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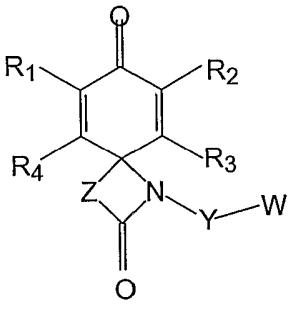
(54) Title: SPIROLACTAMS AND THEIR SYNTHESIS



(I)

(57) 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

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

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

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 US 4,680,388, or hypocholesterolemic 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.

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. US 5,734,061 also describes a process for the preparation of spirocyclic lactams N-substituted with a tertiary amine susbtituent. US 4,680,388 describes procedures to obtain N-sulphate 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.

Dina-Telma et al. in *Tetrahedron Letters*, vol. 35 no 13,2043-246 describe some spirodienone compounds containing a ?-lactam moiety.

Miyazawa, E. et al. in *Heterocycles*, vol 59, 1:149-160 "Synthesis of spiro-fused nitrogen heterocyclic compounds via N-methoxy-N-acylnitrenium ions using phenyliodine (III) bis(trifluoroacetate) in trifluoroethanol" describe another process to obtain functionalised spirolactams including some spirodienones.

Glover, S.A. et al. in *Tetrahedron*, 1987, 43:2577-2592 "N-alkoxy-N-acylnitrenium ions in intramolecular aromatic addition reactions" describe the synthesis in low yields of benzolactams via cyclization of N-alkoxy-N-acylnitrenium ions.

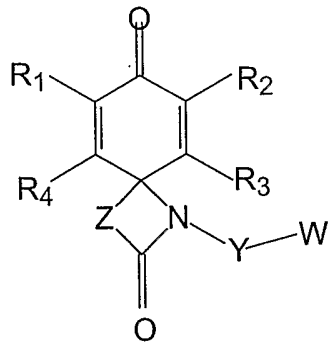
Kawase, M. et al. in *J.Org. Chem.*,1989, 54:3394-3403 "Electrophilic aromatic substitution with N-methoxy-N-acylnitrenium ions generated from N-chloro-N-methoxyamides: syntheses of Nitrogen heterocyclic compounds bearing a N-methoxyamide group" describe among others the synthesis of spiro benzodienone lactams by ipso amidation with a nitrenium ion.

These processes present serious inconvenients 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 cyclohexadienone group, and if necessary with stereospecificity, would be a wellcome contribution to the art.

SUMMARY OF THE INVENTION

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.

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



formula I

wherein R_1 and 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 heterocyclyl, nitro, substituted or unsubstituted amino, mercapto, substituted or unsubstituted arylthio or alkylthio;

R_3 and R_4 are independently selected from H, substituted alkyl, substituted or unsubstituted alkoxy or aryloxy, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl;

Z is $-(CRaRb)_n-$ or $-CH_2-(CRaRb)-$ or $-(CRaRb)-CH_2-$ or $-CH_2-(CRaRb)-CH_2-$, or $-(CH_2)_2-(CRaRb)-$ or $-(CRaRb)-(CH_2)_2-$ 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 alkenyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryloxy, substituted or unsubstituted amino, or halogen;

Y is selected from –O-, -S-, -NRa- or -C(O)-, wherein Ra is as previously defined;

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 usubstituted heterocyclylalkyl, substituted or unsubstituted alkenyl;
or a salt, complex or solvate thereof.

We have drastically increased the stability of these compounds through the selection of an adequate W group.

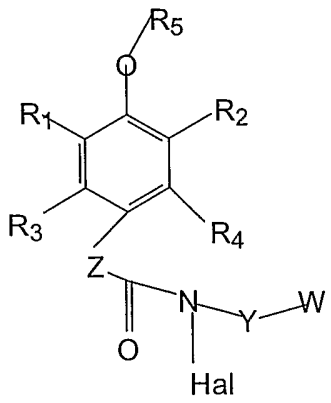
As a further advantage, the compound adopts a preferential conformation in which the W group blocks one of the faces of the benzodienone, directing further reactions on the free face of the benzodienone moeity.

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

In one embodiment the compounds of the invention are as above defined with the proviso that when Z is $-CH_2CH_2-$ then Y is selected from –O-, -S- or -C(O)-.

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 usubstituted heterocyclyl, 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:



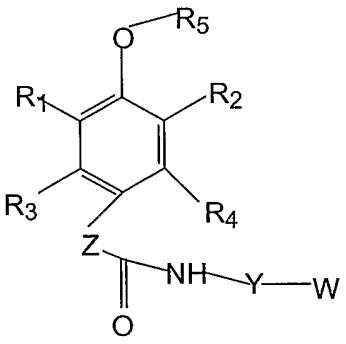
formula III

wherein 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 $-SO_2CF_3$;

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

Preferably the process comprises the additional step (b) of preparing a compound of formula III by reacting a compound of formula IV:



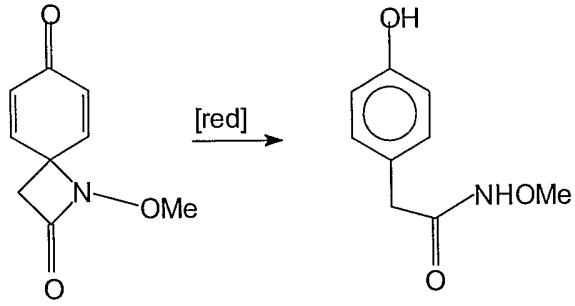
formula IV

wherein wherein R_1, R_2, R_3, R_4, R_5, Z, Y, W are as defined above,
with a Weinreb-type amide halogenating agent; preferably an agent selected from alkyl hypochlorite, alkyl hypobromite, sodium bromite, sodium hypochlorite, benzyltrimethylammonium trihalide, N-halophthalimide , N-halosuccinimide or phenyliodine (III) bis(trifluoroacetate) (PIFA). Most preferred is sodium hypochlorite.

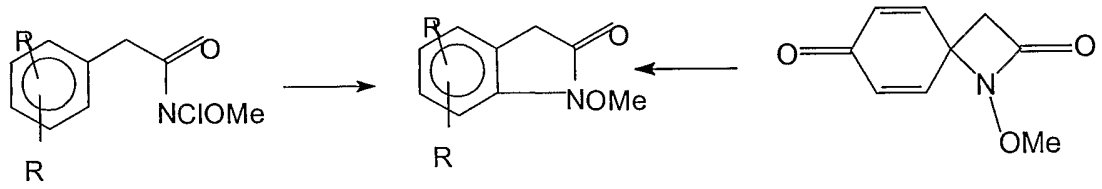
Further, the invention provides intermediate compounds useful in the production of a compound of formula I as defined above, such as compounds III.

DETAILED DESCRIPTION OF THE INVENTION

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:



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 spirolactam 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 reactives 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 rest of 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, alkoxycarbonyl, amino, nitro, mercapto and alkylthio, etc.

"Alkoxy" refers to a radical of the formula-ORalk where Ralk is an alkyl radical as defined above, e. g., methoxy, ethoxy, propoxy, etc. "Aryloxy" refers to a radical of formula –ORar wherein Rar is an aryl radical as defined below.

"Amino" refers to a radical of the formula-NH_2, -NHRa, -NRaRb.

"Aryl" 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, aminoalkyl, acyl and alkoxycarbonyl, 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.

"Heterocyclyl" 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 monocyclic, bicyclic or

tricyclic ring system, which may include fused ring systems; and the nitrogen, carbon or sulfur atoms in the heterocyclyl radical may be optionally oxidised; the nitrogen atom may be optionally quaternized; and the heterocyclyl radical may be partially or fully saturated or aromatic. Examples of such heterocycles include, but are not limited to, azepines, benzimidazole, benzothiazole, furan, isothiazole, imidazole, indole, piperidine, piperazine, 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, tri-isopropylsilyl ether, diethylisopropylsilyl ether, thexyldimethylsilyl ether, triphenylsilyl ether, di-tert-butylmethylsilyl ether; alkyl ethers such as methyl ether, tert-butyl ether, benzyl ether, p-methoxybenzyl ether , 3,4-dimethoxybenzyl ether, trityl ether; allyl ether; alkoxymethyl ether such as methoxymethyl ether, 2-methoxyethoxymethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, 2-(trimethylsilyl)ethoxymethyl ether; tetrahydropyranyl and related ethers; methylthiomethyl ether; Esters such as acetate ester, benzoate ester; pivalate ester; methoxyacetate ester; chloroacetate ester; levulinate 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 SO_3.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 ; alkoxy groups having one or more

oxygen linkages and from 1 to about 12 carbon atoms or 1 to about 6 carbon atoms ; aryloxy such as phenoxy ; alkylthio 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 ; alkylsulfinyl groups including those moieties having one or more sulfinyl linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms ; alkylsulfonyl groups including those moieties having one or more sulfonyl linkages and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms ; aminoalkyl groups such as groups having one or more N atoms and from 1 to about 12 carbon atoms or from 1 to about 6 carbon atoms ; carbocylic aryl having 6 or more carbons, particularly phenyl or naphthyl and aralkyl 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, acetate, maleate, fumarate, citrate, oxalate, succinate, tartrate, malate, mandelate, methanesulphonate and p-toluenesulphonate.

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 within the art.

The compounds of the present invention represented by the above described formula (I) 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_1 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 susbtituted 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- , $-CH_2$-CRaRb- or -CRaRb-CH_2- wherein Ra and Rb are different thus creating a chiral center.

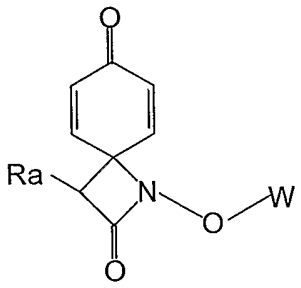
Although the lactam rings of 5 or 6 are also comprised within the scope of the invention, in one embodiment a ß-lactam (n= 1) is preferred because of the further uses that can be given to such compounds.

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. Aralkyl groups and alkenyl 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 p (pi) interactions with the benzodienone moiety. The linker is preferably -CHRa-. 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 diastero- 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 p (pi) interactions and thus modulate properties such as UV absorption.

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

In one embodiment the compounds of formula II are preferred:



Formula II

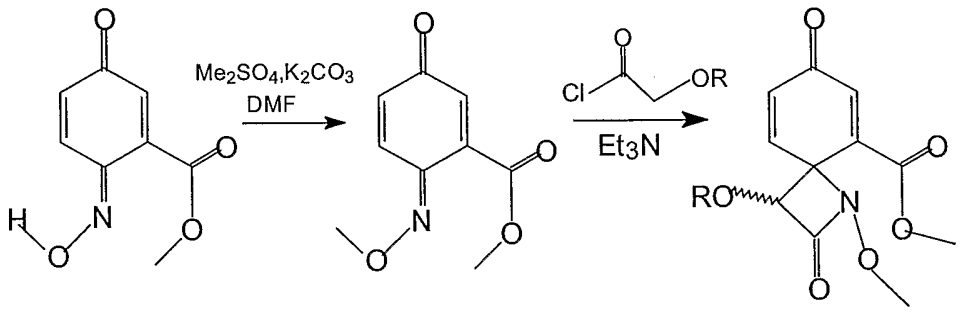
Wherein W and Ra are as above defined. A particularly stable compound according to formula II has W = benzyl.

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 ß-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.

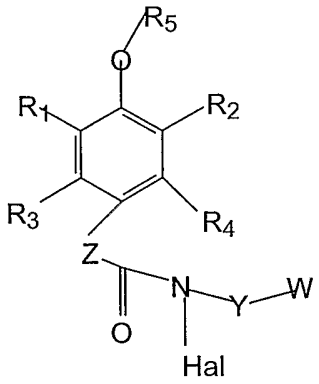
In one embodiment of the process of the invention, a Staudinger type reaction between an activated carboxylic acid and an imine can be used to provide access to the compounds of the invention, such as in the following case:



Alternative to these processes will be apparent to the person skilled in the art.

However, particularly good results are obtained forming the spiro lactam ring through reduction of an aromatic compound via a 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:



formula III

wherein R_1, R_2, R_3, R_4, Z, Y, W are as defined above; R_5 is hydrogen or susbtituted or unsubstituted alkyl; Hal is F, Cl, Br, I or eventually $-SO_2CF_3$;
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.

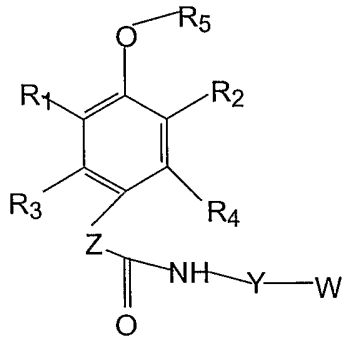
R_5 is preferably an electron-donating group, to promote the ipso addition of the nitrenium ion. Preferably R_5 is alkyl such as methyl, ethyl, propyl, etc. Most preferably it is methyl.

An adequately susbtituted amino group can be used as an alternative to the $-OR_5$ 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 $-OR_5$ 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 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°C to about 10°C is preferred, more preferably of about O°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 prolongued period of time.

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



formula IV

wherein R_1, R_2, R_3, R_4, R_5, 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 phenyliodine (III) bis(trifluoroacetate) (PIFA). Sodium hypochlorite is preferred because of its low cost and availability.

The halogenation is preferably carried out in an apolar sovent, such as acetone, and at a temperature of about -10°C to about 10°C, more preferably of about O°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 I.

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 I 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, epoxydation agents, reduction agents, as well as cycloadditions and Michael reactions.

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

Thus, from the comparison between the ^{1}H 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 π 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 date 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 ^{1}H RMN data. While the spectra for 3a, 3b, 3c y 3d (examples of formula IV) present at 276 nm theirs maximum absorption (λ_{max}) 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 (λ_{max}), and compounds 5c and 5b at 242 y 232 nm, respectively. The variation of 11 nm into the maximum absorption (λ_{max}) 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 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 (CH_2Cl_2 and benzene were distilled over CaH_2). Flash Chromatography was executed on columns loaded with 230-400 mesh silica gel Merck. TLC was carried out on silica gel Merck (Kieselgel 60F-254).

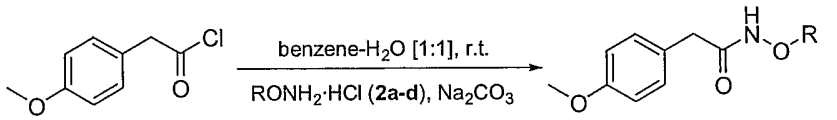
All starting materials were purchased commercially (Aldrich, Fluka and Merck) and used without further purification, except the *N*-alcoxyamine 2d, which was prepared according to a literature procedure (see below). A commercial household bleach solution Mavy® which is stated to be <5% NaOCl was used 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 ^{13}C NMR spectra were measured on a Varian Gemini-200 and a Varian Inova-300 spectrometer with $(CH_3)_4Si$ as an internal reference and $CDCl_3$ as solvent unless otherwise noted. Both ^1H and ^{13}C NMR spectral data are reported in parts per million (δ) relative to residual sign of the solvent ($CDCl_3$, 7.26 ppm and 77.0 ppm for ^1H and ^{13}C NMR, respectively). ^1H and ^{13}C NMR designations are: s (singlet); s br. (broad

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 Química Orgánica General (C.S.I.C.).

Example 1:

General Procedure for the Preparation of the *N*-Alcoxyamides 3a-d from the 4-Methoxyphenylacetyl Chloride (1).



1

2a R = CH_3 **3a** R = CH_3

2b R = CH_2-CH=CH_2 **3b** R = CH_2-CH=CH_2

2c R = CH_2-Ph **3c** R = CH_2-Ph

2d R = (+)-(*R*)-CH(CH_3)Ph **3d** R = (-)-(S)-CH(CH_3)Ph

The *N*-alcoxyamines 2a-c were purchased from Aldrich and Fluka Companies, and used without further purification. The *N*-alcoxyamine 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*-alcoxyamine hydrochloride 2a-d (17.87 mmol) and sodium carbonate (32.50 mmol) in a mixture of benzene (23 ml) and H_2O (23 ml) with ice-water bath cooling, was added 4-methoxyphenylacetyl 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 (2 x 50 ml), dried over Na_2SO_4, filtered and concentrated under reduced pressure to give the corresponding *N*-alcoxyamide 3a-d, which was used in the next reaction without further purification.

Example 2:

***N*-Methoxy-4-methoxyphenylacetamide (3a)**

The compound was obtained from 1 and 2a as described in: Kawase, M.; Kitamura, T.; Kikugawa, Y. *J. Org. Chem.* 1989, *54*, 3394-3403, "Electrophilic aromatic substitution with *N*-methoxy-*N*-acylnitrenium ions generated from *N*-chloro-*N*-methoxyamides: syntheses of nitrogen heterocyclic compounds bearing a *N*-methoxyamide group".

R_f = 0.14 (TLC, hexane-AcOEt, 1:2); yield, 99%; white solid, mp 86-87 °C (lit. mp 83-85 °C); ^{1}H-NMR (200MHz, $CDCl_3$): δ 7.88 (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, OCH_3), 3.71 (3H, s, $NOCH_3$), 3.50 (2H, s, CH_2); ^{13}C-NMR (75MHz, $CDCl_3$): δ 169.1, 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): λ_{max} (ε) = 276 nm (1619 l·mol^{-1}·cm^{-1}); LRMS(EI): m/z 195(M^+, 3), 165(1), 160(1), 148(6), 135(4), 121(100), 91(23), 78(66); E.A. ($C_{10}H_{13}NO_3$): calculated C, 61.53; H, 6.71; found C, 61.61; H, 6.76.

Example 3:

***N*-(*O*-Allylhydroxyl)-4-methoxyphenylacetamide (3b)**

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

R_f = 0.30 (TLC, hexane-AcOEt, 1:2); yield, 99%; white solid, mp 100-101 °C; ^{1}H-NMR (200MHz, $CDCl_3$): δ 7.85 (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, C<u>H</u>=CH_2), 5.31 (1H, s br., CH=C<u>H</u>$_2$), 5.25 (1H, s br., CH=C<u>H</u>$_2$), 4.32 (2H, d, OCH_2), 3.80 (3H, s, OCH_3), 3.49 (2H, s, CH_2); ^{13}C-NMR (75MHz, $CDCl_3$): δ 169.1, 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): λ_{max} (ε) = 276 nm (2070 l·mol^{-1}·cm^{-1}); LRMS(EI): m/z 221(M^+, 37), 180(3), 161(16), 148(33), 135(9), 121(100), 91(17), 78(31); E.A. ($C_{12}H_{15}NO_3$): calculated C, 65.14; H, 6.83; found C, 65.21; H, 6.89.

Example 4:

***N*-Benzyloxy-4-methoxyphenylacetamide (3c)**

Following the same procedure as in example 1 but starting from 2c we obtained compound 3c.

R_f = 0.40 (TLC, hexane-AcOEt, 1:2); yield, 99%; white solid, mp 98-99 °C; ^{1}H-NMR (200MHz, $CDCl_3$): δ 7.71 (1H, s br., NH), 7.34 (5H, s br., Ph), 7.11 (2H, d, J = 8.5 Hz, H-2 and H-6), 6.83 (2H, d, J = 8.5 Hz, H-3 and H-5), 4.86 (2H, s, $OC\underline{H}_2Ph$), 3.79 (3H, s, OCH_3), 3.45 (2H, s, CH_2); ^{13}C-NMR (75MHz, $CDCl_3$): δ 168.9, 158.5, 135.0, 130.0, 129.01, 128.4, 128.3, 126.0, 113.9, 77.8, 55.0, 39.3; IR (KBr): ν 3436, 3159, 2965, 1644, 1611, 1512, 1252, 1059, 1032, 726, 696 cm^{-1}; UV (MeOH): λ_{max} (ε) = 276 nm (1558 $l \cdot mol^{-1} \cdot cm^{-1}$); LRMS(EI): m/z 271($M^+$, 14), 239(2), 211(6), 193(1), 180(2), 165(3), 148(5), 121(71), 91(100), 77(29); E.A. ($C_{16}H_{17}NO_3$): calculated C, 70.83; H, 6.32; found C, 70.87; H, 6.35.

Example 5:

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

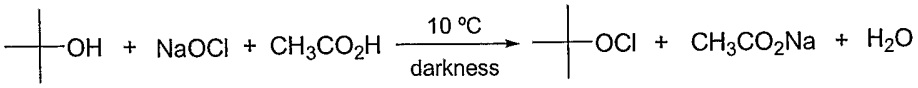
Following the same procedure as in example 1 but starting from 2d we obtained compound 3d.

R_f = 0.32 (TLC, hexane-AcOEt, 1:1); yield, 99%; white solid, mp 60-61 °C; $[\alpha]_D^{20}$ = -168.2° (c 1.1, $CHCl_3$); ^{1}H-NMR (200MHz, $CDCl_3$): δ 7.56 (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, $OC\underline{H}(CH_3)Ph$), 3.78 (3H, s, OCH_3), 3.35 (2H, s, CH_2), 1.53 (3H, d, J = 6.6 Hz, CH_3); ^{13}C-NMR (75MHz, $CDCl_3$): δ 168.5, 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 3202, 3057, 2956, 2927, 2847, 1652, 1609, 1512, 1455, 1301, 1247, 1178, 1035, 700 cm^{-1}; UV (MeOH): λ_{max} (ε) = 276 nm (1841 $l \cdot mol^{-1} \cdot cm^{-1}$); LRMS(EI): m/z 285($M^+$, 3), 268(2), 181(6), 165(2), 148(6), 121(40), 105(100), 91(5), 77(17); E.A. ($C_{17}H_{19}NO_3$): calculated C, 71.56; H, 6.71; found C, 71.62; H, 6.75.

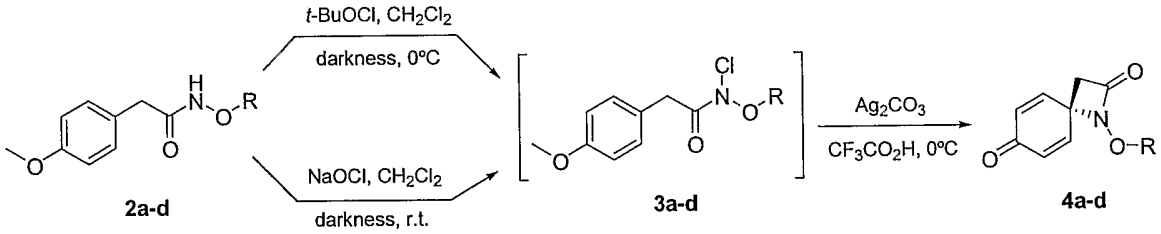
Example 6:

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

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



To a vigorously stirred commercial household 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 Na_2CO_3 solution (50 ml) and then H_2O (50 ml). The product was dried over $CaCl_2$ (1 g) and filtered. The product can be stored in refrigerator over $CaCl_2$ 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_2Cl_2 (30 ml) was added slowly, at 0 °C in the dark, freshly prepared *tert*-butyl hypochlorite (9.21 mmol). Alternatively, sodium hypochlorite such as commercial household bleach solution Mavy® 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_2CO_3 solution (75 ml) with cooling. The precipitated silver salts were filtered through Celite in vacuum, and the pad was washed with CH_2Cl_2. The aqueous solution was extracted with CH_2Cl_2 (3 x 150 ml). The combined extracts was washed with brine (2 x 150 ml), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane-AcOEt) to give the spiro β-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 107-109 °C; ^{1}H-NMR (200MHz, $CDCl_3$): δ 6.91 (2H, d, J = 10.2 Hz, C<u>H</u>=CHCO), 6.46 (2H, d, J = 10.2 Hz, CH=C<u>H</u>CO), 3.77 (3H, s, OCH_3), 2.97 (2H, s, CH_2); ^{13}C-NMR (75MHz, $CDCl_3$): δ 184.2, 162.2, 145.5, 132.5, 65.5, 60.4, 43.6; IR (KBr): ν 3436, 3014, 2934, 1772, 1667, 1630, 1404, 1060, 880 cm^{-1}; UV (MeOH): λ_{max} (ε) = 243 nm (11959 $l \cdot mol^{-1} \cdot cm^{-1}$); LRMS(EI): m/z 179($M^+$, 1), 164(1), 151(2), 137(100), 106(3), 78(6); E.A. ($C_9H_9NO_3$): calculated C, 60.33; H, 5.06; found C, 60.39; H, 5.10.

1-(*O*-Allylhydroxyl)-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 (200MHz, $CDCl_3$): δ 6.89 (2H, d, J = 10.1 Hz, C<u>H</u>=CHCO), 6.44 (2H, d, J = 10.1 Hz, CH=C<u>H</u>CO), 5.97-5.83 (1H, m, CH_2-C<u>H</u>=CH_2), 5.37 (1H, m, CH_2-CH=C<u>H</u>$_2$), 5.32 (1H, m, CH_2-CH=C<u>H</u>$_2$), 4.35 (2H, d, J = 6.3 Hz, OC<u>H</u>$_2$-CH=CH_2), 2.96 (2H, s, CH_2); ^{13}C-NMR (75MHz, $CDCl_3$): δ 183.9, 162.6, 145.7, 131.6, 131.4, 128.7, 77.8, 60.1, 42.9, 12.8; IR (NaCl, CCl_4): ν 3536, 3050, 2927, 1783, 1669, 1631, 1401, 1251,

1052, 940, 880, 839 cm^{-1}; UV (MeOH): λ_{max} (ε) = 243 nm (12549 $l \cdot mol^{-1} \cdot cm^{-1}$); LRMS(EI): m/z 205($M^+$, 1), 177(3), 163(79), 147(34), 133(36), 120(8), 106(89), 78(100); E.A. ($C_{11}H_{11}NO_3$): calculated C, 64.38; H, 5.40; found C, 64.44; H, 5.44.

1-Benzyloxy-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, 68%; pale brown-reddish solid, mp 77-79 °C; ^{1}H-NMR (200MHz, $CDCl_3$): δ 7.32 (5H, m, Ph), 6.55 (2H, d, J = 10.2 Hz, C<u>H</u>=CHCO), 6.17 (2H, d, J = 10.2 Hz, CH=C<u>H</u>CO), 4.88 (2H, s, OC<u>H</u>$_2$Ph), 2.89 (2H, s, CH_2); ^{13}C-NMR (75MHz, $CDCl_3$): δ 183.8, 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): λ_{max} (ε) = 242 nm (9511 $l \cdot mol^{-1} \cdot cm^{-1}$); LRMS(EI): m/z 255($M^+$, 1), 197(41), 121(6), 106(16), 91(100), 78(25); E.A. ($C_{15}H_{13}NO_3$): 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-acetone, 1:5:1). Spiro β-lactam 5c: R_f = 0.40 (TLC, hexane-toluene-acetone, 1:2:1); white solid; yield, 55%.

X-ray crytallography data were obtained using a ENRAF-NONIUS CAD-4 difractometer, using the ? /2T-scan method.

Cristal data

Empirical formula	$C_{15}H_{13}NO_3$
Formula weight	255.26
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, Pcab
Unit cell dimensions	a = 8.358(7) Å
	b = 11.388(2)
	c = 28.213(7)
Volume	2685(2) $Å^3$
Z, Calculated density	8, 1.263 Mg/m^3
Absorption coefficient	0.089 mm^{-1}

F(000) 1072

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

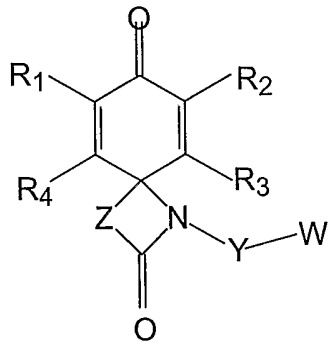
	x	y	z	U(eq)
O(1)	2372(3)	-2592(2)	6076(1)	78(1)
O(2)	2258(3)	3560(2)	5207(1)	82(1)
O(3)	1875(2)	2496(2)	6186(1)	52(1)
C(8)	2467(4)	2563(3)	5332(1)	56(1)
C(1)	2405(4)	-1553(3)	5966(1)	53(1)
C(2)	3914(5)	-896(4)	5948(1)	57(1)
C(3)	3989(4)	189(3)	5793(1)	52(1)
C(4)	2584(4)	821(2)	5609(1)	46(1)
C(5)	1049(4)	180(4)	5679(1)	53(1)
C(6)	967(5)	-902(4)	5838(1)	57(1)
C(7)	2786(5)	1370(3)	5104(1)	58(1)
N	2499(3)	2063(2)	5766(1)	53(1)
C(9)	3158(5)	2886(6)	6497(2)	82(2)
C(10)	2379(4)	3388(3)	6925(1)	58(1)
C(11)	2424(5)	2786(4)	7342(2)	97(1)
C(12)	1723(9)	3243(6)	7740(2)	146(3)
C(13)	975(9)	4264(8)	7720(3)	173(4)
C(14)	874(9)	4870(6)	7318(3)	146(3)
C(15)	1614(5)	4439(4)	6912(2)	94(1)

(-)-(*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; $[\alpha]_D^{20}$ = -63.6° (c 1.0, $CHCl_3$); ^{1}H-NMR (200MHz, $CDCl_3$): δ 7.30-7.17 (5H, m, Ph), 6.67 (1H, dd, J = 10.0, 2.9 Hz, C<u>H</u>=CHCO), 6.23 (1H, dd, J = 10.0, 2.0 Hz, CH=C<u>H</u>CO), 6.11 (1H, dd, J = 10.0, 2,9 Hz, C<u>H</u>=CHCO), 5.81 (1H, dd, J = 10.0, 2.0 Hz, CH=C<u>H</u>CO), 4.88 (1H, q, J = 6.6 Hz, OC<u>H</u>(CH_3)Ph), 2.75 (2H, s, CH_2), 1.44 (3H, d, J = 6.6 Hz, CH_3); ^{13}C-NMR (75MHz, $CDCl_3$): δ 184.2, 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): ν 3289, 2978, 2927, 1784, 1668, 1630, 1512, 1454, 1249, 1050, 700 cm^{-1}; UV (MeOH): λ_{max} (ε) = 232 nm (3083 $l \cdot mol^{-1} \cdot cm^{-1}$); LRMS(EI): m/z 269($M^+$, 1), 181(1), 165(1), 155(1), 148(1), 121(26), 105(100), 77(19) ; E.A. ($C_{16}H_{15}NO_3$): calculated C, 71.36; H, 5.61; found C, 71.40; H, 5.67.

CLAIMS

1. A compound of formula I:



formula I

wherein R_1 and 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 heterocyclyl, nitro, substituted or unsubstituted amino, mercapto, substituted or unsubstituted arylthio or alkylthio;

R_3 and R_4 are independently selected from H, substituted alkyl, substituted or unsubstituted alkoxy or aryloxy, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl;

Z is $-(CRaRb)_n-$ or $-CH_2-(CRaRb)-$ or $-(CRaRb)-CH_2-$ or $-CH_2-(CRaRb)-CH_2-$, or $-(CH_2)_2-(CRaRb)-$ or $-(CRaRb)-(CH_2)_2-$ 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 alkenyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted alkoxy, substituted or unsubstituted aryloxy, substituted or unsubstituted amino, or halogen;

Y is selected from –O-, -S-, -NRa- or -C(O)-, wherein Ra is as previously defined;

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 usubstituted heterocyclylalkyl, substituted or unsubstituted alkenyl;
or a salt, complex or solvate thereof.

2. A compound as defined in claim 1 wherein R_3 and R_4 are H.

3. A compound as defined in claims 1 or 2 wherein R_1 and R_2 are each independently selected from hydrogen, halogen and susbtituted aryl.

4. A compound as defined in claim 3 wherein R_1 and R_2 are H.

5. A compound as defined in anyone of claims 1-4 wherein n is 1.

6. A compound as defined in anyone of claims 1-5 wherein Y is -O- .

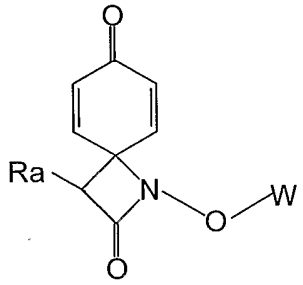
7. A compound as defined in anyone of claims 1-6 wherein W is –CRaRb-Q, wherein Ra and Rb are as previously defined and Q is selected from substituted or unsubstituted aryl, substituted or usubstituted heterocyclyl, substituted or unsubstituted alkenyl.

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 claims 7 or 8 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

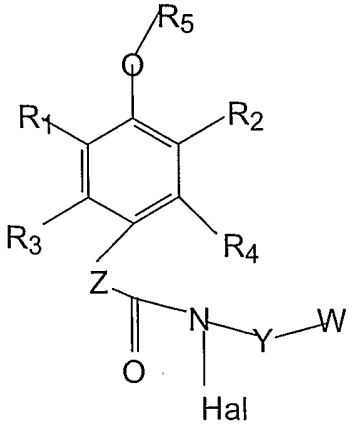
wherein W and Ra are as defined in claim 1; or a salt, complex or solvate thereof.

12. A compound as defined in claim 11, wherein W is $-CH_2$-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 coumpound as defined in any of claims 11-13 wherein Ra is selected form halo, substituted or unsubstituted alkyl, hydroxy, alkoxy, aryloxy group or an hydroxy protected group.

15. A process for producing a spirolactam compound as defined in anyone of claims 1-14 which comprises the step (a) of reacting a compound of formula III:



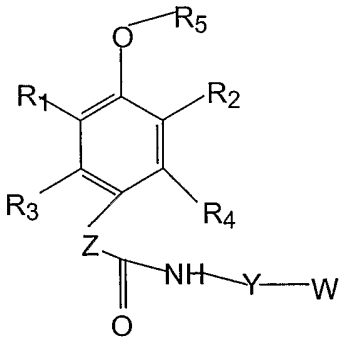
formula III

wherein R_1, R_2, R_3, R_4, Z, Y, W are as defined in claim 1,
R_5 is hydrogen or susbtituted or unsubstituted alkyl;
Hal is F, Cl, Br, I or $-SO_2CF_3$;
with an N-acylnitrenium ion forming agent to produce a compound of formula I.

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

17. A process as defined in claim 15 or 16 wherein the step (a) is carried out in the absence of light.

18. A process according to any of claims 15-17 which comprises the additional step (b) of preparing a compound of formula III by reacting a Weinreb-type amide compound of formula IV:

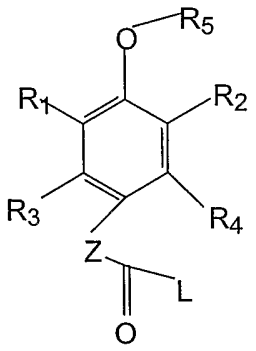


formula IV

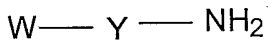
with a a halogenating agent; preferably an agent selected from alkyl hypochlorite, alkyl hypobromite, sodium bromite, sodium hypochlorite, benzyltrimethylammonium trihalide, N-halosuccinimide, N-halophthalimide, or phenyliodine (III) bis(trifluoroacetate) (PIFA).

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

20. A process according to anyone of claims 15-19 which comprises the additional step (c) of producing the compound of formula IV by reacting a compound of formula V with a compound of formula VI:



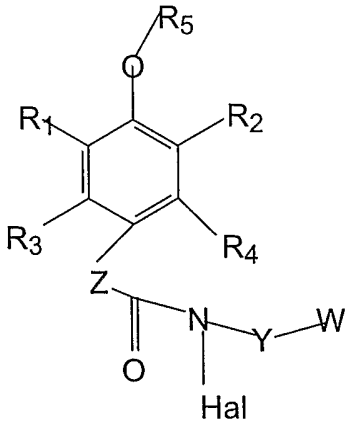
formula V



formula VI

wherein W, Y, Z, R1, R2, R3, R4, R_5 are as previously defined and
L is a nucleophilic leaving group, preferably halogen.

21. A compound of formula III:



formula III

wherein R_1, R_2, R_3, R_4, Z, Y, W are as defined in anyone of claims 1-13;
R_5 is hydrogen or alkyl;
Hal is F, Cl, Br, I or SO_2F_3.

22. Use of a compound as defined in any of claims 1-14 as an UV absorber.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/005146

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D205/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 94/17038 A (BROWNE MARGARET E ; CLADER JOHN W (US); DAVIS HARRY R (US); DUGAR SUND) 4 August 1994 (1994-08-04) cited in the application examples 7,9	1-15
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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
1 July 2005	14/07/2005
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Menegaki, F

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/005146

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	BRAUN, NORBERT ET AL: "Synthesis of Spirolactams from Tyrosine amides and related substances" TETRAHEDRON LETTERS, vol. 39, 1998, pages 4667-4670, XP002303136 compound 14	1-15
A	GLOVER, STEVEN ET AL: "N-alkoxy-N-acylnitrenium ions in intramolecular aromatic addition reactions" TETRAHEDRON, vol. 43, no. 11, 1987, pages 2577-2592, XP002333767 figure 2a; examples 2p,2q,20-22	1-22

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