SYNTHESIS OF HETEROCYCLIC COMPOUNDS BY PHOTOCHEMICAL CYCLIZATIONS

Ana G. Neo
Laboratory of Bioorganic Chemistry and Membrane Biophysics (L.O.B.O.),
Department of Organic and Inorganic Chemistry, Universidad de Extremadura, 10003 Cáceres, Spain
(e-mail: aneo@unex.es)

Abstract. *Photochemical cyclizations permit the access to numerous types of heterocycles and constituent a powerful tool in synthetic organic chemistry. In this type of processes, the light induces a pericyclic ring closing reaction to give an intermediate which evolves, in different manner, to afford a stable final product. Photocyclizations take place in very mild and simple reaction conditions, with great atom economy and, also, in a manner very respectful whit the environment.*

Contents
1. Introduction
2. Photochemical cyclizations in oxidative conditions
  2.1. Application for the synthesis of molecules with biological properties
  2.2. Application for the design of new materials
3. Photochemical cyclizations in the presence of a base
  3.1. Application for the synthesis of molecules with biological properties
  3.2. Application for the design of new materials
4. Cyclization/dehalogenation and related
5. Miscellaneous
6. Conclusion
Acknowledgement
References

1. Introduction
    The study of sunlight effect in nitric acid and the discovery of the principles of photosynthesis by Joseph Priestley (1733–1804) were considered the beginning of photochemistry. In the field of organic chemistry, the photochemistry era was initiated by the investigations of effects of light in santonin by Cannizzaro, and essentially the complete and innovator study of the effect of light in organic compounds developed by Giacomo Ciamician and Paul Silber. After these pioneers, other researchers, as Emanuele Paternò, Otto Schenck, Julius Schmidt, or Alexander Schönberg, have centered your attention in the study of the influence of light in the molecular reactivity.[1,2]

    The early photochemistry investigations were oriented to study the action of solar light in the molecular reactivity, because at this moment, the light nature and their effects at the atomic level were unknown. Presently, is understood that the absorption of UV-visible light by a molecule transfer the electrons from the ground state, to the excited state and the subsequent redistribution of these electrons results in the formation of a product that is not possible to obtain in thermal conditions. Furthermore, photoreactions present other attractive properties, as high atom efficiency, ecofriendly nature, wide range of functional group and heteroatom tolerance, protocol reactions very straightforward and, usually, also they are inexpensive.[3-6]

    All these properties have made photochemical reactions play an important role in the synthesis of great variety of molecules in diverse areas of organic chemistry.[7-13]

    Among the numerous types of photochemical reactions, the light-induced pericyclic ring closing reactions, and particularly, conrotatory 6π-cyclizations are one of the most important. This type of reactions permits the construction, in a single and green process, of aromatic and heteroaromatic polycyclic compounds.[14]

    Usually, 6π-photocyclizations has been classified into oxidation, elimination, and rearrangement. This review is organized following this classification: initially they will show some examples of photocyclizations in oxidative conditions and your application for the synthesis of compounds with biological activity and materials. The second section is about the photocyclizations in basic medium and

their use for the preparation of compounds with biological applications and materials science. Thirdly, they will show eliminative photochemical cyclizations in absence of base and, finally, miscellaneous new reactions involving 6π-photocyclizations and rearrangement.

2. Photochemical cyclizations in oxidative conditions

The photochemical cyclization of stilbene and stilbenoids in the presence of an oxidant, usually namely the Mallory[15] reaction, is probably the most common type of 6π-photocyclizations. In these process, UV irradiation of stilbenes **1** and **2** produces an initial equilibration to a photostationary mixture of *E*- and *Z*-isomers,[16] followed by conrotatory cyclization to the dihydrophenanthrenes **3**. When the irradiation is carried out using an oxidant, the dihydrophenanthrenes **3** delivers the phenanthrenes **4**,[15, 17-20] (Scheme 1). Different oxidants can be used, for example O_2,[21] I_2,[22] catalytic iodine in the presence of an excess of atmospheric oxygen[23] or an excess of iodine and propylene oxide, that acting as a hydroiodic acid scavenger.[24]

This reaction has been widely used for the preparation of various compounds with a heterocycle in place of the benzene ring, denominate phenanthrenoids.[25] These ubiquitous compounds include valuable intermediates and molecules with useful properties.[26-29] Photochemical synthesis of stilbenes and stilbenoids constituted a good alternative to other synthetic methods.[30-32]
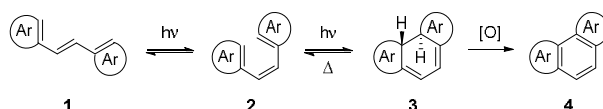
Scheme 1. Synthesis of phenanthrenes and phenanthrenoids by oxidative photocyclization.

2.1. Application for the synthesis of molecules with biological properties

The indolocarbazole (ICZ) nucleus is present in several natural and synthetic molecules that possessing remarkable properties, especially due your ability to inhibit topoisomerase I.[33,34] For example, rebeccamycin,[35] staurosporine[36] or K-252 A,[37] (Figure 1) presents biological activities. The skeleton of these compounds can be obtained by oxidative photocyclization.
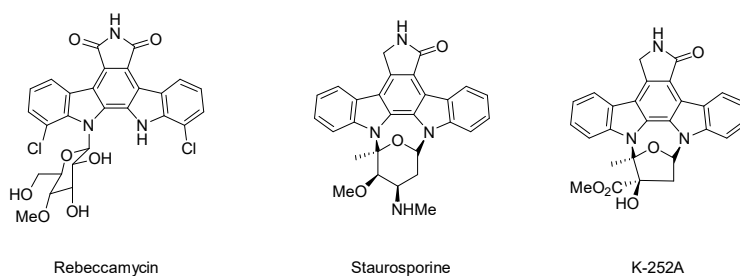

Figure 1. Indolocarbazoles with biological activity.

In one of the two first syntheses of rebeccamycin, the indolocarbazole **6** was synthetize by irradiation of precursor **5** with mercury lamps at 3000 A with iodine catalyst and air (Scheme 2). However, in this case, is more effective the use of Ag$_2$O refluxing in benzene.[38] This photochemical strategy has been also used in other total synthesis of rebeccamycin.[39]

An analogous strategy has been used for the preparation of IPC skeleton of the aza-rebeccamycin analogue **9**. In this propose, the intermediate **7** was irradiated with a medium pressure mercury lamp in benzene using excess of iodine to give the indolocarbazole **8** in 70% yield. Treatment of compound **8** with ammonium hydroxide yielded the aza-rebeccamycine analogue **9** (Scheme 3).[40] In this paper also prepared other aza-rebeccamycin analogues obtaining similar yields in the photochemical cyclization. The aza-rebeccamycins were more selective toward different tumor cell lines tested that the parent compounds.
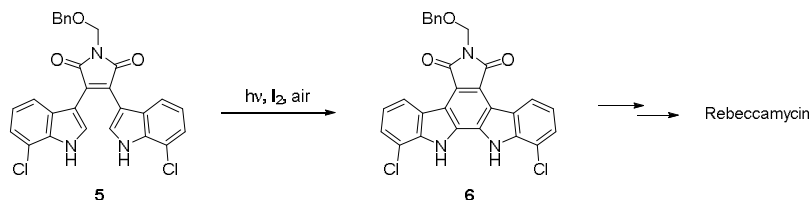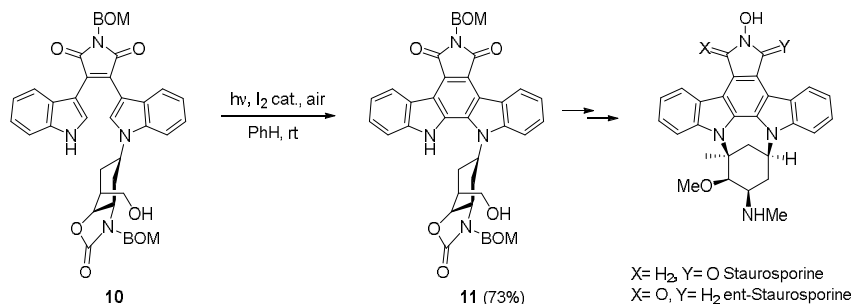
Scheme 2. Synthesis of indolocarbazole by photochemical cyclization.
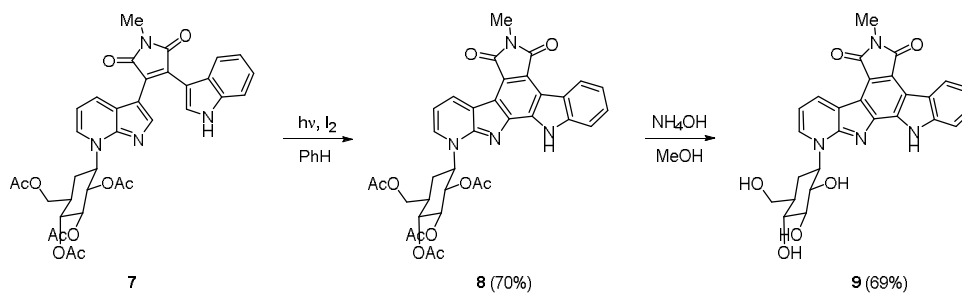
Scheme 3. Photocyclization in the preparation of aza-rebeccamycin analogue.

In similar way, an oxidative photocyclization have been used to obtain the indolopyrrolocarbazole unit **11**. This compound is a key intermediate in the first total synthesis of staurosporine and ent-staurosporine, (Scheme **4**).[41] The photocyclization of compound **10**, in presence of catalytic iodine and air, leaded the pyrrolocarbazole **11** in good yield.

X= H$_2$, Y= O Staurosporine
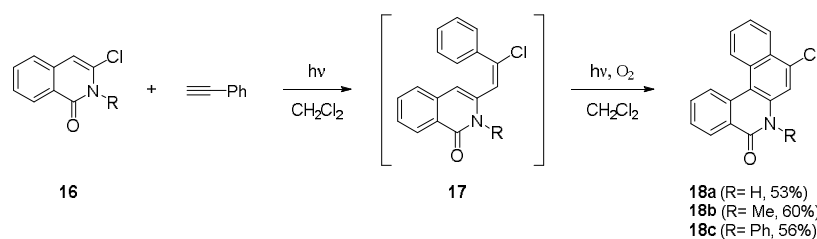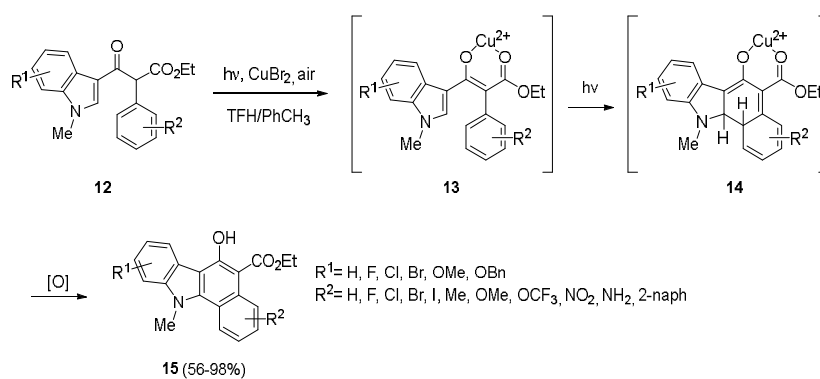X= O, Y= H$_2$ ent-Staurosporine

Scheme 4. Oxidative photocyclization in the synthesis of staurosporine and ent-staurosporine.

A structure related with indolocarbazole skeleton is the benzocarbazole system, which also presents applications in biomedicine and material science. 6-Ethoxycarbonyl-5-hydroxy-benzo[*a*]carbazoles **15** was synthetized by oxidative photocyclization of precursor **12** using air and CuBr$_2$ as oxidants. In this process, Cu(II) complexed with keto-esther **12** to give the intermediate **13**, which suffered an electrocyclization to afforded the dihidrocarbazole **14** that, by oxidation with air or CuBr$_2$, gave the benzo[*a*]carbazole ring **15** (Scheme 5). The photocyclization has be place using a medium-pressure mercury lamp (500 W) at room temperature and many benzo[*a*]carbazole derivatives **15** was obtained with moderate to good yields.[42]

Phenanthridine ring system is a privileged structure prevalent in many natural products that exhibit antifungal, antitumor, antibacterial, and cytotoxic activities.[43,44] The phenanthridine skeleton can be easily prepared by oxidative photocyclization.

For example, benzo[*a*]phenanthridein-5-ones **18** and benzo[*f*]quinolin-3-ones were prepared using two sequential photoreactions. The first one is the photoaddition of 6-chloropyridin-2-ones and

3-chloroisoquinolin-1-ones **16** to phenylacetylene to give the corresponding stilbenoids **17**. The second photoreaction is the oxidative photocyclization of intermediate **17** to give phenanthridines **18** (Scheme 6).[45]

R[1]= H, F, Cl, Br, OMe, OBn
R[2]= H, F, Cl, Br, I, Me, OMe, OCF₃, NO₂, NH₂, 2-naph

15 (56-98%)

Scheme 5. Synthesis of hydroxybenzo[*a*]carbazoles.

18a (R= H, 53%)
18b (R= Me, 60%)
18c (R= Ph, 56%)

Scheme 6. Synthesis of benzo[*a*]phenanthridein-5-ones by two sequential photochemical reactions.

CC-1065 (Figure 2) is a potent antitumor compound in which your central and right fragments selectively interact with DNA in an initial non-covalent binding. Then, adenine nitrogen attacks the cyclopropane on the left part, causing the opening of cyclopropane ring and aromatization of the quinone. The covalent binding between CC-1065 and DNA origins the detention of the DNA replication and, thus, stops the reproduction of cancer cells.[46-48]

Unfortunately, CC-1065 possesses delayed hepatotoxicity,[49] thus, in order to obtain compounds with the antitumor activity of this compound but without their toxicity, diverse number of derivatives has been prepared.[50]
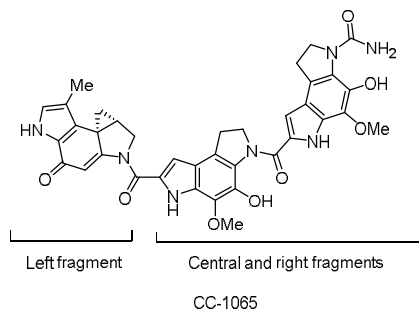

Left fragment   Central and right fragments

CC-1065

Figure 2. Structure of antitumor agent CC-1065.

Different analogues of DNA-alkylating unit of the antitumor compound CC-1065 **19a-f** (Figure 3) were synthetized using a synthetic strategy in which the photochemical reaction is the key step.[51,52]
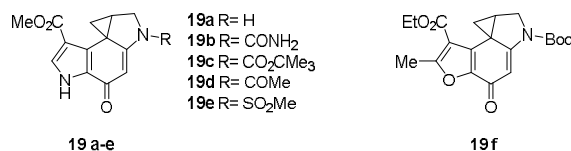

	19a R= H
	19b R= CONH$_2$
	19c R= CO$_2$CMe$_3$
	19d R= COMe
	19e R= SO$_2$Me

Figure 3. Analogues of left-part of CC-1065.

Indole derivatives **19a-f** was obtained from the corresponding phenanthrenoids **21a** and **21b** in eight steps. Indole derivatives **21a** and **21b** were synthetized by an oxidative photocyclization of stilbenoids **20a** and **20b**. Photocyclizations were carry out by irradiation with a medium pressure mercury lamp using catalytic iodine and air in ethanol for the cyclization of **20a**, and stoichiometric iodine and propylene oxide as HI scavenger in benzene in the irradiation of stilbenoid **20b** (Scheme 7).[51,52]
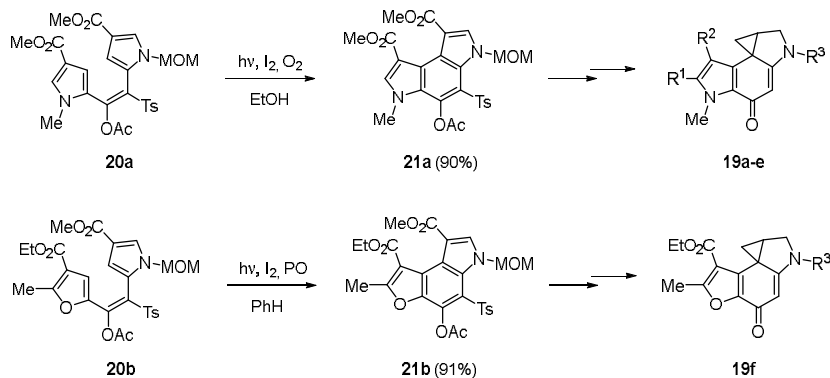
**Scheme 7**. Left-part CC-1065 analogues prepared using a photochemical oxidative cyclization.

This methodology also was applied in the studies on the synthesis of an analogue of CC-1065 containing a benzoindole unit. Thereby, the photochemical cyclization of phenanthrenoids **22a** and **22b** permitted obtain the benzoinidole units **23a** and **23b** in good yields, using a mercury lamp as source of light with stoichiometric iodine and propylene oxide, (Scheme 8).[53,54] Alternatively, **23a** were obtained in quantitative yield by irradiation of **22a** employing catalytic iodine and air in ethanol.

23a R= CO$_2$Me (88%)
23b R= CONEt$_2$ (67%)
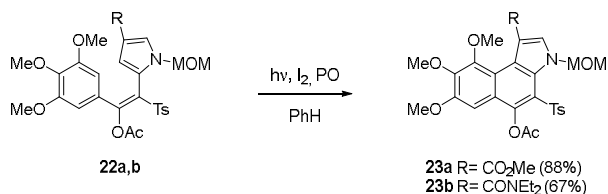
**Scheme 8**. Photochemical synthesis of benzoindole units.

Recently, the G-quadruplex has attracted powerful interest due their potential biological functions, such as gene regulation, gene expression, antitumor potential and DNA nanotechnology.[55,56] Xanthene and xanthone derivatives present properties as G-quadruplex stabilizing ligands.[57] For example, the dimeric xanthone derivative **26** presents a good interaction with quadruplex DNA. This compound was obtained by treatment of compound **25** with piperidine. The precursor **25** was easily achieved by an oxidative

photochemical cyclization of dimeric compound **24** (Secheme 9).[58] The photochemical reaction occurs in a quartz tube under inert atmosphere with an excess of iodine in THF.

24   **25** (80%)   **26**

$R^1 = C_4H_8Cl$
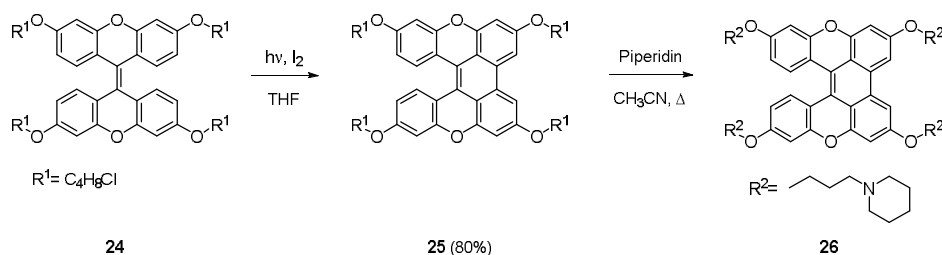
Scheme 9. Photocyclization in the synthesis of dimeric xanthone.

Recently has been published a variation of oxidative phototocyclization for the synthesis of phenanthrenoids. In this process, *N*-(arylsulfonyl)proiolamides **27** suffer a radical Smiles rearrangement following by a C-S bond formation to give **28** that under a Mallory reaction give the phenanthrenoids **29**, (Scheme 10).[59] In this case, UV light at $\lambda = 300$ nm is used under air atmosphere and the products **29** are obtained in excellent yields. The isolation of intermediates **28** confirmed the proposed mechanism. Additionally, the reaction was performed at gram scale using a flow reactor.

27   **28**   **29** (50-84%)
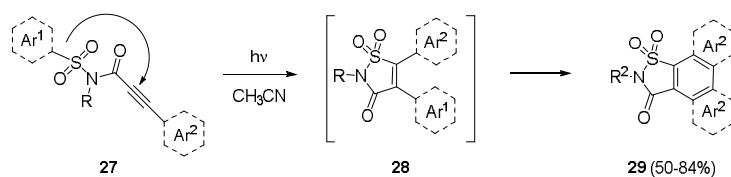
Scheme 10. Synthesis of phenanthrene derivatives from *N*-tosylpropiolamides.

Two examples of 4,5-diarylisothiazol-3(2*H*)-one 1,1-dioxides **28a** and **28b** and diarylisothiazol-dioxides **29a** and **29b** are specified in Figure 4.

Others alternatives of classical Mallory reaction are the used of catalytic potassium iodide or TEMPO in place of conventional iodine-mediated oxidation.[60]
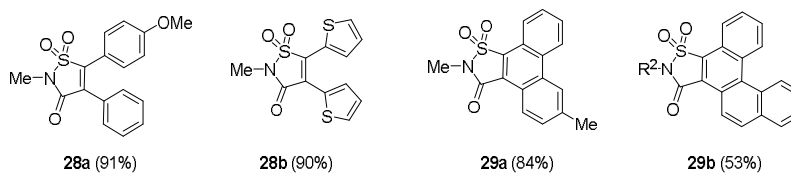

28a (91%)   **28b** (90%)   **29a** (84%)   **29b** (53%)

Figure 4. 4,5-Diarylisothiazol-3(2*H*)-one **28** and 1,1-dioxides and diarylisothiazol-dioxides **29**.

2.2. Application for the design of new materials

The synthesis of expanded π-electron systems of polycyclic aromatic hydrocarbons is very important for the preparation of new materials. Usually, the use of heat and transition metals as catalyst for the preparation of this type of compounds has been reported.[61,62] Other synthetic alternative is the use photochemical cyclizations to prepare this type of compounds. Examples of different compounds prepared using this methodology is given below.

Dithienoquinazolines and benzothienoquinazolines have potential as organic semiconductors (OSC).[63] These structures can be prepared using an oxidative photocyclization.

For example, a family of thienoacene compounds with a fused pyrimidine ring **31a-d** (Figure 5) was prepared by irradiation of 4,5-dithienyl-substituted pyrimidines **30** using iodine as oxidant and propylene oxide to eliminate HI (Scheme 11).[64]
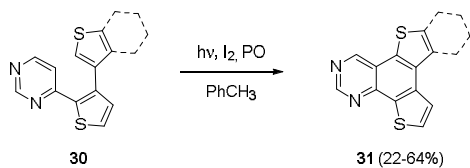
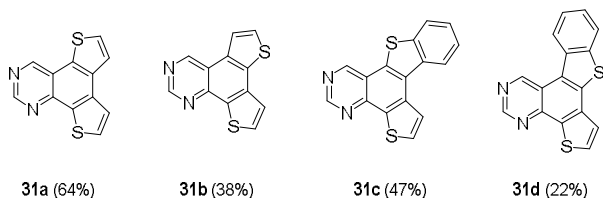**Scheme 11.** Synthesis of potential OSC using UV-light.

31a (64%)   **31b** (38%)   **31c** (47%)   **31d** (22%)

Figure 5. Thienoacene systems obatined by photocyclization.

π-Expanded coumarins presents diverse possible applications in material chemistry, as two-photon fluorescence microscopy, OLEDs, dye-sensitized solar cells or fluorescent probes.[65] The π-expanded coumarin **33** was prepared in 54% yield by irradiation of precursor **32** with a UV-lamp (365 nm) in the presence of air (Scheme 12). Alternatively, **33** can be obtained in good yield (88%) by treatment of compound **32** with BBr$_3$.[66]
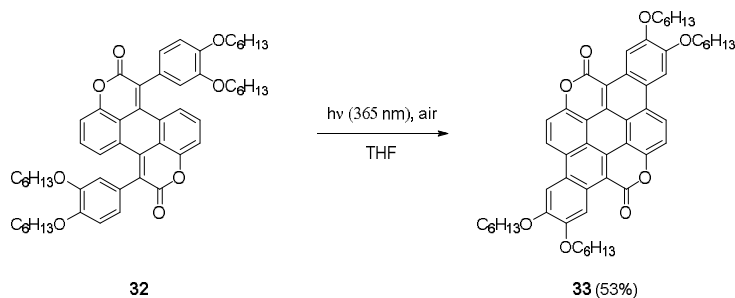

Scheme 12. Synthesis of π-expanded coumarins using UV-lamp.

Nanographenes are a types of relatively large polycyclic aromatic hydrocarbons, PHAs, that presents applications in different fields.[67] Graphene nanoribbons are a type of nanographenes with exceptional applications.[68] Graphene nanoribbons **35**, that presents properties in solar cells, were synthetized in excellent yields by pohotocyclization of **34** using with a common visible light LED and iodine (Scheme 13). The facility of the photocyclizations of substrates **34** is due to their lower energy visible absorptions.[69]

Helicenes are a class of polycyclic compounds constituted by *ortho*-fused benzene or other aromatic rings. These compounds exhibit nonplanar screw-shaped skeletons and presents extraordinary chiro and electronic properties with numerous applications in the field of asymmetric synthesis, molecular recognition and material science.[70,71]

The first helicenes were synthesized in 1903,[72] and since then diverse synthetic approximations are developed for the preparation of these compounds.[70,73,7] One important method for the synthesis of helicenes is the oxidative photocyclization of stilbene derivatives.[75]

34

35 (>95%)
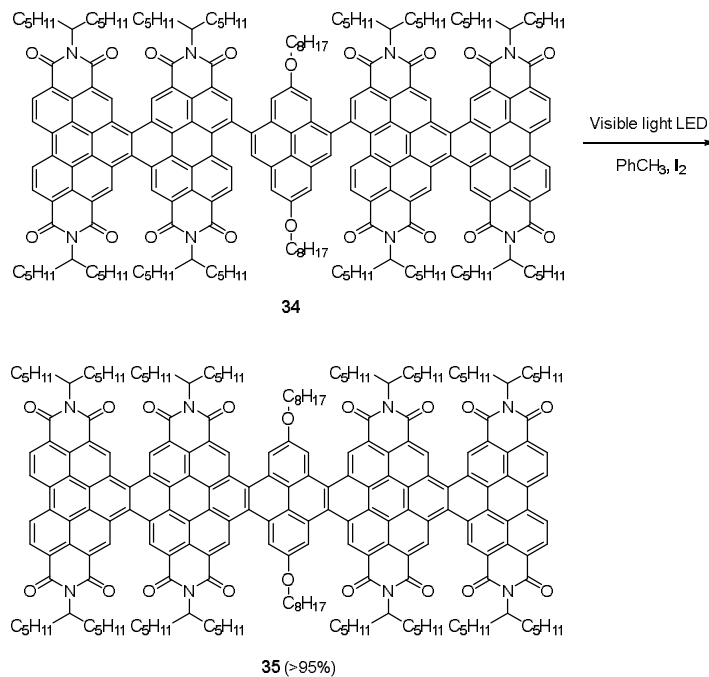
Scheme 13. Photochemical synthesis of graphene nanoribbons.

For example, diverse phenanthrene derivatives **36a-d**, (Figure 6) was obtained by sequential photocyclization of substituted stilbenes **37**, (Scheme 14). The photochemical cyclizations were performed in a home-made micro-flow photoreactor in the presence of catalytic iodine and air, using different solvents depending the susbstrate.[76] The condensed polycyclic aromatic hydrocarbons **36a-d** could be potential application in the field of organic semi- and super-conductor materials.


36a (59%)   **36b** (32%)   **36c** (55%)   **36d** (25%)
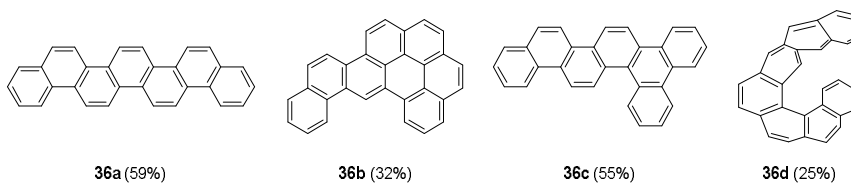
Figure 6. Helicene skeleton prepared by photochemical reaction.

37
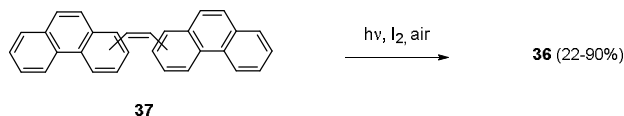
Scheme 14. Preparation of stilbene precursors of helicenes and photocyclization.

The [n]helicenes have involved attention in recent decades due their singular structure and properties produced by their helically extended chiral π systems.[70,73]The preparation of novel helicenes with a great number of π systems is relevant for different points of view, even though the synthesis of higher [n]helicenes is difficult. Nevertheless, [16]helicene has been synthetized by sextuple photocyclizations of precursor **34** using a high-pressure Hg lamp at 90 °C with stoichiometric I_2 and propylene oxide (Scheme 15).[77]
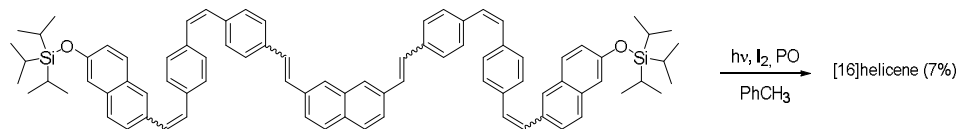
Scheme 15. Synthesis of [16]helicene by multiple photocyclizations.

Corannulene ($C_{20}H_{10}$) is a polycyclic aromatic compound related with fullerene C60 that present optoelectronic properties and charge-transport characteristics with applications in materials science.[78] The corannulene nucleus **40** was obtained by irradiation of compound **39** with a medium pressure Hg lamp using iodine as oxidant and propylene oxide as hydrogen iodine scavenger (Scheme 16).[79]
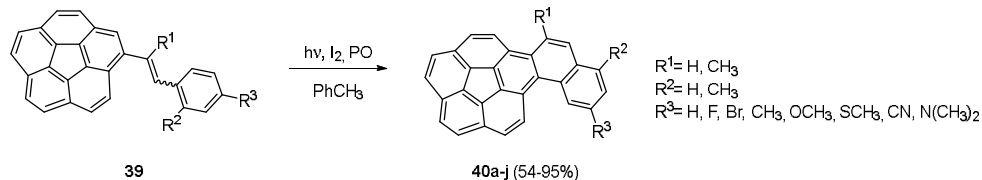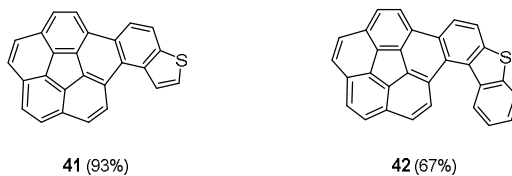

Scheme 16. Synthesis of corannulene nucleus by photocyclization.

This strategy permits the synthesis of different heterocyclic corannulene structures **41** and **42** (Figure 7) in high yields.


Figure 7. Corannulene structures prepared by oxidative photocyclization.

Fluorinated polyaromatic compounds are a type of PHAs that have high significance in areas such as materials science, catalysis, medicine, and biochemistry.[80] Tetrafluoro[6]-helicene **43** and **44** (Figure 8) were obtained by oxidative photocyclization. In Scheme 17 is indicated the synthesis of **44** by irradiation of stilbene **45** in a continuous-flow in a Pyrex glass jacket using iodine (0.67 equivalents).[81]
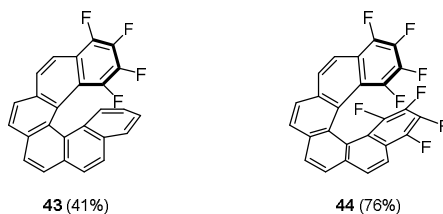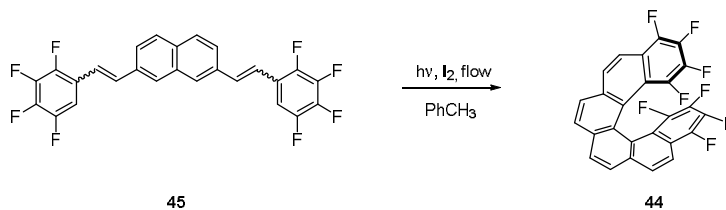

Figure 8. Tetrafluorohelicenes synthetized using a photochemical aproximation.

On the other hand, the synthesis of carbazole derivative diaza[6]helicene **47** is possible by irradiation of stilbenoid **46**. The photocyclization occurs in toluene using 1.3 equivalents of iodine and excess of propylene oxide, in a Rayonet photochemical reactor (Scheme 18).[82]

Scheme 17. Photocyclization of octafluorinated bis-stilbene.
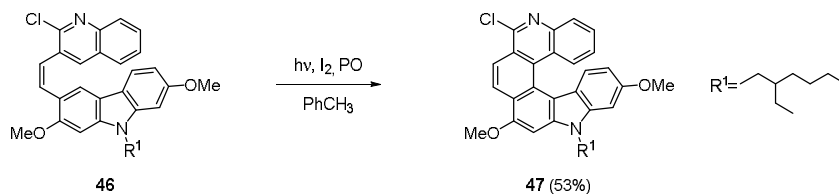
Scheme 18. Synthesis of carbazole-based [6]helicene by photocyclization.

Substitution of chlorine in the quinolone unit permits the resolution of the racemic helicene via diastereomeric separation. The functionalization of (*P*,*S*)-(+)-**47** allows the preparation of chiral materials **48a,b** (Figure 9). These compounds are potential applications in asymmetric synthesis or electronics.[82]
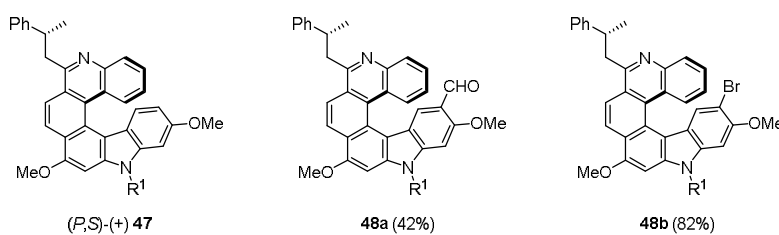


Figure 9. Functionalized diaza[6]helicene.

Thiahelicenes are a subgroup of heterohelicenes containing benzene and thiophene rings. These compounds have an effective conjugation and shows excellent optical and electronic properties, with application in asymmetric synthesis, molecular recognition or material science. The photocylization of precursors type **49** and **51** using visible light and iodine as oxidant afforded [5], [6], [7], [9] and [11]thiahelicenes by (Scheme 19 and Scheme 20).[83]
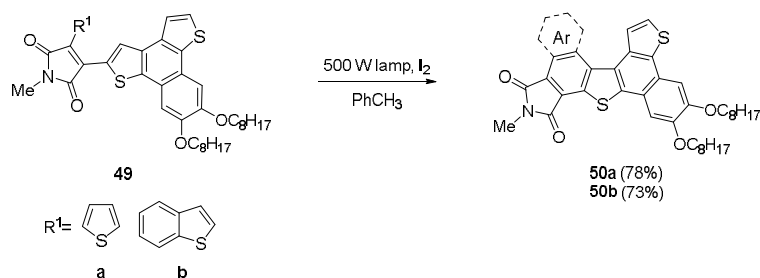
**Scheme 19.** Synthesis of [5], and [6]helicenes using visible light.

Fluoropolymers have interest due their chemical and physical properties such as thermal stability, chemical inertness, ow values for refractive indices or resistance to oxidation. These properties make the

fluoropolymers applications in different fields as petrochemical, microelectronics, chemical engineering, textile treatment or optics.[84]
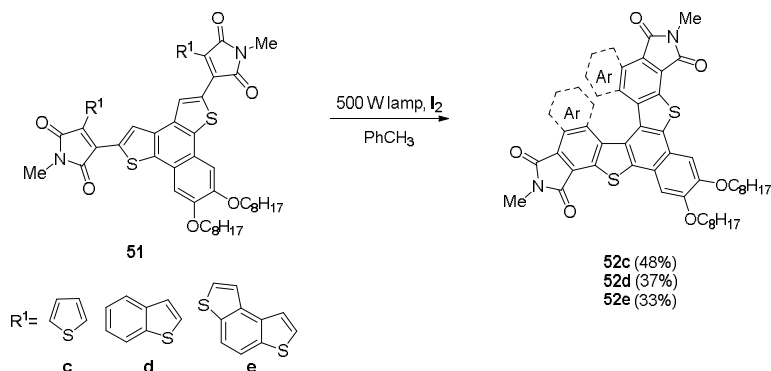
Scheme 20. Synthesis of [7],[9], and [11]helicenes using visible light.

Fluorinated phenanthrenoids **54a-b** were obtained by irradiation of derivatives **43a-b** with light at $\lambda=365$ nm using iodide (0.5 equiv.) and excess of 1,2-epoxybutane (Scheme 21). The polymerization of phenanthrenoids **54** by Suzuki-Miyaura coupling permits to obtain the fluoropolymers **55** and **56** (Figure 10).[85]
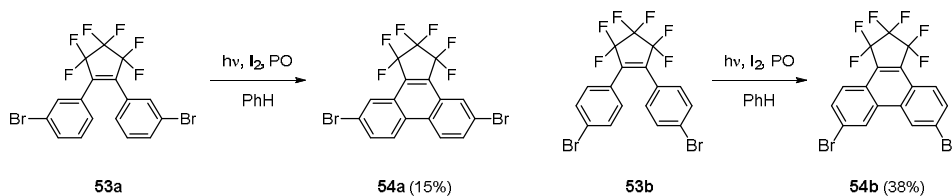
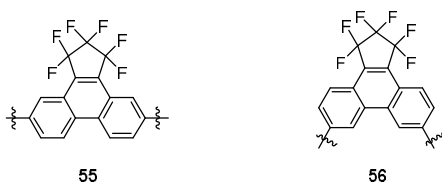**Scheme 21.** Synthesis of fluoromonomers using light irradiation.


Figure 10. Fluoropolymers.

The substitution, in the polycyclic aromatic compounds, of several carbon atoms by other elements permits the modulation of properties of these compounds. Boron-containing compounds was recently used in material science because the changes of certain carbon atoms by boron modifies the electronic properties without altering geometrical properties.[86]

The BN-polyaromatic heterocycle **58** are prepared by irradiation of compound **57** with light (280-400 nm) using 3 equivalents of iodine as oxidant and THF as HI scavenger. Hydrolysis of compound **58** gives the B_2N_2 dibenzoperylene **59** (Scheme 22).[87]
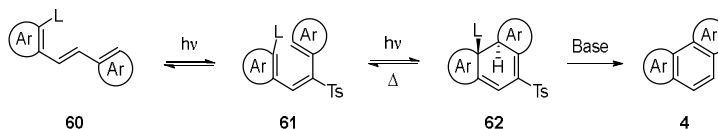
3. Photochemical cyclizations in the presence of a base

A variant of the classical Mallory reaction consists in the photocyclization, in the presence of a base, of a stilbene with a leaving group **60** and **61**, usually Cl or Br, at the ortho position of the phenyl ring. In this

case, the phenanthrene **4** is obtained by elimination of HL from the intermediate substituted dihydrophenathrene **62**[19,88] (Scheme 23).
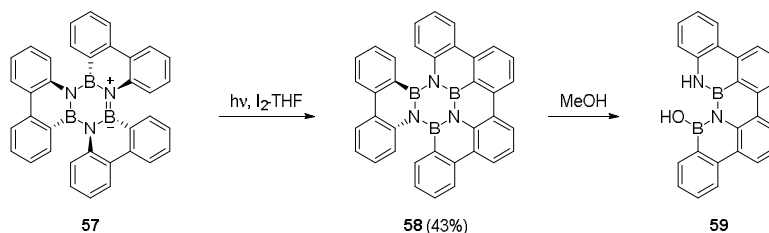


Scheme 22. Synthesis of perylene motif by photocyclization.

Scheme 23. Photocyclization of stilbenes and stilbenoids in the presence of a base.

Another interesting modification involving the irradiation of a stilbene containing a sulfonyl group linked to the central double bond, in the presence of a base.[89] In this method, the irradiation of a tosylstilbene **63**, **64** leads to a tosyldihydrophenanthrene **65** that evolves to the phenanthrene **4** by a base-induced removal of *p*-toluenesulfinic acid (Scheme 24).
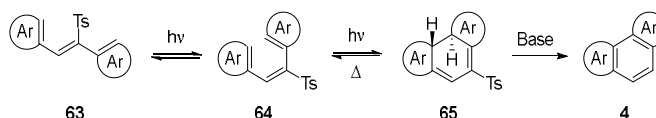
Scheme 24. Photocyclization of stilbenes with a leaving group in the central double bond in basic medium.

The photocyclization of stilbenes and stilbenoids in basic medium has been used for the synthesis of variety type of compounds in diverse fields, as bioscience or functional materials. Then, we explain some examples.

### 3.1. Application for the synthesis of molecules with biological properties

As we have mentioned, the indolocarbazole nucleus is present in numerous bioactive compounds,[33,34] as K-252 A[37] (Figure 1).

In the stereocontrolled total synthesis of (+)-K252A, the intermediate skeleton **67** was obtained in quantitative yield by photochemical cyclization of precursor **66** using sunlight and di-isopropylethylamine (Scheme 25). Different transformations of compound **67** conduce to the (+)-K252A. This methodology can be applied to the synthesis of diverse derivatives of (+)-K252A.[90]

The CC-1065 analogue **68** (Figure 11) presents a benzoindolic skeleton whit a methoxy group located nearby to the alkylating cyclopropane unit. In the synthesis of this compound, the irradiation of stilbenoid **69** with a medium pressure mercury lamp, in the presence of 5 equivalents of DBU, afford the phenanthrenoid **70** in 98% of yield (Scheme 26).[89,9]This methodology can be applied for the synthesis of diverse indole a phenathrene units.[54]

Quinoline scaffold is present in different compounds with a great variety of biological activities as antifungal, antibacterial, or antineoplastic.[92] This heterocyclic system can be prepared by irradiation of **71** with a 500 W medium pressure Hg lamp using O_2 as oxidant and pyridine as base in acetone. In this transformation, photochemical oxidative dehydrogenation of compound **72** give the intermediate **73** that

suffers a photocyclization to yield **74** that by the action of pyridine suffers a dehydrochlorination to give the quinolone derivatives **75** (Scheme 27).[93]
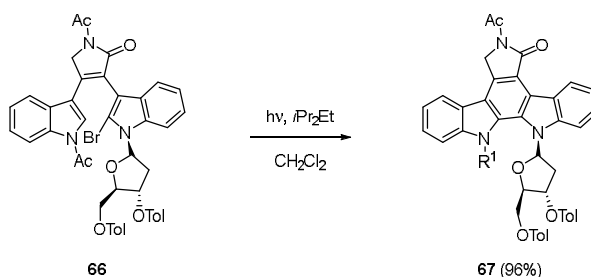
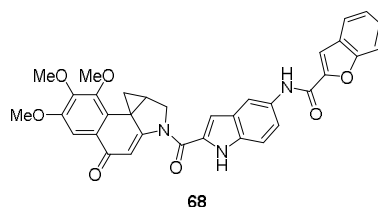**Scheme 25**. Photochemical synthesis of indolocarbazole unit using sunlight.

Figure 11. CC-1065 bulky analogue.
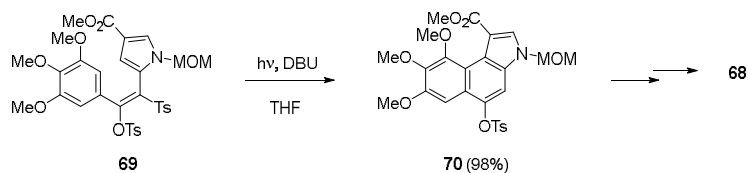
Scheme 26. Photocyclization of stilbenoinds in basic medium.
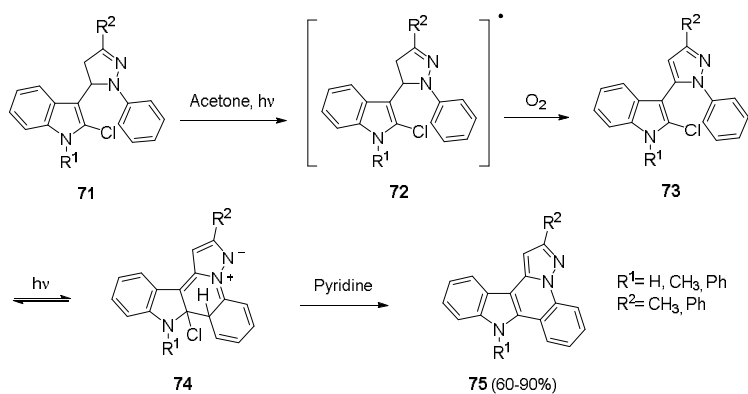
Scheme 27. Photochemical synthesis of quinolone derivatives.

3.2. Application for the design of new materials

Different nanographenes and graphene nanoribbons fragments **76-78** (Figure 12) were prepared by photochemical cyclization and dehydrochlorination of various aryl chlorides. In this strategy, different stilbenoids were irradiated with 16x7.2 W lamps @300 nm or 450 W medium pressure mercury lamps, in

acetone using a base, or in benzene, to give different nanographenes in excellent yields. Scheme 28 shows an example of this procedure.[94]

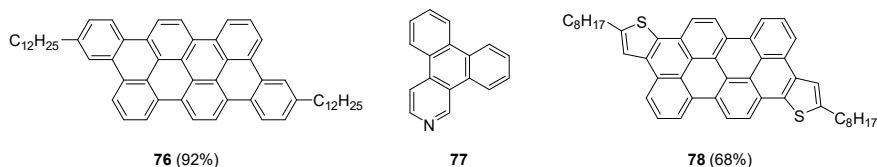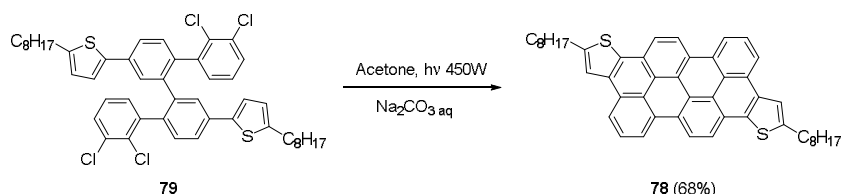**Figure 12**. Some examples of nanagraphenes prepared by photochemical cyclodehydrochlorination.

Scheme 28. Regioselective synthesis of π-conjugated molecules.

## 4. Cyclization/dehalogenations and related

Stilbenes and stilbenoids with a leaving group on the ortho position of one aromatic ring in **60** and **61** can be suffering a variant of Mallory photocyclization. Upon photocyclization, the intermediate **62** have an H atom situated at the adjacent carbon of the X group and suffers the loss of HL giving the phenanthrenes or phenanthrenoids **4** (Scheme 29).[95,96]

L= F, Cl, Br, I, OMe, etc...
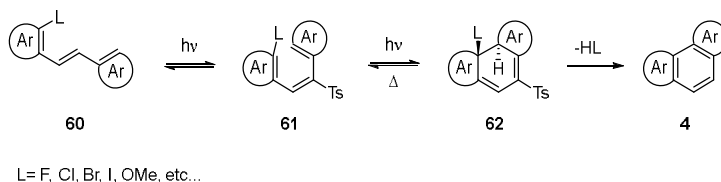
Scheme 29. Photocyclodehydrohalogenation reaction of stilbenes and stilbenoids.

In this type of photocyclization, neither photosensitizers nor base are necessaries. Different examples of this reaction will be explained.

A wide variety of fluorinated stilbenes and stilbenoids possessing a fluorine atom at the ortho position **80** are irradiated in absence of oxidant to give the corresponding phenanthrenes and phenanthrenoids **81** with loss of HF (Scheme 30). This reaction take place in acetonitrile or toluene, depending of the stilbene, in a Rayonette photochemical reactor prepared with 254 nm ultraviolet lamps. The photocyclodehidrofluorination (PCDHF) permitted to obtained selectively fluorinated polynuclear phenanthrenes with potential interest in materials science (Figure 13).[97]
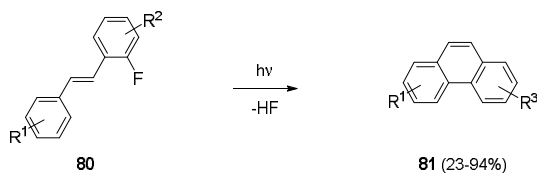
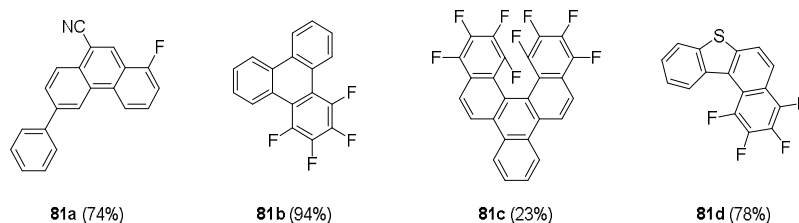**Scheme 30.** Photocyclodehidrofluorination.

Figure 13. Some examples of PCDHF.

Phenanthrene-fused thiophenes have are a type of compounds that presents numerous applications in material science, for example as organic light-emitting diodes or organic photovoltaics.[98,26]

Diverse thiophene derivatives **83** were synthesized by photocyclization of 3,4-diarylthiophenes **82**, in a solvent mixture of benzene and acetonitrile at λ=254 nm (Scheme 31). In this direct arylation, the position of the chlorine substituent defines the selectivity of the photocyclization. The reaction take place at room temperature in a RPR-100 reactor with sixteen lamps at λ=254 nm or λ=300 nm and the products are obtained with excellent yields.[99]
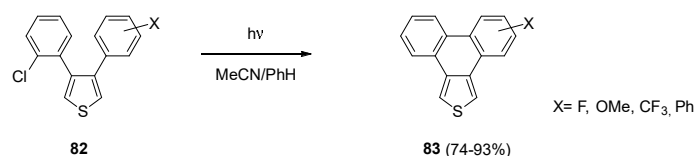
Scheme 31. Synthesis of 3,4-diarylthiophenes by photocyclization.

N-heteroaromatic systems are prevalent in many natural and synthetic biologically active compounds and also in materials science.[100,101] Phenanthridine scaffold are present in diverse compounds with a wide exhibition of biological activity, as, antifungal, antitumor, antibacterial, or cytotoxic activities.[102]

Irradiation of phenanthro[9,10-*d*]imidazoles **84** with UV-light (λ=254 nm) promote the intramolecular direct arylation of **78** yielding the formation of phenanthridines **85** (Scheme 32). This reaction take place in absence of oxidant or base and the products are obtained with high yields. This methodology permits the synthesis of different imidazophenanthridines that are blue-emitters, and presents strong fluorescence in solution.[103]
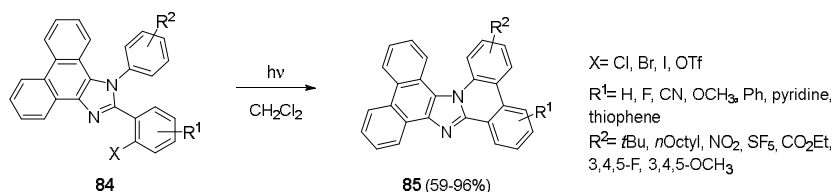
Scheme 32. Photochemical arylation of phenanthro[9,10-*d*]-imidazoles.

This procedure was applied for the synthesis of higher aromatic systems. For example, phenanthro[9′,10′:4,5]imidazo[1,2-*f*]-phenanthridines **87** and **88** was synthetized by irradiation of phenanthro[9,10-*d*]-imidazoles **86** with a 2-halogenoaryl substituent (Scheme 33).[103]

Substituted phenanthridines **93** can be prepared from derivatives **89** by a photocyclization that involves the loose of a halogen (Scheme 34). In the proposed mechanism, compounds **89** suffers the photoinduced loos of a halogen generating the intermediate radical **90** that cycle to give the radical **91** that evolves to yield the dihydropenanthridine derivative **92**. *In situ* oxidation of **92** gives different phenanthridine derivatives **93** up to 95% yield.[104]

Scheme 33. Synthesis of phenanthro[9′,10′:4,5]imidazo[1,2-*f*]-phenanthridines.
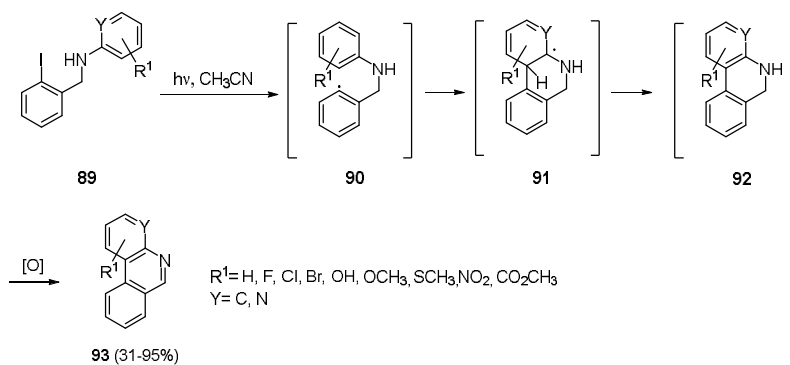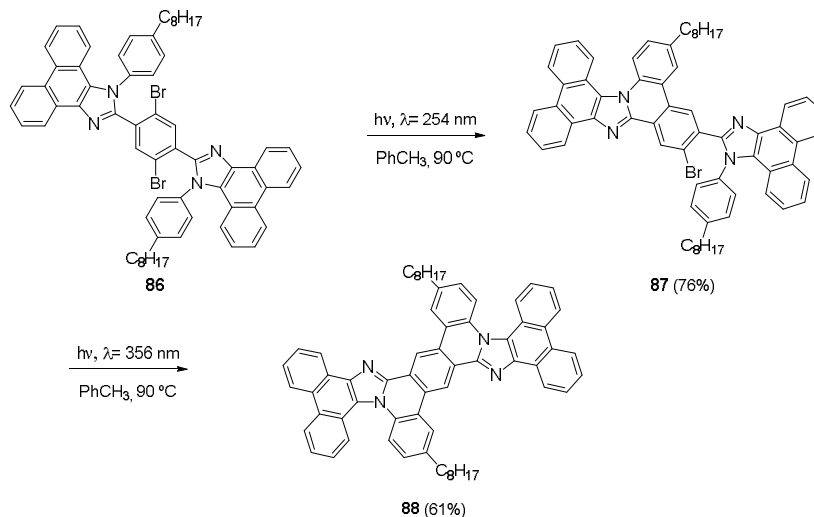
Scheme 34. Synthesis of phenanthridine derivatives.

This strategy has been used for the irradiation of isoxazol **94a** and oxazine **94b** to give phenanthridines **95a** and **95b**, respectively (Figure 14).

Figure 14. Photocyclization performance of sensitive heterocylic systems.
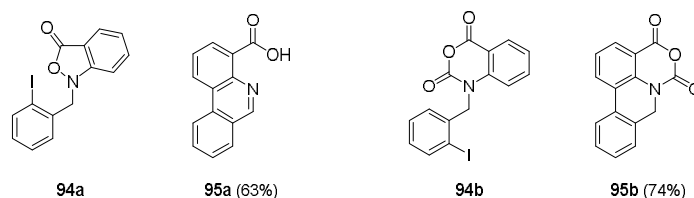
π-Conjugated thiophene-based compounds presents numerous applications in materials science.[105] [1]Benzothieno[3,2-*b*][1]benzothiophene derivatives (BTBTs) **98** was prepared by a photolysis of methyl-thiophenyl bromides **96** that afforded the vinyl radicals **97** that cyclized *in situ* to yield benzothiophenes **98** (Scheme 35). Diverse benzothieno-benzothiophene derivatives **98** are obtained by irradiation of **96** in dichloromethane with a high-pressure mercury lamp.[106] Some examples are indicated in Figure 15.

Scheme 35. Synthesis of 3,4-diarylthiophenes by photocyclization.
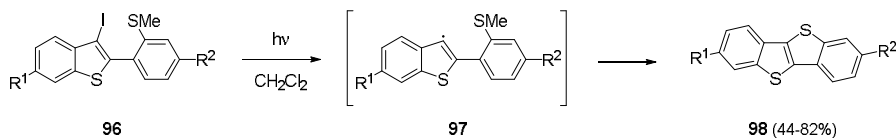
R^1 and R^2= H, Cl, CH$_3$, tBu, OCH$_3$, CO$_2$Ph, CO$_2$CH$_3$ in different combination

98a BTBT (64%)   98b (70%)   98c (82%)   98d (74%)

Figure 15. Some examples of BTBTs.

Pyrazole and its derivatives constitute one of the most important class of heterocycles due to their wide using areas.[107]

The photocyclization of 3,4-diaryl-1H-pyrazoles **99** gave the dihidydrophenathrenoids **100** that dehydrated to give the 2H-phenanthro[9,10-c]pyrazoles **101** (Scheme 36). The photocyclization was carried out in a mixture of EtOH-H$_2$O using a medium-pressure mercury lamp (500 W) under an argon atmosphere.[108]
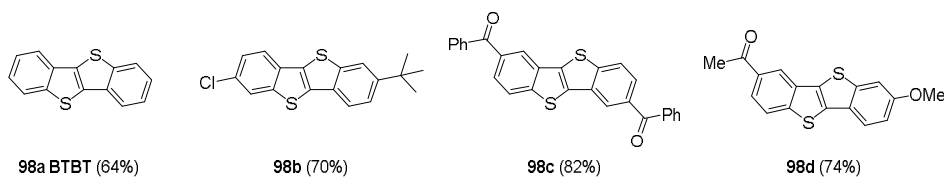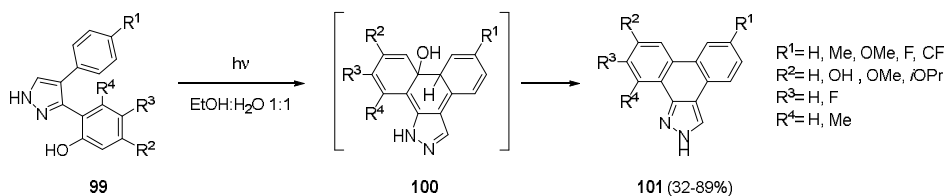

R^1= H, Me, OMe, F, CF
R^2= H, OH , OMe, iOPr
R^3= H, F
R^4= H, Me

Scheme 36. Photochemical synthesis of 2H-phenanthro[9,10-c]pyrazoles.

Carbazole scaffold is present in a multiple compounds with applications in biomedicine and materials science.[109,110] Benzocarbazole derivatives **104** was prepared by photocyclization/dehydratation of indoles **102** (Scheme 37). Some examples of diverse polyaromatic compounds **104** are indicated in Figure 16. The photocyclization take place in moderate yields using a Vilber Lourmat VL-6.LM lamp (365 nm, 6 W) in N-methyl-2-pyrrolidone.[111]
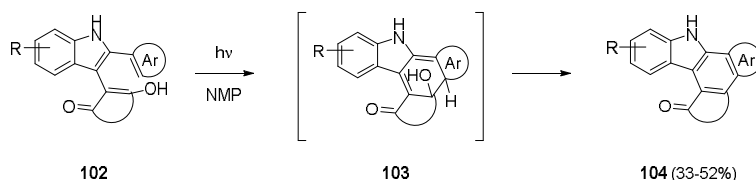
Scheme 37. Synthesis of benzocarbazole scaffolds.

A similiar reaction permits the synthesis of benzo[H]-naphth[1,2-f]quinazolines and benzo[H]-phenanthren[9,10-f]quinazoines **106** by photocyclization and dehydration of hydroxyphenyl-pyrimidines derivatives **105** (Scheme 38). The photocyclization occurs by irradiation of **99** with a high-pressure mercury lamp in a mixture of EtOH:H$_2$O or EtOH:H$_2$O:dioxane.[112]

Figure 16. Some benzocarbazoles prepared by photocyclization.

Scheme 38. Polybenzoquinazolines by photocyclization of hydroxyphenyl -pyrimidines.
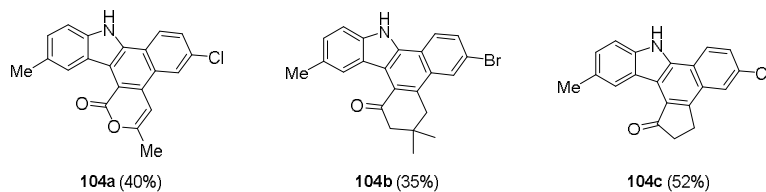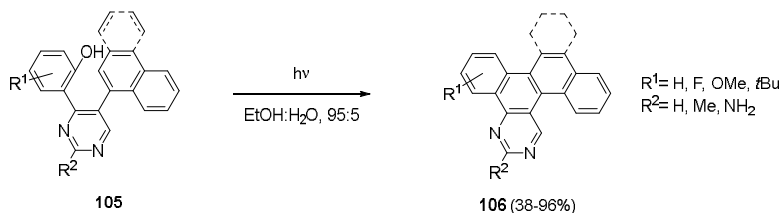
5. Miscellaneous

Recently, Lvov and col. have reported a novel photochemical process that consists in a 6π electrocyclization of diarylethenes **107** to give naphthalene amide **110**. Initially, the irradiation of stilbenoids **107** gave the dihydrophenanthrenoid **108** that suffers two sequential 1,9- and 1,3-hydrogen shifts and ring opening to the afford the product **110** (Scheme 39). The photochemical reaction take place in CDCl$_3$ in a quartz vessel using UV-light (λ=365 nm, 6W).[113]
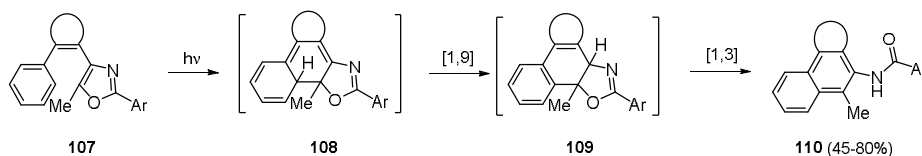
Scheme 39. Photoreaction of diarylethenes.

In a similar approach, the irradiation of diverse diarylethenes **111** (Figure 17) permits the synthesis of functionalized naphthalene derivatives **112**, in good yields (45-90%), by a 6π-cyclization followed by a sigmatropic rearrangement. Some examples of naphthalene derivatives are indicated in Figure 17.[114]
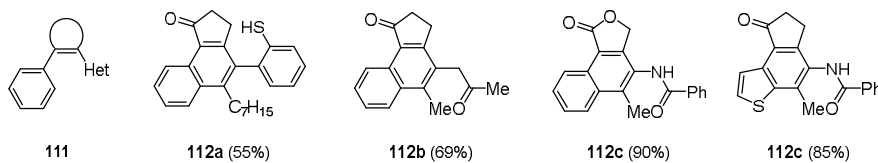
Figure 17. Naphthalene derivatives obtained by photocyclization of diarylethenes.

Another interesting photochemical promoted cyclization is the synthesis of indolines **117** from enamines **113**. The irradiation with visible light of enamines **113**, using Ir(ppy)$_3$ as photosensitizer, generate the excited triplet state **114** that by an electrocyclization gave the diradical **115** that evolving the zwitterionic intermediate **116**, which leads to the indoline **117** by 1,2-hydrogen shifts (Scheme 40). Some examples of obtained indoline derivatives are indicating in Figure 18.[115] Indolines **117** are obtained in highest yields and high diastereoselectivity.

Other example of fused heterocyclic systems obtained by a 6π cyclization mediated by light and iridium photosensitizer is indicated in Scheme 41. In this approach, the irradiation of enones **118** with 12 W

blue LED with Ir(Fppy)$_3$ (0.05 mol%) generated the intermediate **119** that evolves to the final product **121** by a hydrogen sigmatropic transposition followed by an epimerization. Quantum calculation with the model **122** (Figure 19) demonstrates that the reaction take place thought the triplet excited state **119**.[116] Some examples of dihydrobenzofurans, dihydroindoles and dihydrothiophenes synthetized using this strategy are indicated in Figure 19.

Scheme 40. Synthesis of indolines by photocyclization.

117a (70%), 4,0:1 dr *trans/cis*   **117b** (78%), 19:1 dr   **117c** (72%), 4:1 dr   **117c** (62%),4:1 dr

Figure 18. Some examples of isoindolines.

118   **119**   **120**   **121** (23-96%), d.r. > 20:1
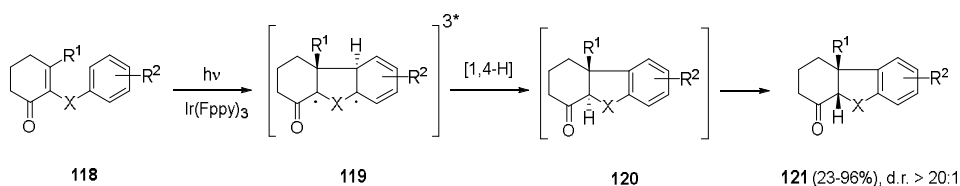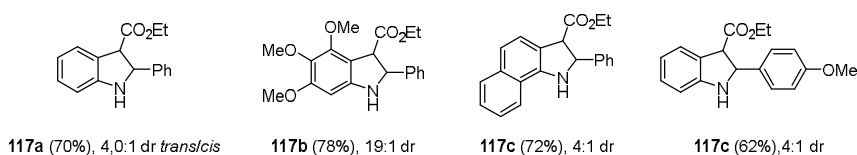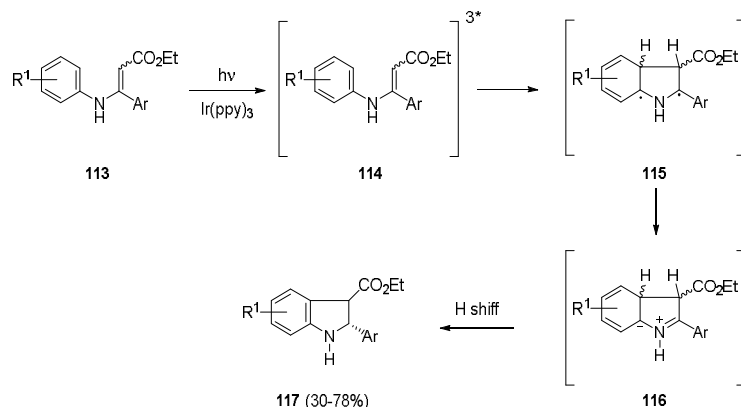
X= O, S, NR
R^1= H, Me, Et, CH$_2$Ph
R^2= F, Cl, Br, I, Me, OMe, Allyl, CF$_3$, CO$_2$Et, NMe$_2$

Scheme 41. Photocyclization of enones whit visible and iridium photosensitizer.

122   **121a** (93%)   **121b** (91%)   **121c** (77%)

Figure 19. Model of quantum calculations and examples of heterocyclic ring systems synthetized.
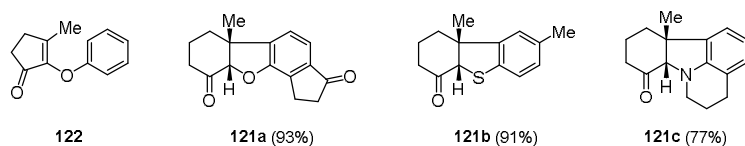
In a recent photochemical reaction reported by Bach,[117] *cis*-hexahydrocarbazol-4-ones **126** were synthetized from *N*-alkoxycarbonyl-*N*-aryl-β-enaminones **123**. In this process, upon irradiation at λ=366 nm, enaminones **123** suffers a 6π-photocyclization to give the intermediate **124**. This zwitterion experiment a [1,4] hydrogen migration to afford the *trans*-hexahydrocarbazol-4-ones **125** that epimerize to yield the

cis-hexahydrocarbazol-4-ones **126** (Scheme 42). The reaction takes place in CH_2Cl_2 and the epimerization occurs in silica, yielding the products **126** in moderate to excellent yields (44−98%)

123   **124**   **125**   **126** (44-98%)
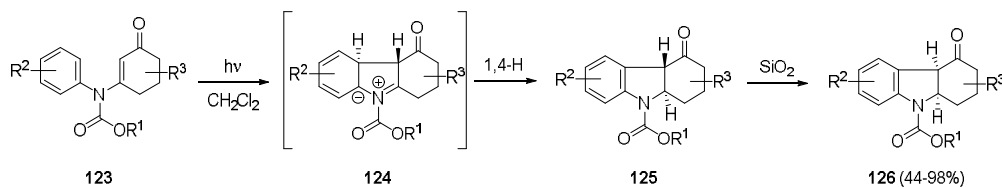
Scheme 42. Preparation of *cis*-hexahydrocarbazol-4-ones.

Carbazole is a prevalent scaffold in diverse natural and synthetic molecules with a great variety of applications.[118] The irradiation of diarylamines and triarylamines **127** with visible light, Cu catalyst, iodine (1 equivalent) and a HI scavenger in continuous flow permits the preparation of *N*-aryl- and *N*-alkyl-bearing carbazoles **128** (Scheme 43).[119]

127   **128** (50-95%) R^1= Alkyl, Aryl
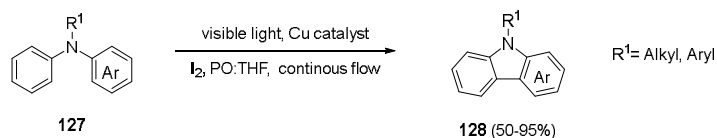
Scheme 43. Photochemical synthesis of carbazoles.

The first 6π-photocyclization of dienynes catalized by $Cu(OTf)_2$ is depicted in Scheme 44. In this procedure, coordination of dienynes **129** with Cu(II) gave intermediate **130** that cyclized to produce **131** which suffered a [1,5-H] shift to afforded **132**, and finally, dissociation of Cu(II) conduced to phenanthrene product **133**. This mechanism is supported by computer calculations. All reactions were carried using ultraviolet light (λ=254 nm) in dicholoromethane under argon atmosphere.[120]
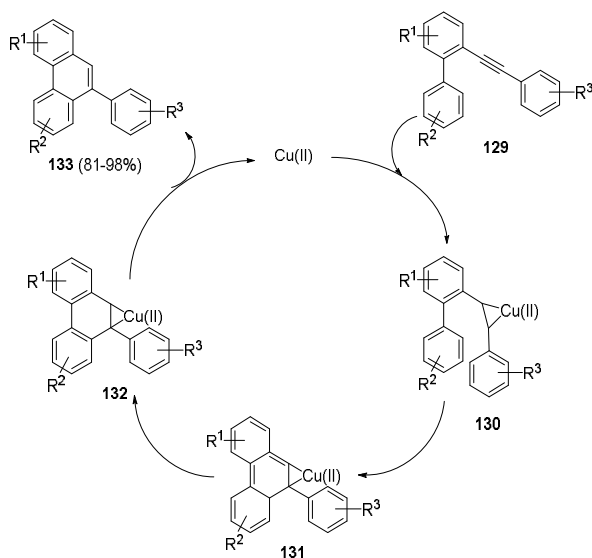
Scheme 44. 6π-Photocyclization of dienynes.

α,α′-Diaryl ketone scaffold is present in a great variety of compounds with applications in pharmaceutical chemistry [121] and materials science.[122] This nucleus can be synthetized by a photocyclization and rearrangement. Accordingly, the irradiation of (*E*)-3-arylvinyl-4*H*-chromen-4-ones **134** with high-pressure mercury lamp (500 W) in ethanol produce a conrotatory 6π-electrocyclization to give the intermediate **135** that suffers a 1,9 migration of hydrogen to give **136**. The *in sit*u aromatization of compound **136** yield the α,α′-diaryl ketone derivatives **137** (Scheme 45). This photoinduced rearrangement takes place in good yields under Ar atmosphere.[123]

R^1= H, F, Cl, CH$_3$
Ar= Ph, naphthalene, furan, thiophene
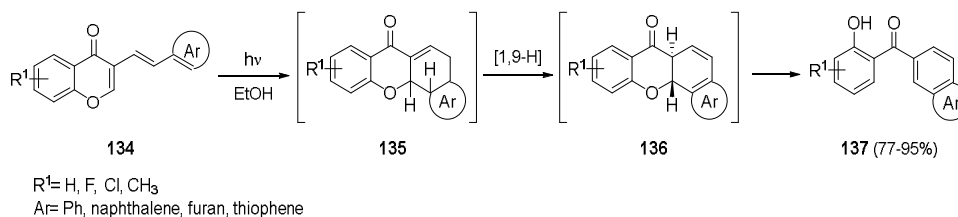
Scheme 45. Photoinduced rearrangement of arylvinylchromenones.

6. Conclusion

Photochemical cyclizations are a potent tool for the synthesis of diverse heterocycles with applications in different fields. This type of reactions permits the formation of bonds that in thermal conditions in not possible to obtain.

Photocyclization in oxidative conditions, in the presence of a base, eliminatives or photocyclizations followed by a rearrangement permit the access of multiple skeletons as phenanthrenes, phenanthrenoids, phenanthridines, indoles, cabarzoles, and diverse expanded π-electron systems. Also, these processes are green, experimentally very simple with tolerance to diverse functional groups and also preceded whit high atom efficiency.

However, despite all the reactions that have been discovered, new photocyclizations continues investigated in order to obtain higher efficient and ecofriendly processes.

References
1. Albini, A.; Dichiarante, V. *Photochem. Photobiol. Sci.* **2009**, *8*, 248-254.
2. Roth, H. D. *Angew. Chem. Int. Ed.* **1989**, *28*, 1193-1207.
3. Oelgemöller, M. *Chem. Rev.* **2016**, *116*, 9664-9682.
4. Protti, S.; Dondi, D.; Fagnoni, M.; Albini, A. *Green Chem.* **2009**, *11*, 239-249.
5. Beeler, A. B. *Chem. Rev.* **2016**, *116*, 9629-9630.
6. Neckers, D. C.; Cai, X. *Annual Reports Section "B" (Organic Chemistry)* **2009**, *105*, 380-397.
7. Dekeukeleire, D.; He, S. L. *Chem. Rev.* **1993**, *93*, 359-380.
8. Bach, T.; Hehn, J. P. *Angew. Chem. Int. Ed.* **2011**, *50*, 1000-1045.
9. Griesbeck, A. G.; Henz, A.; Hirt, J. *Synthesis* **1996**, *1996*, 1261.
10. Meier, H.; Cao, D. *Chem. Soc. Rev.* **2013**, *42*, 143-155.
11. Hoffmann, N. *J. Photochem. Photobiol. C-Photochem. Rev.* **2014**, *19*, 1-19.
12. Schultz, D. M.; Yoon, T. P. *Science* **2014**, *343*, 1239176-1239176-8.
13. Hoffmann, N. *Chem. Rev.* **2008**, *108*, 1052-1103.
14. Laarhoven, W. H. *Recl. Trav. Chim. Pays-Bas* **1983**, *102*, 185-204.
15. Mallory, F. B.; Wood, C. S.; Gordon, J. T.; Lindquist, L. C.; Savitz, M. L. *J. Am. Chem. Soc.* **1962**, *84*, 4361-4362.
16. Lewis, G. N.; Magel, T. T.; Lipkin, D. *J. Am. Chem. Soc.* **1940**, *62*, 2973-2980.

17. Parker, C. O.; Spoerri, P. E. *Nature* **1950**, *166*, 603-603.
18. Buckles, R. E. *J. Am. Chem. Soc.* **1955**, *77*, 1040-1041.
19. Mallory, F. B.; Mallory, C. S., *Organic Reactions*. Wiley: New York, 1984; Vol. 30.
20. Jørgensen, K. B. *Molecules* **2010**, *15*, 4334-4358.
21. Bromberg, A.; Muszkat, K. A. *J. Am. Chem. Soc.* **1969**, *91*, 2860-2866.
22. Laarhoven, W. H.; Peters, W. H. M.; Tinnemans, A. H. A. *Tetrahedron* **1978**, *34*, 769-777.
23. Laarhoven, W. H. *Rec. Trav. Chim. Pays Bas* **1983**, *102*, 241-254.
24. Liu, L.; Yang, B.; Katz, T. J.; Poindexter, M. K. *J. Org. Chem.* **1991**, *56*, 3769-3775.
25. Antelo, B.; Castedo, L.; Delamano, J.; Gómez, A.; López, C.; Tojo, G. *J. Org. Chem.* **1996**, *61*, 1188-1189.
26. Anthony, J. E. *Chem. Rev.* **2006**, *106*, 5028-5048.
27. Kovács, A.; Vasas, A.; Hohmann, J. *Phytochem.* **2008**, *69*, 1084-1110.
28. Tóth, B.; Hohmann, J.; Vasas, A. *J. Nat. Prod.* **2018**, *81*, 661-678.
29. Meier, H. *Angew. Chem. Int. Ed.* **1992**, *31*, 1399-1420.
30. Iuliano, A.; Piccioli, P.; Fabbri, D. *Org. Lett.* **2004**, *6*, 3711-3714.
31. Bu, M.-j.; Lu, G.-p.; Cai, C. *Org. Chem. Front.* **2016**, *3*, 630-634.
32. Mamane, V.; Hannen, P.; Fürstner, A. *Chem. Eur. J.* **2004**, *10*, 4556-4575.
33. Sánchez, C.; Méndez, C.; Salas, J. A. *Nat. Prod. Rep.* **2006**, *23*, 1007-1045.
34. Li, T.; Du, Y.; Cui, Q.; Zhang, J.; Zhu, W.; Hong, K.; Li, W. *Marine drugs* **2013**, *11*, 466-488.
35. Nettleton, D. E.; Doyle, T. W.; Krishnan, B.; Matsumoto, G. K.; Clardy, J. *Tetrahedron Lett.* **1985**, *26*, 4011-4014.
36. Omura, S.; Iwai, Y.; Hirano, A.; Nakagawa, A.; Awaya, J.; Tsuchiya, H.; Takahashi, Y.; Masuma, R. *J. Antibiot.* **1977**, *30*, 275-282.
37. Kase, H.; Iwahashi, K.; Matsuda, Y. *J. Antibiot.* **1986**, *39*, 1059-1065.
38. Kaneko, T.; Wong, H.; Okamoto, K. T.; Clardy, J. *Tetrahedron Lett.* **1985**, *26*, 4015-4018.
39. Gallant, M.; Link, J. T.; Danishefsky, S. J. *J. Org. Chem.* **1993**, *58*, 343-349.
40. Messaoudi, S.; Anizon, F.; Peixoto, P.; David-Cordonnier, M.-H.; Golsteyn, R. M.; Léonce, S.; Pfeiffer, B.; Prudhomme, M. *Bioorg. Med. Chem.* **2006**, *14*, 7551-7562.
41. Link, J. T.; Raghavan, S.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1995**, *117*, 552-553.
42. Li, Y.; Pang, Z.; Zhang, T.; Yang, J.; Yu, W. *Tetrahedron* **2015**, *71*, 3351-3358.
43. Nakanishi, T.; Suzuki, M. *J. Nat.l Prod.* **1998**, *61*, 1263-1267.
44. Yu, Y.; Cai, Z.; Yuan, W.; Liu, P.; Sun, P. *J. Org. Chem.* **2017**, *82*, 8148-8156.
45. Wang, R.; Lu, S. C.; Zhang, Y. M.; Shi, Z. J.; Zhang, W. *Org. Biomol. Chem.* **2011**, *9*, 5802-5808.
46. Hanka, L. J.; Dietz, A.; Gerpheide, S. A.; Kuentzel, S. L.; Martin, D. G. *J. Antibiot.* **1978**, *31*, 1211-1217.
47. Boger, D. L.; Garbaccio, R. M. *Acc. Chem. Res.* **1999**, *32*, 1043-1052.
48. Reynolds, V. L.; Kaplan, D. J.; Hurley, L. H.; Molineux, I. J.; Swenson, D. H. *Biochemistry* **1985**, *24*, 6228-6237.
49. McGovren, J. P.; Clarke, G. L.; Pratt, E. A.; Dekoning, T. F. *J. Antibiot.* **1984**, *37*, 63-70.
50. Lutz, F. T.; Birgit, K. *Anti-Cancer Agents Med. Chem.* **2009**, *9*, 304-325.
51. Castedo, L.; Delamano, J.; Enjo, J.; Fernández, J.; Grávalos, D. G.; Leis, R.; López, C.; Marcos, C. F.; Ríos, A.; Tojo, G. *J. Am. Chem. Soc.* **2001**, *123*, 5102-5103.
52. Enjo, J.; Castedo, L.; Tojo, G. *Org. Lett.* **2001**, *3*, 1343-1344.
53. Neo, A. G.; López, C.; López, A.; Castedo, L.; Tojo, G. *Tetrahedron* **2013**, *69*, 11010-11016.
54. Neo, A. G.; López, C.; Romero, V.; Antelo, B.; Delamano, J.; Pérez, A.; Fernández, D.; Almeida, J. F.; Castedo, L.; Tojo, G. *J. Org. Chem.* **2010**, *75*, 6764-6770.
55. Tian, T.; Chen, Y.-Q.; Wang, S.-R.; Zhou, X. *Chem* **2018**, *4*, 1314-1344.
56. Asamitsu, S.; Bando, T.; Sugiyama, H. *Chem. Eur. J.* **2019**, *25*, 417-430.
57. Altieri, A.; Alvino, A.; Ohnmacht, S.; Ortaggi, G.; Neidle, S.; Nocioni, D.; Franceschin, M.; Bianco, A. *Molecules* **2013**, *18*, 13446-13470.
58. Franceschin, M.; Nocioni, D.; Biroccio, A.; Micheli, E.; Cacchione, S.; Cingolani, C.; Venditti, A.; Zizza, P.; Bianco, A.; Altieri, A. *Org. Biomol. Chem.* **2014**, *12*, 9572-9582.

59. Chen, M.; Yang, C.; Wang, Y.; Li, D.; Xia, W. *Org. Lett.* **2016**, *18*, 2280-2283.
60. Matsushima, T.; Kobayashi, S.; Watanabe, S. *J. Org. Chem.* **2016**, *81*, 7799-7806.
61. Watson, M. D.; Fechtenkötter, A.; Müllen, K. *Chem. Rev.* **2001**, *101*, 1267-1300.
62. Jin, T.; Zhao, J.; Asao, N.; Yamamoto, Y. *Chem. Eur. J.* **2014**, *20*, 3554-3576.
63. Cinar, M. E.; Ozturk, T. *Chem. Rev.* **2015**, *115*, 3036-3140.
64. Verbitskiy, E. V.; Slepukhin, P. A.; Valova, M. S.; Cheprakova, E. M.; Schepochkin, A. V.; Rusinov, G. L.; Charushin, V. N. *Eur. J. Org. Chem.* **2014**, *79*, 8133-8141.
65. Tasior, M.; Kim, D.; Singha, S.; Krzeszewski, M.; Ahn, K. H.; Gryko, D. T. *J. Mat. Chem. C* **2015**, *3*, 1421-1446.
66. Weclawski, M. K.; Tasior, M.; Hammann, T.; Cywinski, P. J.; Gryko, D. T. *Chem. Commun.* **2014**, *50*, 9105-9108.
67. Narita, A.; Wang, X.-Y.; Feng, X.; Müllen, K. *Chem. Soc. Rev.* **2015**, *44*, 6616-6643.
68. Bai, J.; Huang, Y. *Mat. Sci. Eng.: R: Reports* **2010**, *70*, 341-353.
69. Sisto, T. J.; Zhong, Y.; Zhang, B.; Trinh, M. T.; Miyata, K.; Zhong, X.; Zhu, X. Y.; Steigerwald, M. L.; Ng, F.; Nuckolls, C. *J. Am. Chem. Soc.* **2017**, *139*, 5648-5651.
70. Gingras, M. *Chem. Soc. Rev.* **2013**, *42*, 1051-1095.
71. Shen, Y.; Chen, C.-F. *Chem. Rev.* **2012**, *112*, 1463-1535.
72. Meisenheimer, J.; Witte, K. *Chem. Ber.* **1903**, *36*, 4153-4164.
73. Gingras, M. *Chem. Soc. Rev.* **2013**, *42*, 968-1006.
74. Gingras, M.; Félix, G.; Peresutti, R. *Chem. Soc. Rev.* **2013**, *42*, 1007-1050.
75. Hoffmann, N. *J. Photochem. Photobiol. C: Photochemi. Rev.* **2014**, *19*, 1-19.
76. Fujino, S.; Yamaji, M.; Okamoto, H.; Mutai, T.; Yoshikawa, I.; Houjou, H.; Tani, F. *Photochem. Photobiol. Sci.* **2017**, *16*, 925-934.
77. Mori, K.; Murase, T.; Fujita, M. *Angew. Chem. Int. Ed.* **2015**, *54*, 6847-6851.
78. Nestoros, E.; Stuparu, M. C. *Chem. Commun.* **2018**, *54*, 6503-6519.
79. Rajeshkumar, V.; Stuparu, M. C. *Chem. Commun.* **2016**, *52*, 9957-9960.
80. Brooke, G. M. *J. Fluorine Chem.* **1997**, *86*, 1-76.
81. Církva, V.; Jakubík, P.; Strašák, T.; Hrbáč, J.; Sýkora, J.; Císařová, I.; Vacek, J.; Žádný, J.; Storch, J. *J. Org. Chem.* **2019**, *84*, 1980-1993.
82. Bucinskas, A.; Waghray, D.; Bagdziunas, G.; Thomas, J.; Grazulevicius, J. V.; Dehaen, W. *J. Org. Chem.* **2015**, *80*, 2521-2528.
83. Waghray, D.; Dehaen, W. *Org. Lett.* **2013**, *15*, 2910-2913.
84. Ameduri, B. *Chem. Eur. J.* **2018**, *24*, 18830-18841.
85. Fukumoto, H.; Ando, M.; Shiota, T.; Izumiya, H.; Kubota, T. *Macromolecules* **2017**, *50*, 865-871.
86. Campbell, P. G.; Marwitz, A. J. V.; Liu, S.-Y. *Angew. Chem. Int. Ed.* **2012**, *51*, 6074-6092.
87. Müller, M.; Behnle, S.; Maichle-Mössmer, C.; Bettinger, H. F. *Chem. Commun.* **2014**, *50*, 7821-7823.
88. Lewis, F. D.; Kalgutkar, R. S.; Yang, J.-S. *J. Am. Chem. Soc.* **2001**, *123*, 3878-3884.
89. Almeida, J. F.; Castedo, L.; Fernandez, D.; Neo, A. G.; Romero, V.; Tojo, G. *Org. Lett.* **2003**, *5*, 4939-4941.
90. Kobayashi, Y.; Fujimoto, T.; Fukuyama, T. *J. Am. Chem. Soc.* **1999**, *121*, 6501-6502.
91. Neo, A. G.; Pérez, A.; López, C.; Castedo, L.; Tojo, G. *J. Org. Chem.* **2009**, *74*, 3203-3206.
92. Musiol, R.; Jampilek, J.; Kralova, K.; Richardson, D. R.; Kalinowski, D.; Podeszwa, B.; Finster, J.; Niedbala, H.; Palka, A.; Polanski, J. *Bioorg. Med. Chem.* **2007**, *15*, 1280-1288.
93. Zhang, Y.; Wang, R.; Shi, Z.; Zhang, W. *Synthesis* **2011**, *2011*, 1711-1716.
94. Daigle, M.; Picard-Lafond, A.; Soligo, E.; Morin, J. F. *Angew. Chem. Int. Ed.* **2016**, *55*, 2042-2047.
95. Lenz, G. R. *J. Org. Chem.* **1974**, *39*, 2839-2845.
96. Mallory, F. B.; Mallory, C. W. *J. Org. Chem.* **1983**, *48*, 526-532.
97. Li, Z.; Twieg, R. J. *Chem. Eur. J.* **2015**, *21*, 15534-15539.
98. Perepichka, I. F.; Perepichka, D. F., *Handbook of Thiophene-Based Materials*. 2009.
99. Schnapperelle, I.; Bach, T. *Chem. Eur. J.* **2014**, *20*, 9725-9732.
100. Koch, M. A.; Schuffenhauer, A.; Scheck, M.; Wetzel, S.; Casaulta, M.; Odermatt, A.; Ertl, P.; Waldmann, H. *Proc Natl Acad Sci U S A* **2005**, *102*, 17272-17277.

101. Gao, Z.; Liu, Y.; Wang , Z.; Shen, F.; Liu, H.; Sun, G.; Yao, L.; Lv, Y.; Lu, P.; Ma, Y. *Chem. Eur. J.* **2013**, *19*, 2602-2605.
102. Krane, B. D.; Fagbule, M. O.; Shamma, M.; Gözler, B. *J. Nat. Prod.* **1984**, *47*, 1-43.
103. Skonieczny, K.; Gryko, D. T. *J. Org. Chem.* **2015**, *80*, 5753-5763.
104. Linsenmeier, A. M.; Williams, C. M.; Bräse, S. *J. Org. Chem.* **2011**, *76*, 9127-9132.
105. Takimiya, K.; Osaka, I.; Mori, T.; Nakano, M. *Acc. Chem. Res.* **2014**, *47*, 1493-1502.
106. Kitamura, T.; Morita, K.; Nakamori, H.; Oyamada, J. *J. Org. Chem.* **2019**, *84*, 4191-4199.
107. Elguero, J., *Comprehensive Heterocyclic Chemistry III,* Pergamon Press, Elsevier Sci.: Tarrytown, NY, 1996; Vol. III.
108. Wang, Q.; Zhang, Z.; Du, Z.; Hua, H.; Chen, S. *Green Chem.* **2013**, *15*, 1048-1054.
109. Schmidt, A. W.; Reddy, K. R.; Knölker, H.-J. *Chem. Rev.* **2012**, *112*, 3193-3328.
110. Chen, Q.; Liu, D.-P.; Luo, M.; Feng, L.-J.; Zhao, Y.-C.; Han, B.-H. *Small* **2014**, *10*, 308-315.
111. Melekhina, V. G.; Mityanov, V. S.; Lichitsky, B. V.; Komogortsev, A. N.; Lyssenko, K. A.; Krayushkin, M. M. *Eur. J. Org. Chem.* **2019**, *2019*, 1335-1340.
112. Wei, W.; Li, C.; Wang, T.; Liu, D.; Zhang, Z. *Tetrahedron* **2016**, *72*, 5037-5046.
113. Lvov, A. G.; Shirinian, V. Z.; Kachala, V. V.; Kavun, A. M.; Zavarzin, I. V.; Krayushkin, M. M. *Org. Lett.* **2014**, *16*, 4532-4535.
114. Lvov, A. G.; Shirinian, V. Z.; Zakharov, A. V.; Krayushkin, M. M.; Kachala, V. V.; Zavarzin, I. V. *J. Org. Chem.* **2015**, *80*, 11491-11500.
115. Wu, C.-J.; Cao, W.-X.; Lei, T.; Li, Z.-H.; Meng, Q.-Y.; Yang, X.-L.; Chen, B.; Ramamurthy, V.; Tung, C.-H.; Wu, L.-Z. *Chem. Commun.* **2017**, *53*, 8320-8323.
116. Munster, N.; Parker, N. A.; van Dijk, L.; Paton, R. S.; Smith, M. D. *Angew. Chem. Int. Ed.* **2017**, *56*, 9468-9472.
117. Modha, S. G.; Pöthig, A.; Dreuw, A.; Bach, T. *J. Org. Chem.* **2019**, *84*, 1139-1153.
118. Roy, J.; Jana, A. K.; Mal, D. *Tetrahedron* **2012**, *68*, 6099-6121.
119. Hernandez-Perez, A. C.; Collins, S. K. *Angew. Chem. Int. Ed.* **2013**, *52*, 12696-12700.
120. Jin, R.; Chen, J.; Chen, Y.; Liu, W.; Xu, D.; Li, Y.; Ding, A.; Guo, H. *J. Org. Chem.* **2016**, *81*, 12553-12558.
121. Sahu, N. K.; Balbhadra, S. S.; Choudhary, J.; Kohli, D. V. *Curr. Med. Chem.* **2012**, *19*, 209-225.
122. Perez-Prieto, J.; Galian, R.; Miranda, M. *Mini-Rev. Org. Chem.* **2006**, *3*, 117-135.
123. Fan, J.; Wang, T.; Li, C.; Wang, R.; Lei, X.; Liang, Y.; Zhang, Z. *Org. Lett.* **2017**, *19*, 5984-5987.