SPIROLACTAMS AND THEIR SYNTHESIS

Inventors: Pedro Noheda Marin, Madrid (ES); Manuel Bernabe Pajares, Madrid (ES); Sergio Maroto Quintana, Madrid (ES); Nuria Tabares Cantero, Madrid (ES)

Correspondence Address:
MORGAN & FINNEGAN, L.L.P.
3 WORLD FINANCIAL CENTER
NEW YORK, NY 10281-2101 (US)

Assignee: LABORATORIOS DEL DR. ESTEVE, S.A., Barcelona (ES)

Appl. No.: 11/568,897
PCT Filed: May 10, 2005
PCT No.: PCT/EP05/05146
§ 371(c)(1), (2), (4) Date: Nov. 2, 2007

Related U.S. Application Data
Continuation-in-part of application No. 11/047,860, filed on Feb. 1, 2005, and which is a continuation-in-part of application No. 10/853,639, filed on May 25, 2004, now Pat. No. 7,297,788, and which is a continuation-in-part of application No. 10/846,466, filed on May 14, 2004, now Pat. No. 7,291,728.

Foreign Application Priority Data
May 10, 2004 (ES) .................................. P200401123
May 10, 2004 (EP) .................................. 04380104.2
May 20, 2004 (EP) .................................. 04076477.1
May 27, 2004 (ES) .................................. P200401285
Dec. 30, 2004 (EP) .................................. 04380295.8

Publication Classification
Int. Cl. C07D 205/12 (2006.01)
U.S. Cl. .............................................. 548/952

ABSTRACT
New spirolactams of formula (I) having a cycloexadienone moiety which are highly stable due to pi interactions between the W group and the dienone moiety. They are useful as UV absorbers and as intermediates for the synthesis of active biomolecules.
SPIROLACTAMS AND THEIR SYNTHESIS

FIELD OF THE INVENTION

[0001] The present invention relates to new spirolactam compounds, to synthetic processes and intermediate compounds for their preparation and to their use as UV absorbers.

BACKGROUND OF THE INVENTION

[0002] Lactams are compounds of high interest due to their biological activities, for example well known β-lactams such as some penicillins, cephalosporins and carbapenems have antibacterial activity.

[0003] Spirolactams are one particular class of lactams that have shown interesting biological properties. Some spiro-fused azetidinones have been described as having antibacterial activity, see U.S. Pat. No. 4,680,388, or hypcholesterolemic properties, see for example WO 94 17038. Additionally, if these compounds have the adequate functionality they are valuable intermediates towards different families of compounds. The spirolactam ring is the equivalent of an alpha amino or hydroxy aminoacid and opens many possibilities in diastero and/or enantioselective synthesis.

[0004] There are few synthetic processes available for this class of compounds. WO 96 27587 describes the catalytic enantioselective synthesis of certain spirolactams that involves a large number of steps. U.S. Pat. No. 5,734,061 also describes a process for the preparation of spirocyclic lactams N-substituted with a tertiary amine substitutent. U.S. Pat. No. 4,680,388 describes procedures to obtain N-sulfate substituted spirolactams. These processes and the intermediates used in them are directed to very particular compounds and therefore lack a wider applicability due to the absence of reactive functional groups.


[0006] Miyazawa, F. et al. in Heterocycles, vol 59, 1:149-160 "Synthesis of spirofused nitrogend heterocyclic compounds via N-methoxy-N-acyliminium ions using phenylmagnesium (III) bis(trifluoroacetate) in trifluoroethanol" describe another process to obtain functionalised spirolactams including some spiroidones.


[0009] These processes present serious inconvenient relating to their yields and to the limited stability of the spiro-fused lactams obtained. Thus, any efficient process for producing functionalised spirolactam compounds in high yield, with various functionalities such as a cyclohexadiene group, and if necessary with stereospecificity, would be a welcome contribution to the art.

SUMMARY OF THE INVENTION

[0010] The invention provides very stable spiro-fused lactams having UV absorbing properties and which are useful as intermediate compounds in the preparation of a variety of highly functionalised chemical structures, including, if necessary, diastero and/or enantioselective processes.

[0011] In one aspect the invention provides a compound of formula I:

\[
\begin{align*}
&\text{R}_1 \quad \text{R}_2 \\
&\text{R}_3 \quad \text{R}_4 \\
&\text{R}_5 \quad \text{R}_6
\end{align*}
\]

wherein \( \text{R}_1 \) and \( \text{R}_2 \) are independently selected from H, halogen, protected or unprotected hydroxy, protected or unprotected silyloxy, substituted or unsubstituted alkyl or cycloalkyl, substituted or unsubstituted alkoxy or aryloxy, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclic, nitro, substituted or unsubstituted amino, mercapto, substituted or unsubstituted arylthio or alkylthio;

[0012] \( \text{R}_3 \) and \( \text{R}_4 \) are independently selected from H, substituted alkyl, substituted or unsubstituted alkoxy or aryloxy, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclic;

[0013] \( \text{R}_5 \) and \( \text{R}_6 \) are independently selected from hydrogen, substituted or unsubstituted alkoxy substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclic, substituted or unsubstituted alkoxy, substituted or unsubstituted aryloxy, substituted or unsubstituted amino, or halogen;

[0014] \( \text{Z} \) is \(-(\text{CRaRb})_n-\) or \(-\text{CH}_2-(\text{CRaRb})-\) or \(-(\text{CRaRb})-\text{CH}_2-\) or \(-\text{CH}_2-(\text{CRaRb})-\text{CH}_2-\), or \(-\text{CH}_2-(\text{CRaRb})-\text{CH}_2-\) wherein \( n \) is a number selected from 1, 2, 3 and Ra and Rb are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclic, substituted or unsubstituted alkoxy, substituted or unsubstituted aryloxy, substituted or unsubstituted amino, or halogen;

[0015] \( \text{Y} \) is selected from \(-\text{O}-\), \(-\text{S}-\), \(-\text{NRa}-\) or \(-\text{C(O)-}\), wherein Ra is as previously defined;

[0016] \( W \) is a group with sufficient electronic density to stabilize the compound through p (pi) interactions with the benzodienone moiety such as a group selected from substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted alkylalkyl;

[0017] or a salt, complex or solvate thereof.

[0018] We have drastically increased the stability of these compounds through the selection of an adequate \( W \) group.
[0019] As a further advantage, the compound adopts a preferential conformation in which the W group blocks one of the faces of the benzodienone, directing further reactions on the free face of the benzodienone moiety.

[0020] In addition, we have found that these compounds present interesting UV absorption properties which can be modulated according to the substituents used.

[0021] In one embodiment the compounds of the invention are as above defined with the proviso that when Z is \(-\text{CH}_2\text{CH}_2\) then Y is selected from \(-\text{O}-\), \(-\text{S}-\) or \(-\text{C(\text{O})-}\).

[0022] In another embodiment W is preferably a group having unsaturated bonds or aromatic groups, more preferably it comprises at least a group selected from substituted or unsubstituted aryl, substituted or unsubstituted heterocyclic, substituted or unsubstituted alkenyl. More preferably it is selected from substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted alkenyl. The invention also provides a process for producing a compound of formula I which comprises a step (a) of reacting a compound of formula III:

```
formula III
```

wherein wherein \(R_1\), \(R_2\), \(R_3\), \(R_4\), \(Z\), \(Y\), \(W\) are as defined above, with a Weinreb-type amide halogenating agent; preferably an agent selected from alkyl hypochlorite, alkyl hypoh bromite, sodium bromite, sodium hypochlorite, benzyl trimethylammonium trihalide, N-halophthalimide, N-halo succinimide or phenylidine (III) bis(trifluoroacetate) (PHFA). Most preferred is sodium hypochlorite.

[0028] Further, the invention provides intermediate compounds useful in the production of a compound of formula I as defined above, such as compounds III.

**DETAILED DESCRIPTION OF THE INVENTION**

[0029] Previously described compounds such as N-methoxy substituted spiro-lactams benzodienones are poorly stable and tend to reverse to compounds structurally related to the starting products during their synthesis or purification because of an easily triggered reduction process:

```
[red]  \(\text{O} \rightarrow \text{OH} \)
```

[0030] Additionally, during their synthesis or during their purification, and depending on the substitution of the phenyl alkylamides starting materials, other aromatic heterocycles tend to be produced because of their higher stability, such as for example (see *J. Org. Chem.*, 1989, 54: 2294-3403, scheme I):
We have now found a new class of compounds containing the spirrolactam group and presenting a benzodienone functionality that are remarkably stable and open to a large number of possibilities for further use. The stability is present during synthesis and also in purification processes. In these compounds the above mentioned reactions are avoided.

Without being bound by theory, we believe that the high stability is provided by p interactions between the W group attached to the the Y group such as hydroxilamino and the benzodienone functionality. This configuration has a further advantage in that the W group covers one face of the benzodienone group, acting as a protecting group for one of the faces and directing the attack of further reagents to the other face.

In our copending application PCT/EP2005/..., filed the same day as the present application, the reactivity of the compounds of the invention is advantageously used to provide a broad range of intermediate compounds useful for the synthesis of biologically active molecules.

In the above definition of compounds of formula (I) and in the description the following terms have the meaning indicated:

“Alkyl” refers to a straight or branched hydrocarbon chain radical consisting of carbon and hydrogen atoms, containing no saturation, having one to eight carbon atoms, and which is attached to the molecule by a single bond, e. g., methyl, ethyl, n-propyl, i-propyl, n-butyl, t-butyl, n-pentyl, etc. Alkyl radicals may be optionally substituted by one or more substituents such as halo, hydroxy, alkoxy, carboxy, cyano, carbonyl, acyl, alkoxy carbonyl, aminino, nitro, mercapto and alkylthio, etc.

“Alkoxy” refers to a radical of the formula-ORalkyl where Ralkyl is an alkyl radical as defined above; e. g., methoxy, ethoxy, propoxy, etc. “Aryloxy” refers to a radical of formula —OR wherein R is an aryl radical as defined below.

“Amino” refers to a radical of the formula-NH2, —NR, —NRSR.

“Aril” refers to a phenyl, naphthyl, phenantryl or anthracyl radical. The aryl radical may be optionally substituted by one or more substituents such as hydroxy, mercapto, halo, alkyl, phenyl, alkoxy, haloalkyl, nitro, cyano, dialkylamino, aminokyl, acyl and alkoxy carbonyl, etc. as defined herein.

“Aralkyl” refers to an aryl group linked to an alkyl group such as benzyl and phenethyl.

“Cycloalkyl” refers to a saturated carbocyclic ring having from 3 to 8 carbon atoms.

“Heterocyclic” refers to a heterocyclic radical, i.e. a stable 3- to 15-membered ring which consists of carbon atoms and from one to five heteroatoms selected from the group consisting of nitrogen, oxygen, and sulfur, preferably a 4-to-8-membered ring with one or more heteroatoms, more preferably a 5- or 6-membered ring with one or more heteroatoms. For the purposes of this invention, the heterocycle may be a monocylic, bicyclic or tricyclic ring system, which may include fused ring systems; and the nitrogen, carbon or sulfur atoms in the heterocyclic radical may be optionally oxidised; the nitrogen atom may be optionally quarternized; and the heterocyclic radical may be partially or fully saturated or aromatic. Examples of such heterocycles include, but are not limited to, azepines, benzoimidazole, benzothiazole, furan, isothiazole, imidazole, indole, piperidine, pipеразине, purine, quinoline, thiadiazole, tetrahydrofuran.

“Hydroxyl protecting group” refers to a group that blocks the OH function for further reactions and can be removed under controlled conditions. The hydroxyl protecting groups are well known in the art, representative protecting groups are silyl ethers such as trimethylsilyl ether, triethylsilyl ether, tert-butyldimethylsilyl ether, tert-butyldiphenylsilyl ether, triisopropylsilyl ether, diethyldimethylsilyl ether, diphenylmethylsilyl ether, triphenylsilyl ether, trityl methylsilyl ether, di-tert-butyldimethylsilyl ether; alkyl ethers such as methyl ether, tert-butyl ether, benzyl ether, p-methoxybenzyl ether, 3,4-dimethoxybenzyl ether, trityl ether; allyl ether; alkoxyethyl ether such as methoxyethyl ether, 2-methoxyethoxyethyl ether, benzoxymethyl ether, p-methoxybenzoxymethyl ether, 2-(trimethylsilyl)ethoxyethyl ether; tetrahydropropyl and related ethers; methylthiomethyl ether. Esters such as acetate ester, benzoate ester; pivalate ester; methoxyacetate ester; chloroacetate ester; levulinic ester; Carbonates such as benzyl carbonate, p-nitrobenzyl carbonate, tert-butyl carbonate, 2,2,2-trichloroethyl carbonate, 2-(trimethylsilyl)ethyl carbonate, allyl carbonate; and sulphates such as SO3 py. Additional examples of hydroxyl protecting groups can be found in reference books such as Greene and Wuts’ “Protective Groups in Organic Synthesis”, John Wiley & Sons, Inc., New York, 1999.

References herein to substituted groups in the compounds of the present invention refer to the specified moiety that may be substituted at one or more available positions by one or more suitable groups, e. g., halogen such as fluoro, chloro, bromo and iodo; cyano; hydroxyl; nitro; azido; alkanoyl such as a C1-6 alkanoyl group such as acyl and the like; carboxamido; alkyl groups including those groups having 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms and more preferably 1-3 carbon atoms; alkenyl and alkynyl groups including groups having one or more unsaturated linkages and from 2 to about 12 carbon or from 2 to about 6 carbon atoms; alkoxys groups having one or more oxygen linkages and from 1 to about 12 carbon atoms or 1 to about 6 carbon atoms or aroyloxy such as phenoxyl; alkythio groups including those moieties having one or more thioether linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; alkylsulfanyl groups including those moieties having one or more sulfanyl linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms; carbocyclic aryl having 6 or more carbons, particularly phenyl or naphthyl and aril such as benzyl. Unless otherwise indicated, an optionally substituted group may have a substituent at each substitutable position of the group, and each substitution is independent of the other.
Unless otherwise stated, the compounds of the invention are also meant to include compounds which differ only in the presence of one or more isotopically enriched atoms. For example, compounds having the present structures except for the replacement of a hydrogen by a deuterium or tritium, or the replacement of a carbon by a $^{13}$C- or $^{14}$C-enriched carbon or $^{15}$N-enriched nitrogen are within the scope of this invention.

Salts of compounds of the invention are also part of the invention. They can be synthesized from the parent compound which contains a basic or acidic moiety by conventional chemical methods. Generally, such salts are, for example, prepared by reacting the free acid or base forms of these compounds with a stoichiometric amount of the appropriate base or acid in water or in an organic solvent or in a mixture of the two. Generally, nonaqueous media like ether, ethyl acetate, ethanol, isopropanol or acetonitrile are preferred. Examples of the acid addition salts include mineral acid addition salts such as, for example, hydrochloride, hydrobromide, hydroiodide, sulphate, nitrate, phosphate, and organic acid addition salts such as, for example, acetic, maleic, fumaric, citric, oxalate, succinate, tartrate, malate, mandelate, methanesulphonate and p-toluene-sulphonate.

The compounds of the invention may be in crystalline form either as free compounds or as solvates (e.g. hydrates) and it is intended that both forms are within the scope of the present invention. Methods of solvation are generally known in the art.

The compounds of the present invention represented by the above described formula (1) may include enantiomers depending on the presence of chiral centres or isomers depending on the presence of multiple bonds (e.g. Z, E). The single isomers, enantiomers or diastereoisomers and mixtures thereof fall within the scope of the present invention.

In the compounds of formula I, $R_3$ and $R_4$ are preferably H. Other substituents such as halogen or unsubstituted alkyl are more difficult to produce because of the formation of indol type of compounds instead of the lactam.

In the compounds of formula I, substituents $R_2$ and $R_2$ should preferably not be strongly electrophilic because during the synthesis, and depending on the method used, they could difficult the attack of the nitrenium ion. Preferably they are each independently selected from hydrogen, halogen or substituted aryl. More preferably they are both hydrogen.

In the compounds of formula I, the group Z gives rise to a ring of 4, 5 or 6 members. Substitution on position Z creates a stereogenic center that could induce selective functionalisation on the benzodienone moiety. In a preferred embodiment Z is $-(CH_2)_n-$. In another preferred embodiment Z is $-CRaRb-$. In another preferred embodiment Z is $-CRaRb-CH_2-$. Wherein Ra and Rb are different thus creating a chiral center.

Although the lactam rings of 5 or 6 are also comprised within the scope of the invention, in one embodiment a $\beta$-lactam (n=1) is preferred because of the further uses that can be given to such compounds.

The group Y in the compounds of formula I, plays a role in the stability and conformation and also during its synthesis. In an embodiment Y is preferably $-O-$, although other atoms are not excluded as long as the final product is stable.

As we already mentioned, the W group is important for the stabilization of the compound of formula I. Preferably it comprises unsaturated bonds or aromatic groups to increase the pi interaction. Aroylalkyl groups and alkynyl groups are preferred since they give the best stability. In a particular embodiment, W is $-CRaRb-Q$ or $-SiRaRb-Q$ since the stability of the conformation is further improved by the presence of a $-CRaRb-$ or a $-SiRaRb-$ linker between Y and the substituent Q which has $\pi(\pi)$ interactions with the benzodienone moiety. The linker is preferably $-CHR-$. In this case a stereogenic center is introduced which allows for the selectivity or specificity of any further reaction, distinguishing the two double bonds of the benzodienone. This will advantageously open the way to diastereo- and/or enantioselective synthesis in addition to the selection for one face which is mentioned above. Depending on the size of Ra it can also modulate the $\pi(\pi)$ interactions and thus modulate properties such as UV absorption.

In one embodiment the W is an aroyl group. Among the aryl groups, substituted or unsubstituted phenyl and naphthyl are preferred. Heterocyclylalkyl groups are also envisaged.

In one embodiment the compounds of formula II are preferred:

![Formula II](image)

Wherein W and Ra are as above defined. A particularly stable compound according to formula II has W=benzyl.

In one embodiment Ra is H in the compound of formula II.

In another preferred embodiment Ra is an halo, substituted or unsubstituted alkyl, hydroxy, alkoxy, aryloxy group or an hydroxy protected group, thus introducing a chiral center in the $\beta$-lactam ring.

The compounds of formula (I) or (II) defined above can be obtained by available synthetic procedures. Some examples of these procedures are described in the documents mentioned above.

In one embodiment of the process of the invention, a Staudinger reaction between an activated carboxylic acid and an imine can be used to provide access to the compounds of the invention, such as in the following case:
Alternative to these processes will be apparent to the person skilled in the art.

However, particularly good results are obtained by forming the spiro lactum ring through reduction of an aromatic compound via an N-acylnitrenium ion.

Therefore in one aspect the invention is directed to a process of preparing a compound of formula I as defined above which comprises the step (a) of reacting a compound of formula III:

![Diagram of formula III]

wherein $R_1$, $R_2$, $R_3$, $R_4$, $Z$, $Y$, $W$ are as defined above; $R_5$ is hydrogen or substituted or unsubstituted alkyl; Hal is F, Cl, Br, I or eventually $-\text{SO}_2\text{CF}_3$;

with an N-acylnitrenium ion forming agent to produce a compound of formula I.

If Hal is an halogen, an adequate precipitating agent will be able to form the nitrenium ion. In general silver salts give good results, other salts can be used.

$R_5$ is preferably an electron-donating group, to promote the ipso addition of the nitrenium ion. Preferably $R_5$ is alkyl such as methyl, ethyl, propyl, etc. Most preferably it is methyl.

An adequately substituted amino group can be used as an alternative to the $-\text{OR}_4$ group, in this case the addition of the nitrenium ion will generate the iminium salt of the benzodienone which by hydrolysis generates the benzodienone. In this alternative, it is preferred that the substituents on the N atom be electro-donating groups, such as dialkylamine. Another possibility is to use an halogen group instead of $-\text{OR}_4$ as described in *J. Org. Chem.*, 2003, 68: 6739-6744.

The reaction is preferably carried out in the absence of light to avoid undesired radical reactions such as the formation of the alkoxyamide starting material rather than ipso amidation (addition), or decomposition of compounds of formula III.

Preferably the solvent should be polar, such as for example trifluoroacetic acid or acetic acid. A temperature of about $-10^\circ$ C. to about $10^\circ$ C. is preferred, more preferably of about O$^\circ$ C. The reaction can be carried out under inert atmosphere if necessary. The obtained product of formula I can be purified following standard procedures such as evaporation, chromatography, phase separation (extraction). As previously mentioned the product is stable and can be stored for a prolonged period of time.

The compound of formula III is preferably prepared from a Wernig-type amide compound of formula IV:

![Diagram of formula IV]

wherein $R_1$, $R_2$, $R_3$, $R_4$, $Z$, $Y$, $W$ are as defined above, by reaction with an halogenating agent. The halogenating agent is preferably an agent selected from alkyl hypochlorite, alkyl hypobromite, sodium bromite, sodium hypochlorite, benzyltrimethylammonium trihalide, N-halosuccinimide, N-halophthalimide or phenylidene (III) bis(trifluoroacetate) (PIFA). Sodium hypochlorite is preferred because of its low cost and availability.

The halogenation is preferably carried out in an apolar solvent, such as acetone, and at a temperature of about $-10^\circ$ C. to about $10^\circ$ C., more preferably of about O$^\circ$ C. The reaction is preferably carried out in absence of light to avoid undesired radical reactions.

The compounds of formula IV are either commercially available or easily prepared following known procedures as described for example in the above mentioned references.
The processes above described provide a quick and easy way (3 steps) to obtain the stable compounds of formula 1.

The possibility of the preparation of new lactams, which are stable, densely functionalised and well suited to control further reactions opens a large number of possibilities for further use. The compounds of formula 1 are useful starting materials to produce a variety of chemical structures of interest. The double bond can be subjected to electrophilic attacks with for example hydroxylating agents, epoxidation agents, reduction agents, as well as cycloadditions and Michael reactions.

RMN and UV spectroscopic data (see examples section) for compounds described by formula 1, are in complete agreement with the presence of interactions between their benzodienone portion and the Y-X substitution for the cases in which the Y-electrons are adequately orientated.

Thus, from the comparison between the 1H RMN data (chemical shifts and coupling constants) for compounds 3a, 3b, 3c y 3d (examples of formula IV) and compounds 5a, 5b, 5c y 5d (examples of formula I) it became evident that compounds 5c and 5d have to present the above indicated interactions. For compound 5d, the huge difference between the four signals assigned to the four protons of its benzodienone portion has to be correlated to the interaction between this moiety and its Y—X portion. In addition, we propose that this interaction is enhanced by a Thorpe-Ingold effect.

Furthermore, the UV data for compounds 3a, 3b, 3c y 3d (examples of formula IV) and compounds 5a, 5b, 5c y 5d (examples of formula I) (see examples section) support our conclusions from their 1H RMN data. While the spectra for 3a, 3b, 3c y 3d (examples of formula IV) present at 276 nm theirs maximum absorption (λmax) and this is with independence of theirs Y—W substitution or Y—X, respectively, the situation for examples of formula I is completely different. Compounds 5a and 5b present at 243 nm theirs maximum absorptions (λmax) and compounds 5c and 5b at 242 and 232 nm, respectively. The variation of 11 nm into the maximum absorption (λmax) between compound 5d and compound 5a is assigned to the interaction between its benzodienone portion moiety and its Y—X portion.

The knowledge of the structural basis (the establishment of π interactions between their benzodienone portion and the Y—X substitution) for the above features spans the scope of their accessibility and applicability. From their absorption data it is clear that both the range of absorption and the possibility to modulate this range by selection of the appropriate substituents makes these compounds useful materials as UV absorbers.

The following examples are intended to exemplify the invention, and should not be construed as limiting the disclosure of the claimed invention.

EXAMPLES

General Methods and Materials.

All reactions described below were carried out under argon atmosphere unless otherwise noted. The solvents used were distilled and dried under argon atmosphere before use (CH₂Cl₂ and benzene were distilled over CaH₂).

Flash Chromatography was executed on columns loaded with 230-400 mesh silica gel Merck. TLC was carried out on silica gel Merck (Kieselgel 60F₂₅₄).

All starting materials were purchased commercially (Aldrich, Fluka and Merck) and used without further purification, except the N-alkoxymidamide 2d, which was prepared according to a literature procedure (see below). A commercial household bleach solution Maxy® which is stated to be <5% NaOCl was used for the preparation of t-butyl hypochlorite following the procedure described below.

Melting points (mp) were determined on a Reichert Microscopic Hot-Stage and are uncorrected. 1H and 13C NMR spectra were measured on a Varian Gemini-200 and a Varian Inova-300 spectrometer with (CH₃)₂Si as an internal reference and CDCl₃ as solvent unless otherwise noted. Both 1H and 13C NMR spectral data are reported in parts per million (δ) relative to residual sign of the solvent (CDCl₃, 7.26 ppm and 77.0 ppm for 1H and 13C NMR, respectively). 1H and 13C NMR designations are: s (singlet); d (doublet); t (triplet); q (quartet); m (multiplet). Infrared (IR) spectra were recorded on a Perkin-Elmer FT-IR spectrometer. UV spectra were recorded on a Perkin-Elmer 402 spectrometer. Low-resolution mass (LRMS) spectra were obtained on a Hewlett Packard 5973 MSD spectrometer with a direct inlet system (EI) at 70 eV. Microanalytical data (E.A.) were obtained on a Perkin-Elmer 240C and Heraus CHN—O instruments at the Instrumental Analysis Department of Instituto de Quimica Orgánica General (C.S.I.C.).

Example 1

General Procedure for the Preparation of the N-Alkoxymidamides 3a–d from the 4-Methoxyphenylacetyl Chloride (1)

The N-alkoxamines 2a–c were purchased from Aldrich and Fluka Companies, and used without further purification. The N-alkoxymidamide 2d was prepared following the procedure described in: Brown, D. S.; Gallagher, P. T.; Lightfoot, A. P.; Moody, C. J.; Slawin, A. M. Z.; Swann, E. Tetrahedron 1995, 51, 11473-11488.

To a vigorously stirred solution of N-alkoxymidamide hydrochloride 2a–d (17.87 mmol) and sodium carbonate...
(32.50 mmol) in a mixture of benzene (23 ml) and H2O (23 ml) with ice-water bath cooling, was added 4-methoxyphenylacetamide chloride (1). The mixture was stirred at room temperature for 12 h under an argon atmosphere and the progress of the reaction was monitored by TLC (hexane-AcOEt, 1:2). Then, AcOEt (50 ml) was added and the organic layer separated. This process was repeated three times. The combined extracts were washed with brine (2x50 ml), dried over Na2SO4, filtered and concentrated under reduced pressure to give the corresponding N-acylamide (3a-d), which was used in the next extraction without further purification.

Example 2

N-Methoxy-4-methoxyphenylacetamide (3a)


[0086] Rp = 0.14 (TLC, hexane-AcOEt, 1:2); yield, 99%; white solid, mp 86-87°C (lit. mp 83-85°C); 1H-NMR (200 MHz, CDCl3); δ 87.88 (1H, s, br, NH), 7.19 (2H, d, J = 8.7 Hz, H-2), 6.88 (2H, d, J = 8.7 Hz, H-3), 3.81 (3H, s, OCH3), 3.71 (3H, s, NOCH3), 3.50 (2H, s, CH2), 3.49 (2H, s, CH2); 13C-NMR (75 MHz, CDCl3); δ 8169.1, 158.5, 130.1, 126.1, 113.9, 63.8, 55.1, 39.1; IR (KBr); ν 3467, 3159, 2967, 1644, 1612, 1513, 1252, 1063, 1033 cm-1; UV (MeOH); λmax (ε) = 276 nm (1619 1 mol-1 cm-1); LRMS (EI): m/z 271 (M+, 41), 239 (2), 211 (6), 193 (1), 180 (2), 165 (3), 148 (5), 121 (71), 91 (100), 77 (29); E.A. (C16H17NO3); calculated C, 70.83; H, 6.32; found C, 70.87; H, 6.35.

Example 3

N-(O-Allyhydroxy)-4-methoxyphenylacetamide (3b)

[0087] Following the same procedure as in example 1 but starting from 2b we obtained compound 3b.

[0088] Rp = 0.30 (TLC, hexane-AcOEt, 1:2); yield, 99%; white solid, mp 100-101°C; 1H-NMR (200 MHz, CDCl3); δ 87.85 (1H, s, br, NH), 7.18 (2H, d, J = 8.5 Hz, H-2 and H-6), 6.87 (2H, d, J = 8.5 Hz, H-3 and H-5), 5.89 (1H, m, CH=CH2), 5.31 (1H, s, br, CH=CH2), 5.25 (1H, s, br, CH=CH2), 4.32 (2H, d, OCH3), 3.80 (3H, s, OCH3), 3.49 (2H, s, CH2), 3.47 (2H, s, CH2); 13C-NMR (75 MHz, CDCl3); δ 8169.1, 158.5, 131.9, 130.0, 126.2, 120.2, 113.8, 76.9, 55.0, 39.2; IR (KBr); ν 3467, 2967, 1641, 1609, 1514, 1253, 1057 cm-1; UV (MeOH); λmax (ε) = 276 nm (2070 1 mol-1 cm-1); LRMS (EI): m/z 285 (M+, 3), 280 (2), 186 (16), 165 (2), 148 (6), 121 (40), 105 (100), 91 (5), 77 (17); E.A. (C16H17NO3); calculated C, 71.56; H, 6.71; found C, 71.62; H, 6.75.

Example 5

(-)-(S)—N-(1-Phenylethoxy)-4-methoxyphenylacetamide (3d)

[0091] Following the same procedure as in example 1 but starting from 2d we obtained compound 3d.

[0092] Rp = 0.32 (TLC, hexane-AcOEt, 1:1); yield, 99%; white solid, mp 60-61°C; [α]20D = +168.2° (c 1.1, CHCl3); 1H-NMR (200 MHz, CDCl3); δ 87.61 (1H, s, br, NH), 7.32 (5H, m, Ph), 6.98 (2H, d, J = 7.1 Hz, H-2 and H-6), 6.77 (2H, d, J = 7.1 Hz, H-3 and H-5), 4.98 (1H, m, OCH(2)CH3), 3.78 (3H, s, OCH3), 3.35 (2H, s, CH2), 1.53 (5H, d, J = 6.6 Hz, CH3); 13C-NMR (75 MHz, CDCl3); δ 8168.5, 158.1, 140.6, 129.7, 128.0, 127.8, 126.6, 126.3, 113.5, 82.5, 54.7, 38.8, 20.4; IR (KBr); ν 3200, 3057, 2956, 2927, 2847, 1652, 1609, 1512, 1455, 1301, 1247, 1178, 1035, 700 cm-1; UV (MeOH); λmax (ε) = 276 nm (1841 1 mol-1 cm-1); LRMS (EI): m/z 285 (M+, 3), 280 (2), 186 (16), 165 (2), 148 (6), 121 (40), 105 (100), 91 (5), 77 (17); E.A. (C16H17NO3); calculated C, 71.56; H, 6.71; found C, 71.62; H, 6.75.

Example 6

General Procedure for the Preparation of the Spiro-Lactams 5a-d

[0093] First, the compound t-Butyl Hypochlorite was prepared following the procedure described in: Mintz, M. J.; Walling, C. Org. Syntheses 1969, 49, 9-12.

\[
\text{OH} + \text{NaOCl} + \text{CH}_3\text{COOH} \xrightarrow{10^\circ \text{C}} \text{OCl} + \text{CH}_3\text{COONa} + \text{H}_2\text{O}
\]

[0094] To a vigorously stirred commercial bleach solution (500 ml) was added, at 10°C in the dark and in a single portion, a solution of tert-butyl alcohol (37 ml, 0.39 mol) and glacial acetic acid (24.5 ml, 0.43 mol). The reaction mixture was stirred for about 3 min, and then was poured into separatory funnel. The lower aqueous layer was discarded, and the oily yellow organic layer was washed first with 10% aqueous Na2CO3 solution (50 ml) and then H2O (50 ml). The product was dried over CaCl2 (1 g) and filtered. The product can be stored in refrigerator over CaCl2 in amber glass bottles. The t-butyl hypochlorite isolated by this procedure could be used in the next reaction without further purification.
To a stirred solution of a N-alcoxyamide 3a-d (7.37 mmol) in CH$_2$Cl$_2$ (30 ml) was added slowly, at 0°C. in the dark, freshly prepared tert-butyl hypochlorite (0.21 mmol). Alternatively, sodium hypochlorite such as commercial household bleach solution Mavex® is used, at room temperature in the dark. The resulting mixture was stirred at 0°C. (or in the case of bleach added, at room temperature) in the dark under an argon atmosphere until the disappearance of starting material by TLC (hexane-AcOEt, 1:2) was observed (the time required was generally less than 30 min). The solvent was evaporated in the dark under reduced pressure and the residue, the N-chloro-N-alcoxyamide 4a-d as a yellow solid (Rf=0.83, hexane-AcOEt, 1:2), was used in the next reaction without further purification.

The solid N-chloro-N-alcoxyamide 4a-d cooled at 0°C. under argon atmosphere, was added a solution of silver carbonate (14.74 mmol) in TFA (30 ml) in the dark with stirring. The mixture was stirred until the reaction was complete, generally 30 min (TLC monitoring, hexane-AcOEt, 1:2), and then the solvent was removed under pressure below 35°C. The residue was basified with 5% aqueous Na$_2$CO$_3$ solution (75 ml) with cooling. The precipitated silver salts were filtered through Celite in vacuum, and the pad was washed with CH$_2$Cl$_2$. The aqueous solution was extracted with CH$_2$Cl$_2$ (3x150 ml). The combined extracts were washed with brine (2x150 ml), dried over Na$_2$SO$_4$ and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane-AcOEt) to give the spiro-b lactam 5a-d.

1-Methoxy-1-azaspiro[3.5]nona-5,8-diene-2,7-dione (5a)

Flash chromatography (hexane-AcOEt, 1:1). R$_f$=0.33 (TLC, hexane-AcOEt, 1:2); yield, 43%; pale brown solid, mp 77-79°C; $^1$H-NMR (200 MHz, CDCl$_3$): 8.91 (2H, d, J=10.2 Hz, CH$_3$-CH=CHCO), 6.46 (2H, d, J=10.2 Hz, CH=CHCO), 3.77 (3H, s, OCH$_3$), 2.97 (2H, s, CH$_2$); $^1$C-NMR (75 MHz, CDCl$_3$): δ184.2, 162.2, 145.5, 132.5, 65.5, 60.4, 43.6; IR (KBr): ν=3456, 3014, 2934, 1772, 1767, 1630, 1404, 1060, 880 cm$^{-1}$; UV (MeOH): $\lambda$$_{max}$ (e)=245 nm (11959 l mol$^{-1}$ cm$^{-1}$); LRMS(ELI): m/z 179(M$,^+)$, 164(1), 151(2), 137(100), 106(3), 78(6); E.A. (C$_7$H$_{12}$NO$_2$): calculated C, 60.33; H, 5.06; found C, 60.39; H, 5.10.

1-(O-Allyloxy)-1-azaspiro[3.5]nona-5,8-diene-2,7-dione (5b)

Flash chromatography (hexane-AcOEt, 3:2). R$_f$=0.40 (TLC, hexane-AcOEt, 1:2); yield, 68%; yellow oil; $^1$H-NMR (200 MHz, CDCl$_3$): 6.89 (2H, d, J=10.1 Hz, CH$_3$-CH=CHCO), 6.44 (2H, d, J=10.1 Hz, CH=CHCO), 5.97-5.83 (1H, m, CH$_2$-CH$_2$-CH$_3$), 5.37 (1H, m, CH$_2$-CH$=$CH$_2$), 5.32 (1H, m, CH$_2$-CH$=$CH$_2$), 4.35 (2H, d, J=6.5 Hz, OCH$_3$-CH$=$CH$_2$), 2.96 (2H, s, CH$_2$); $^1$C-NMR (75 MHz, CDCl$_3$): δ185.9, 162.6, 145.7, 131.6, 121.4, 128.7, 77.8, 60.1, 42.9, 33.8, IR (NaCl, CCL$_4$): ν=3536, 3050, 2927, 1783, 1669, 1641, 1501, 1251, 1251, 840, 880, 839 cm$^{-1}$; UV (MeOH): $\lambda$$_{max}$ (e)=243 nm (12549 l mol$^{-1}$ cm$^{-1}$); LRMS(ELI): m/z 205(M$,^+)$, 177(3), 163(79), 147(34), 133(36), 120(8), 106(79), 78(100); E.A. (C$_7$H$_{12}$NO$_2$): calculated C, 64.38; H, 5.40; found C, 64.44; H, 5.44.

1-Benzylxloxy-1-azaspiro[3.5]nona-5,8-diene-2,7-dione (5c)

The purity of spiro-lactam 5c is related to the concentration of the household bleach solution used. $^1$H NMR spectra have to be used for the determination of spiro-lactam/N-alcoxyamide (5c:3c) ratio. By TLC both compounds have the same R$_f$ (0.40, hexane-AcOEt, 1:2).

Flash chromatography (hexane-AcOEt, 2:1). R$_f$=0.40 (TLC, hexane-AcOEt, 1:2); yield, 88%; pale brown-reddish solid, mp 77-79°C; $^1$H-NMR (200 MHz, CDCl$_3$): 87.32 (5H, m, Ph), 6.55 (2H, d, J=10.2 Hz, CH$_3$-CH=CHCO), 6.17 (2H, d, J=10.2 Hz, CH=CHCO), 4.88 (2H, s, OCH$_3$-Ph), 2.89 (2H, s, CH$_2$); $^1$C-NMR (75 MHz, CDCl$_3$): δ184.2, 162.9, 145.0, 134.2, 130.9, 128.7, 128.6, 128.1, 78.7, 60.0, 42.9; IR (KBr): ν=3459, 3043, 2963, 1764, 1672, 1630, 1375, 1056, 886, 841, 768, 737, 696 cm$^{-1}$; UV (MeOH): $\lambda$$_{max}$ (e)=242 nm (9511 l mol$^{-1}$ cm$^{-1}$); LRMS(ELI): m/z 255(M$,^+)$, 197(41), 126(16), 106(16), 91(100), 78(25); E.A. (C$_7$H$_{12}$NO$_2$): calculated C, 70.58; H, 5.13; found C, 70.63; H, 5.18.

However, compounds 5c and 3c were separated by Flash chromatography (hexane-toluene-aceton, 1:5:1). Spireo-b lactam 5c: R$_f$=0.40 (TLC, hexane-toluene-aceton, 1:2:1); white solid; yield, 55%.
X-ray crystallography data were obtained using an ENRAF-NONIUS CAD-4 diffractometer, using the \(\theta/2\theta\)-scan method.

---

**Cristal data**

<table>
<thead>
<tr>
<th>Empirical formula</th>
<th>(C_{13}H_{29}NO_3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formula weight</td>
<td>255.36</td>
</tr>
<tr>
<td>Temperature</td>
<td>293(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 A</td>
</tr>
<tr>
<td>Crystal system, space group</td>
<td>Orthorhombic, Pca2b</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td></td>
</tr>
<tr>
<td>(a = 8.358(7)) A</td>
<td></td>
</tr>
<tr>
<td>(b = 11.388(2)) A</td>
<td></td>
</tr>
<tr>
<td>(c = 28.213(7)) A</td>
<td></td>
</tr>
<tr>
<td>Volume</td>
<td>2685(2) A</td>
</tr>
<tr>
<td>(Z_{r}), Calculated density</td>
<td>8, 1.263 Mg/m(^3)</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.089 mm(^{-1})</td>
</tr>
</tbody>
</table>

F(000) 1072

**Atomic coordinates (x,10\(^4\)) and equivalent isotropic displacement parameters (\(\AA^2\times10^3\)).** U(eq) is defined as one third of the trace of the orthogonalized \(U_{ij}\) tensor.

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>U(eq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O(1)</td>
<td>2372(3)</td>
<td>-292(2)</td>
<td>6070(1)</td>
<td>78(1)</td>
</tr>
<tr>
<td>O(2)</td>
<td>2258(3)</td>
<td>3560(2)</td>
<td>520(1)</td>
<td>82(1)</td>
</tr>
<tr>
<td>O(3)</td>
<td>1875(2)</td>
<td>2496(2)</td>
<td>6180(1)</td>
<td>52(1)</td>
</tr>
<tr>
<td>C(4)</td>
<td>2467(4)</td>
<td>2563(3)</td>
<td>5332(1)</td>
<td>56(1)</td>
</tr>
<tr>
<td>C(1)</td>
<td>2465(4)</td>
<td>-1553(3)</td>
<td>5968(1)</td>
<td>53(1)</td>
</tr>
<tr>
<td>C(2)</td>
<td>3014(5)</td>
<td>-896(4)</td>
<td>5948(1)</td>
<td>57(1)</td>
</tr>
<tr>
<td>C(3)</td>
<td>3986(4)</td>
<td>189(3)</td>
<td>5797(1)</td>
<td>52(1)</td>
</tr>
<tr>
<td>C(4)</td>
<td>2584(4)</td>
<td>821(2)</td>
<td>5601(1)</td>
<td>46(1)</td>
</tr>
<tr>
<td>C(5)</td>
<td>1094(4)</td>
<td>180(4)</td>
<td>5579(1)</td>
<td>53(1)</td>
</tr>
<tr>
<td>C(6)</td>
<td>967(5)</td>
<td>-90(2)</td>
<td>5838(1)</td>
<td>57(1)</td>
</tr>
<tr>
<td>C(7)</td>
<td>2786(5)</td>
<td>1370(3)</td>
<td>5104(1)</td>
<td>58(1)</td>
</tr>
<tr>
<td>N</td>
<td>2459(3)</td>
<td>2063(2)</td>
<td>5766(1)</td>
<td>53(1)</td>
</tr>
<tr>
<td>C(9)</td>
<td>3158(5)</td>
<td>2886(6)</td>
<td>6497(2)</td>
<td>82(2)</td>
</tr>
<tr>
<td>C(10)</td>
<td>2379(4)</td>
<td>3388(3)</td>
<td>6029(1)</td>
<td>58(1)</td>
</tr>
<tr>
<td>C(11)</td>
<td>2424(5)</td>
<td>2786(4)</td>
<td>7342(2)</td>
<td>97(1)</td>
</tr>
<tr>
<td>C(12)</td>
<td>1723(9)</td>
<td>3243(6)</td>
<td>7740(2)</td>
<td>146(3)</td>
</tr>
<tr>
<td>C(13)</td>
<td>575(9)</td>
<td>4264(8)</td>
<td>7723(3)</td>
<td>173(4)</td>
</tr>
<tr>
<td>C(14)</td>
<td>874(9)</td>
<td>4870(6)</td>
<td>7813(3)</td>
<td>146(3)</td>
</tr>
<tr>
<td>C(15)</td>
<td>1614(5)</td>
<td>4430(4)</td>
<td>6912(2)</td>
<td>94(1)</td>
</tr>
</tbody>
</table>

\[\text{(-)-(S)-1-(1-Phenylethoxy)-1-azaspiro[3.5]nona-5,8-diene-2,7-dione (5d)}\]

---

**Flash chromatography** (hexane-AcOEt, 3:2). R\(_f\)=0.47 (TLC, hexane-AcOEt, 1:2); yield, 55%; brown oil; \([\text{c}]\)\(_D\)=63.6° (c 1.0, CHCl\(_3\)); \(^1\text{H}-\text{NMR}\) (200 MHz, CDCl\(_3\)); \(87.30-7.17\) (51H, m, Ph), 6.67 (1H, dd, J=10.0, 2.9 Hz, CH=CH=CH=CO), 6.23 (1H, dd, J=10.0, 2.0 Hz, CH=CH=CO), 6.11 (1H, dd, J=10.0, 2.9 Hz, CH=CH=CO), 5.81 (1H, dd, J=10.0, 2.0 Hz, CH=CH=CO), 4.88 (1H, q, J=6.6 Hz, OC=CH(CH\(_2\))\(_3\)Ph), 2.75 (2H, s, CH\(_2\)), 1.44 (3H, d, J=6.6 Hz, CH\(_3\)). \(^1\text{H}-\text{NMR}\) (75 MHz, CDCl\(_3\)): 8184.2, 163.8, 145.4, 144.9, 140.1, 131.9, 130.5, 128.9, 128.6, 127.1, 85.0, 60.5, 43.4, 20.7; IR (NaCl, CCl\(_4\)), \(v\) 3289, 2978, 2927, 1784, 1668, 1630, 1512, 1454, 1249, 1050, 700 cm\(^{-1}\); UV (MeOH): \(\lambda_{\text{max}}\) (\(e\)) 232 nm (3083 mol\(^{-1}\)cm\(^{-1}\)); \(\lambda_{\text{max}}\) (EISi): \(m/z\) 269(M\(^+\)), 181(1), 165(1), 155(1), 148(1), 121(26), 105(100), 79(19); E.A. (C\(_{13}\)H\(_{29}\)NO\(_3\)): calculated C, 71.56; H, 5.61; found C, 71.40; H, 5.67.

1. A compound of formula I:

\[
\begin{align*}
\text{R}_1 & - \text{O} - \text{R}_2 \\
\text{R}_3 & - \text{O} - \text{R}_4
\end{align*}
\]

wherein \(\text{R}_1\) and \(\text{R}_3\) are independently selected from H, halogen, protected or unprotected hydroxy, protected or unprotected silyloxy, substituted or unsubstituted alkyl or cycloalkyl, substituted or unsubstituted alkox or aryloxo, substituted or unsubstituted aryl, substituted or unsubstituted heterocycleryl nitro, substituted or unsubstituted amino, mercapto, substituted or unsubstituted arylthio or alkylthio;

\(\text{R}_3\) and \(\text{R}_4\) are independently selected from H, substituted alkyl, substituted or unsubstituted alkox or aryloxy, substituted or unsubstituted aryl, substituted or unsubstituted heterocycleryl; \(Z\) is \(-\text{CRaRb}(\text{Ra} \neq \text{Rb})\) or \(-\text{CH}_{2}\) or \(-\text{CH}_{2}-\text{CRaRb}(\text{Ra} \neq \text{Rb})\) or \(-\text{CH}_{2}-\text{CRaRb}(\text{Ra} \neq \text{Rb})\) or \(-\text{CH}_{2}-\text{CRaRb}(\text{Ra} \neq \text{Rb})\) where \(n\) is a number selected from 1, 2, 3 and Ra and Rb are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted alkene, substituted or unsubstituted aryl, substituted or unsubstituted heterocycleryl, substituted or unsubstituted alkox or aryloxy, substituted or unsubstituted amino, or halogen;

\(Y\) is selected from \(-\text{O}-, -\text{S}-, -\text{NRa}-\) or \(-\text{C(O)}-\), wherein Ra is as previously defined;

\(W\) is a group with sufficient electronic density to stabilize the compound through \(\pi\) (pi) interactions with the benzodienone moiety such as a group selected from substituted or unsubstituted arylalkyl, substituted or unsubstituted heterocyclerylalkyl, substituted or unsubstituted alkylene;

or a salt, complex or solvate thereof.

2. A compound as defined in claim 1 wherein \(\text{R}_3\) and \(\text{R}_4\) are H.

3. A compound as defined in claim 1 wherein \(\text{R}_1\) and \(\text{R}_2\) are each independently selected from hydrogen, halogen and substituted aryl.

4. A compound as defined in claim 3 wherein \(\text{R}_1\) and \(\text{R}_2\) are H.

5. A compound as defined in claim 1 wherein \(n\) is 1.

6. A compound as defined in claim 1 wherein \(Y\) is \(-\text{O}-\).

7. A compound as defined in claim 1 wherein \(W\) is \(-\text{CRaRb}-\text{Q}\), wherein Ra and Rb are as previously defined and Q is selected from substituted or unsubstituted aryl, substituted or unsubstituted heterocycleryl, substituted or unsubstituted alkylene.

8. A compound as defined in claim 7 wherein Ra and Rb in the group W are both H.

9. A compound as defined in claim 7 wherein Q is aryl, preferably phenyl.
10. A compound as defined in claim 7 wherein Ra is H and Rb is alkyl.

11. A compound of formula II:

![Formula II]

wherein W and Ra are as defined in claim 1; or a salt, complex or solvate thereof.

12. A compound as defined in claim 11, wherein W is —CH₂-Q, and Q is substituted or unsubstituted aryl, substituted or unsubstituted alkenyl; preferably substituted or unsubstituted phenyl or substituted or unsubstituted vinyl.

13. A compound as defined in claim 12, wherein Q is phenyl.

14. A compound as defined in claim 11 wherein Ra is selected from halo, substituted or unsubstituted alkyl, hydroxy, alkoxy, aryl group or an hydroxy protected group.

15. A process for producing a spirolactam compound as defined in claim 1 which comprises the step (a) of reacting a compound of formula III:

![Formula III]

wherein R₁, R₂, R₃, R₄, Z, Y, W are as defined in claim 1,
R₅ is hydrogen or substituted or unsubstituted alkyl;
Hal is F, Cl, Br, I or —SO₂CF₃;
with an N-acyliminium ion forming agent to produce a compound of formula I.

16. A process as defined in claim 15 wherein the N-acyliminium ion forming agent is an halogen precipitating agent, preferably a silver salt.

17. A process as defined in claim 15 wherein the step (a) is carried out in the absence of light.

18. A process according to claim 15 which comprises the additional step (b) of preparing a compound of formula III by reacting a Weinreb-type amide compound of formula IV:

![Formula IV]

with a halogenating agent; preferably an agent selected from alkyl hypochlorite, alkyl hypobromite, sodium bromite, sodium hypochlorite, benzyltrimethylammonium tribromide, N-haloisuccinimide, N-halophthalimide, or phenyliodine (III) bis(trifluoroacetate) (PIFA).

19. A process according to claim 18 wherein the halogenating agent is alkyl hypochlorite, preferably tert-butyl hypochlorite, or sodium hypochlorite.

20. A process according to claim 15 which comprises the additional step (c) of producing the compound of formula V by reacting a compound of formula V with a compound of formula VI:

![Formula V]

wherein W, Y, Z, R₁, R₂, R₃, R₄, R₅ are as previously defined and L is a nucleophilic leaving group, preferably halogen.

21. A compound of formula III:

![Formula III]

wherein R₁, R₂, R₃, R₄, Z, Y, W are as defined in claim 1;
R₅ is hydrogen or alkyl;
Hal is F, Cl, Br, I or SO₂F₃.

22. Use of a compound as defined in claim 1 as an UV absorber.

* * * * *