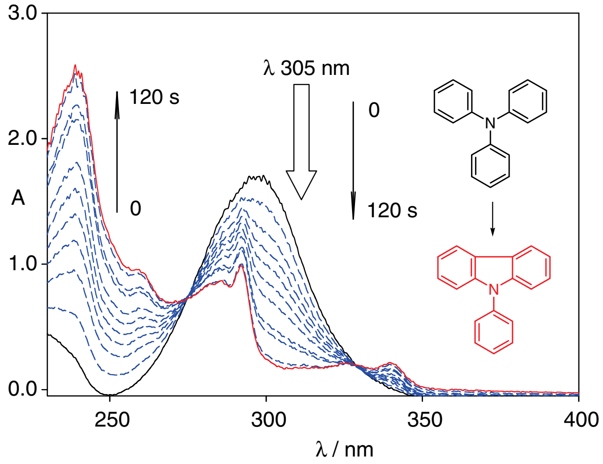


Figure 1.8 Photochemical conversion of triphenylamine into *N*-phenylcarbazole. At 305 nm the photoproduct has only a modest absorption, and irradiation at that wavelength leads to a regular conversion that can be continued up to completion. This would not be the case if the irradiation were carried out at a shorter wavelength (because the inner filter effect by the photoproduct would progressively slow down the reaction), or if using a solvent that absorbs competitively, such as acetone.

occurrence), it may hinder completing the photoreaction when it is photostable (the so-called "inner filter" effect), or it may lead to a mixture of primary and secondary photoproducts when the product itself is photoreactive.

The desirable situation where it is possible to irradiate the reagent at a wavelength where the product absorbs much less is shown in Figure 1.8. Under this condition, the conversion takes place at a regular pace and one arrives at a quantitative conversion, or close to it. When this does not apply, it may be difficult to bring the reaction to completion and/or to avoid the formation of secondary photoproducts. These are the actual limitations to the synthetic use of photochemical reactions, and they involve a general concentration limit (a clean reaction is rarely obtained above a 0.01–0.1 M concentration). Although there is no simple and general way to overcome this negative aspect, several methods are available that allow many cases to perform better.

Significant – and sometimes spectacular – improvements may be obtained by circulating the solution by means of a peristaltic pump; this is particularly the case when exposing a thin layer to the lamp at any time, rather than stirring the whole of the solution and thus having a longer optical path. "Falling film photoreactors" are commercially available in which a solution from a reservoir is sprayed onto the top of a (cooled) lamp, using a peristaltic pump, although a cheap, home-made device has been shown to be almost equally effective. For this, good results have been obtained by coiling a plastic tubing (that is transparent to the light used. and preferably made from fluorinated polyolefins for purpose of chemical resistance) around the cooling well of a medium-pressure lamp, and circulating the solution. In this way, considerable volumes (up to several liters) can be irradiated in a limited

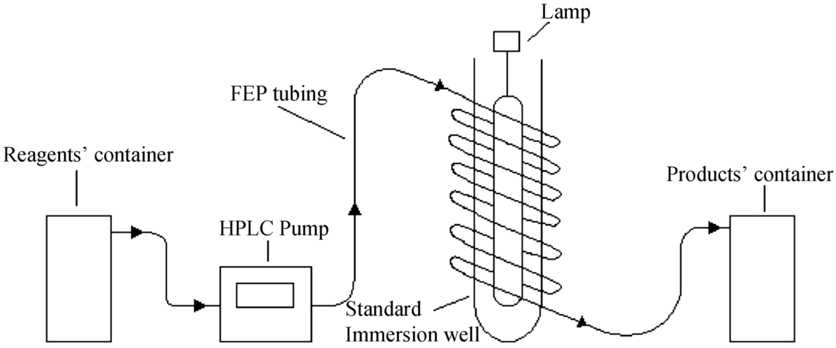


Figure 1.9 The circulation of a solution around an immersion well fitted with a medium-pressure mercury lamp.

overall time, with a better conversion and yield than when irradiating in a static reactor (see Figure 1.9). In this case, a tubing with an internal diameter sufficiently wide (e.g., >1 mm) so as to avoid any build-up of pressure must be used. Under such conditions, the tubing may be used to connect several lamps in series, so that the irradiated volume and amount of reagent transformed reach industrially significant levels. In fact, when using such an inexpensive set-up with a single lamp, a daily production on the order of 500 g has been achieved [11].

An alternative approach is that of *process intensification through miniaturization*, which involves the application of microreactors to photochemical reactions. For this, the reactors were created by engraving thin grooves on a variety of surfaces; the grooves are then covered by a transparent plate, which enables the solution to be circulated through the resultant channels. The short optical path so formed may lead to partial absorption, but also ensures homogeneous excitation – a condition that is difficult to achieve otherwise (as indicated above). "Home-made" continuous flow microreactors have been described in the literature, and shown to have significant advantages in terms of the photochemical reactions carried out (see Figure 1.10) [12].

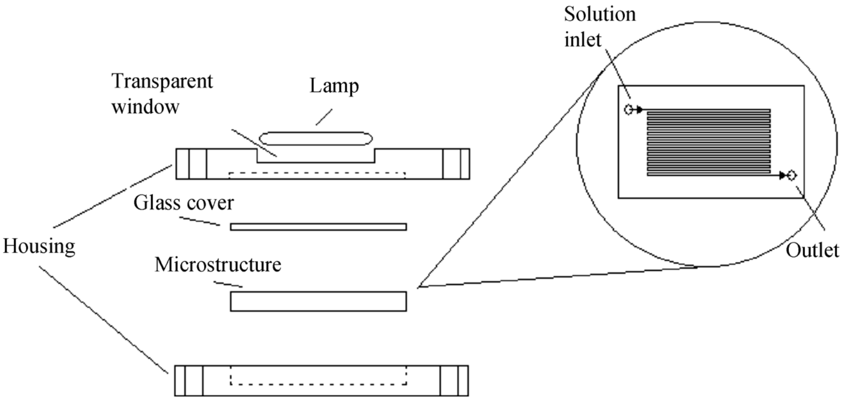


Figure 1.10 A flow microreactor for photochemical reactions.

Another way to minimize secondary photoreactions is to use lamps with a narrow λ range emission, as this may match the reagent absorption better than that of the primary product. Low-pressure Hg arcs with almost exclusive emission at 254 nm can be advantageous in this sense, and even better LEDs that are available for various λ ranges. The merging of these two ideas – that is, illuminating planar microreactors with a set of LEDs mounted on a flat support – may combine the advantage of both choices and thus best exploit the spatially limited output of these light sources. Indeed, this may be a future solution to this problem [13].

The above considerations regarding concentrated solutions imply that a solid-state photochemical reaction is practicable only when the product formed does not hinder the penetration of light down to the inner molecules of the reagent. In the opposite case, the crystals may undergo a conspicuous change in appearance when exposed to light; however, dissolving the crystals and analyzing the solution shows that the photodecomposition is next to negligible, because only the first layer has reacted. Nonetheless, a considerable number of crystal-phase photochemical reactions have been reported, and advantage has been taken of the potential of this method for selective reactions, at least in some cases rationalized on the basis of the crystal structure [14], and including enantioselective processes by using chiral auxiliaries. The irradiation of a thin layer of small-dimension crystals, either on a glass plate or on the internal walls of a rotating tube, may produce good results; for example, a solution can be slowly evaporated in a rotating tube held horizontally, and the thin coat obtained then irradiated [14]. An alternative, which has been shown to be convenient in some cases, is to irradiate a microcrystals suspension obtained by adding a solution of the reagent in a water-miscible solvent (e.g., acetone) to neat water, while stirring [15]. Irradiation with the reagent adsorbed onto a variety of matrices has likewise been reported [16].

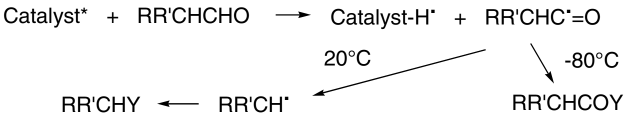
1.3.2
Effect of Impurities, Oxygen, and Temperature

The lifetime of the excited state is short, in the order of $\tau < 1\,\mu s$ for triplets, and $\tau < 1$ ns for singlets. Thus, in order that a chemical reaction competes with an unproductive physical decay, it must be quite fast. This has both positive and negative implications. On the plus side, it makes the effect of impurities relatively small, such that the extensive purification of reagents and solvents is not generally required, provided that neither absorbing impurities (this can easily be monitored with UV spectroscopy) nor highly reactive molecules (e.g., alkenes as impurities in alkanes, which react easily with ketones) are present. The exception here is oxygen, which quenches excited states at a diffusion-controlled rate. In many air-equilibrated organic solvents the amount of oxygen present in solution is in the range 0.002 to 0.003 M (0.0005 M in water), which is high enough to quench more than 90% of long-lived triplets. The effect is much smaller with singlets or with short-lived triplets.

The effect can easily be eliminated by flushing the solution with an inert gas for some minutes, so that the amount of oxygen dissolved drops by approximately three orders of magnitude (this is frequently carried out also with radical reactions). At any rate, it is advisable to carry out at least the first tests under "deoxygenated" conditions (or rather with a low oxygen concentration) because O_2 may react also with any further intermediates that are often formed along the reaction path, such as radicals or radical ions. To summarize, taking into account that oxygen interferes only with some families of photochemical reactions – and likewise that moisture is a problem only in some cases – the very fact that excited states are highly reactive and short-lived often makes photochemical reactions easier to carry out than "typical" procedures of advanced organic synthesis. In fact, photochemistry requires nothing like the exhaustive dehydration and purification of solvents needed by most reactions via enolates or transition-metal catalysis. On the negative side is the fact that, in bimolecular reactions, a large trap concentration is required to capture the short-lived excited state, often a great excess with respect to the reagent.

Again, for the same reasons, photochemical reactions generally are little affected by changes in temperature, or at least are reactions of the excited states (though there are exceptions). However, the course of the overall process which occurs on irradiation may change dramatically, generally due to an effect on the system before or after the actual photochemical step [17]. For example, when the reagent is liable to some equilibrium, the temperature may affect distribution between the forms, so that a different reagent would be excited at a different temperature. (In the same way, a compound may be hydrogen-bonded in certain solvents, such that the excitation produces a different excited state that results in a photochemistry which differs from that seen in a non-hydrogen-bonding solvent.) On the other hand, photochemical reactions do create (in most cases) a ground-state product (i.e., the lowest-lying species at that configuration), although this need not be a stable particle in absolute terms. Indeed, the photochemical reaction quite often produces a highly reactive species (a radical, an ion, a nitrene, etc.), the fate of which depends more on the conditions than that of the excited state, and results in an overall dependence on the temperature. In fact, the "cold" generation of highly reactive intermediates is an important advantage of photochemical reactions. For example, the generation of alkyl radicals by thermal hydrogen abstraction from α-substituted aldehydes leads unavoidably to decarbonylation. However, the highly favored hydrogen abstraction by an excited photocatalyst is also effective at low (e.g., −80 °C) temperatures, when decarbonylation is slowed down, so that different end-products are obtained at different temperatures (Scheme 1.2) [6].

In fact, this characteristic has even more general implications. Photochemical reactions tend to be (relatively) independent of the conditions (except when the nature of the excited state changes, see above), and thus the primary photoproduct can be created under different conditions (temperature, viscosity, proticity, etc.), a fact that provides such methods with an unparalleled versatility.



Scheme 1.2

1.3.3
Safety

Intense light sources (including solar light) may be dangerous for the skin (UV-B, 280–320 nm causes erythema, while UV-C below 280 nm is genotoxic) and the eyes. An annoying *conjunctivitis* may result from exposure to short-wavelength light, with the onset of pain occurring some hours after the exposure, without warning. In general, it is difficult to avoid indirect or reflected radiation, the only practical approach being *always* to wear protective glasses (specially designed to block UV light) when working close to an irradiation apparatus. It is advisable to switch off the lamps before approaching the apparatus, even when wearing such glasses. This may be problematic with high-pressure, but not low-pressure, arcs. A photochemical safety cabinet which switches off automatically when opened is available commercially, but careful behavior is probably sufficient. Attention must also be paid to the formation of toxic ozone, and irradiations should always be carried out under a fume hood. With high-power lamps, nitrogen flushing in the close vicinity of the arc should be contemplated so as to avoid ozone building up to dangerous concentrations. Obviously, mercury-polluted exhausted lamps should be disposed of correctly and safely.

1.3.4
Planning a Photochemical Synthesis

To summarize, it may be concluded that with the range of lamps available, the most convenient choice would be two pairs (each of 15 W) of low-pressure arcs with their emission centered at 254, 305, 350 and 370 nm; an alternative (which is likely to become more common in the future) would be a set of LEDs. Quartz tubes would be a sensible acquisition for any synthetic laboratory as they allows an exploration of the viability of photochemical steps. The limited precautions and safety requirements involved with photochemistry make it a much more easily used method than many of the reactions that involve thermal/oxygen/moisture-labile and/or toxic/flammable reagents, or a delicate catalyst that are routinely considered and carried out in synthetic laboratories. With photochemistry, an experiment can be easily conducted, with failure by beginners more likely due to naïve oversight (see below) than to an inadequate experimental capability. An experiment with a time-honored method, such as the exposure to solar light, may also be appropriate, at least as a first indication, for reagents absorbing in the near UV spectrum. There are also not negligible advantages in this case of using a freely available source requiring no investment at all!

Some of the key parameters useful for planning a photochemical reaction are summarized in Table 1.1 and Figure 1.1. Thus, a lamp must be chosen that emits where the putative photoreactive molecule absorbs (check the absorption spectrum). A check must also be made that neither the material from which the apparatus is built nor the solvent absorb at that wavelength. In practice, with a low-pressure mercury arc, a quartz apparatus and a solvent chosen among alkanes, alcohols, ethers or

Table 1.2 Some key indications for planning a photochemical reaction.

Lamp	**Irradiation (nm)**	**Einstein (min^{-1} cm^{-2})**	**Volume irradiated (ml)**	**Time taken to convert a 5×10^{-2} M solution ($\Phi = 1$) (h)**
Low-pressure Hg	ext, 254[a)]	$\approx 4\times10^{-6}$	10–100	0.25
Phosphor-coated	ext, 305[a)]	$\approx 1\times10^{-6}$	10–100	1
	ext, 350[a)]	$\approx 8\times10^{-7}$	10–100	1.2
Medium-pressure Hg	imm, 300–400[b)]	$\approx 10^{-5}$	80–1000	0.1
LED	ext, 310[c)]	$\approx 2\times10^{-8}$	1–10	40
LED	ext, 400[c)]	$\approx 1\times10^{-6}$	1–10	1
Solar light	ext, 330–400	$\approx 10^{-7}$	Any	10

[a)] In a multilamp apparatus fitted with six 15 W lamps.
[b)] For the range indicated, the lamp emits also in the visible.
[c)] Six LEDs circularly placed around the test tube containing the solution.

simple haloalkanes, should be used. Acetonitrile is a common choice as solvent because it adds to the overall transparency in the UV its low chemical reactivity. A wider choice is possible when utilizing the UV-A spectrum.

When planning the scale of the experiment, the data listed in Table 1.2 might be of value. The quantities indicated are: (i) the light flux (in Einstein, moles of photons) on a 1 cm^2 surface close to the lamp; and (ii) the time required for converting a 5×10^{-2} M solution by using that lamp, assuming that all of the flux is absorbed, the quantum yield is unitary, and that there is no inner filter effect (in other words, the minimal time required for converting the above amount).

Clearly, the amount of reagent converted depends on the volume that can be illuminated, and thus on the surface of the lamp. Further consider that in an immersion well apparatus, all of the flux is absorbed, whereas with an external illumination the fraction absorbed will vary considerably. Phosphor-coated lamps and LEDs, for example, may have the same flux density (at $\lambda > 360$ nm), but the former lamp is larger and a much larger overall flux is emitted. The problem then is to place the vessel with the solution in such a way that a large fraction of the flux is absorbed. This target is achieved in a multilamp apparatus with mirror walls, where volumes of 100 ml or more can be effectively irradiated (i.e., according to Figure 1.2 rather than to Figure 1.3). In contrast, while the flux from a LED is readily directed towards the sample, the total emission is weak and only a few milliliters of solution will be irradiated by using about ten LEDs (which is still useful for explorative reactions).

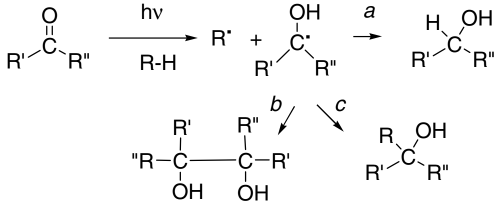
It can be seen that amounts of up to a few grams can be converted in 5–10 h in the case of complete absorption and unitary quantum yield (ignoring any internal filter effect). Lower quantum yields or an incomplete absorption proportionally lengthens the time required for the transformation. It is most likely safe to say that exploratory reactions on the 100 mg scale can be carried out in a reasonable time, provided that $\Phi \geq 0.1$–0.05. Even reactions with a quantum yield at the lower limit or below may be interesting for a preparation if the reaction is clean. Given the minimal safety precautions required, leaving the reaction for a few hours or even overnight in a tube exposed to the light of a low-pressure Hg arc may often be a convenient choice as a test experiment. Larger amounts require additional planning, however, the best approach probably being to use a flow system that, as shown above, can even be implemented by using a home-made apparatus and subsequently developed to the kilogram scale.

1.4
Photochemical Steps in Synthetic Planning

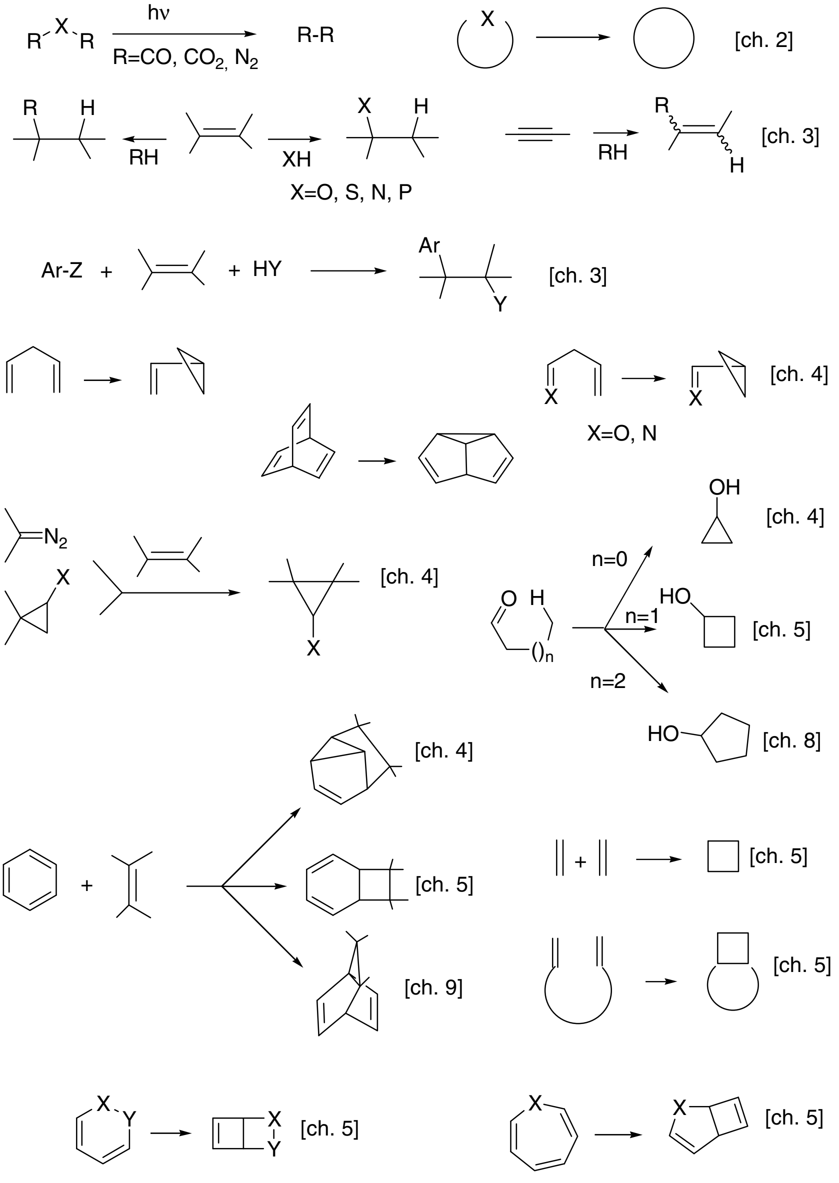
A number of excellent textbooks of organic photochemistry are available, and the reader is directed to these to acquire an appropriate introduction to the field of organic chemistry (for example, see [18]). Presentations of the synthetic aspects of organic photochemistry are likewise available in books and reviews [19–21], arranged according to the chemical function reacting or to the type (mechanism) of the reaction involved.

In this handbook, it was deemed more appropriate to present the reactions according to the transformation occurring, in the way that an appreciated treatise such as Theilheimer does (albeit more simply). This should help when considering a photochemical alternative if planning a synthesis. Unfortunately, this choice has the drawback that very little is said regarding the general features of any photochemical reaction, let alone the detailed mechanism. Moreover, a single reaction may be mentioned in different chapters if it leads to different synthetic targets, whereas reactions that have nothing in common are dealt with in the same chapter when their synthetic targets are the same.

No attention is given to the "mechanistic" importance of a reaction; rather, an attempt has been made to concentrate on reactions that have an actual (potential) synthetic role. This is not always an obvious selection, because photochemistry has not been sufficiently used in such syntheses, and mechanistic studies are not necessarily a reliable guide towards this aim. As an example, hydrogen abstraction by ketones (Scheme 1.3), which probably is the most thoroughly studied photochemical reaction, is not mechanistically discussed. Neither is presented the resultant photoreduction of ketones (Scheme 1.3, path *a*), because this will hardly ever become a sensible synthetic alternative for the reduction. However, other reactions arising from the same primary photoprocess, namely bimolecular reduction (path *b*) and



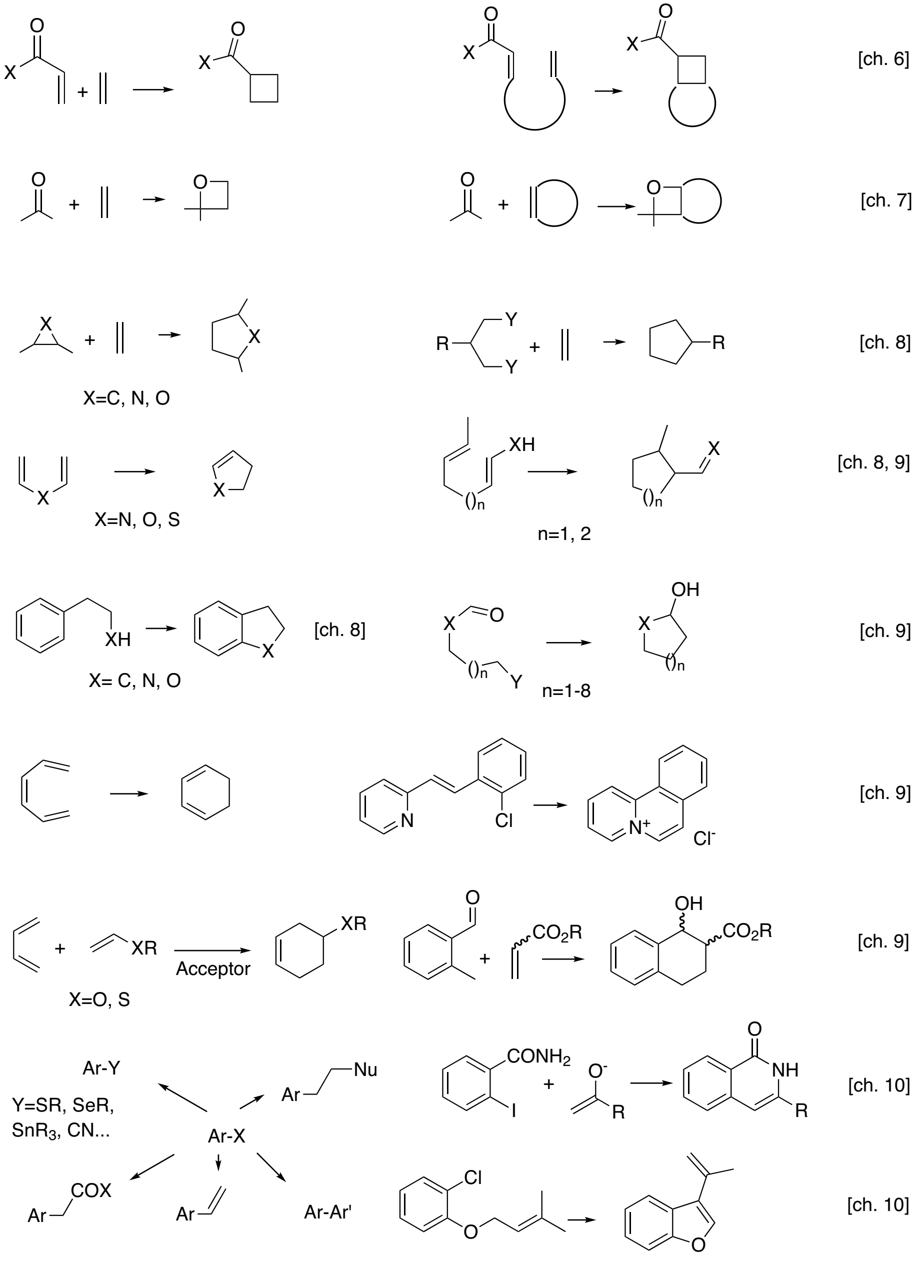
Scheme 1.3



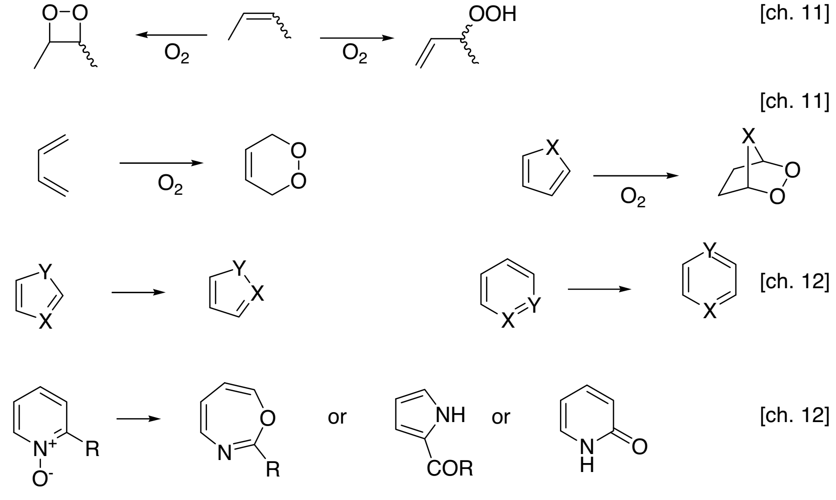
Scheme 1.4 The chapter number where each reaction is discussed is shown in square brackets.

coupling (path *c*), are presented in the appropriate chapter according to the characteristics of the (carbon–carbon) bond formed (in a open-chain compound, forming a ring, of which dimension).

The general schemes for some of the main photochemical reactions are reported in Scheme 1.4 (the relevant chapter number is shown in square brackets).



Scheme 1.4 (*Continued*)



Scheme 1.4 (*Continued*)

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