Photoinduced [2+2] cycloadditions (the Paterno–Büchi reaction) of 1-acetylisatin with enol ethers—regioselectivity, diastereoselectivity and acid catalysed transformations of the spirooxetane products †

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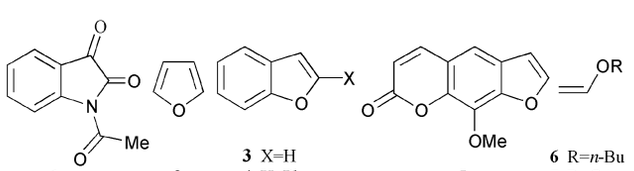
Photoinduced [2+2] cycloadditions (the Paterno–Büchi reaction) of 1-acetylisatin **1** with cyclic enol ethers (furan **2**, benzofuran **3**, 2-phenylbenzofuran **4**, 8-methoxypsoralen **5**) and acyclic enol ethers (*n*-butyl vinyl ether **6** and vinyl acetate **7**) afford the spiro(3*H*-indole-3,2′-oxetane)s **8**–**21** in benzene in high total yield (82–96%) and with high regio- and diastereoselectivity *via* the nπ* triplet state of **1** without single electron transfer (SET) involvement. The cycloaddition regioselectivity is determined by the formation of the most stable 1,4-diradical intermediate. As a result, head-to-head products with an acetal structure are formed for the cyclic 1,3-dienes **2**–**5**, while for the acyclic monoalkenes **6** and **7**, head-to-tail products are preferentially formed. The diastereoselectivity, which favors the thermodynamically less stable *syn*-spirooxetanes for all the alkenes **2**–**7**, can be rationalized by considering the sterically more favorable 1,4-diradical conformers suitable for efficient intersystem crossing (ISC) and C–C bond formation according to the Salem–Rowland rules. Acid treatment of the oxetanes derived from furan and benzofuran results in oxetane ring opening and provides a convenient and high yielding access to the 3-(furan-3-yl)indole derivatives.

Introduction

Recent research interest in the photoinduced [2+2] cycloadditions between carbonyl compounds and alkenes (the Paterno–Büchi reaction [1,2]) concentrates on the different factors that influence the regio- and stereo-selectivity, and the exploitation of the synthetic applications, taking advantage of the propensity of the oxetane products to undergo ring opening in different fashions depending on reaction conditions to furnish products with delicate structures.[2d,3,4,5] Alkenes with their C=C bond linked to a heteroatom such as enol ethers,[3a,6–9] silyl enol ethers [5b,5c,10] and enamines [5a,11] are known to be good substrates in the Paterno–Büchi reaction. In particular, the regioselectivity and diastereoselectivity in the photocycloadditions of aldehydes and ketones with cyclic enol ethers and enamines such as furan, dihydrofuran [3a,6–9] and dihydropyrroles [5a,11a–c] have been scrutinised closely. Synthetic applications have been made of these cycloadditions, especially in the synthesis of natural products or of new compounds with possible biological activities .[3,4,5] However, Paterno–Büchi reactions of cyclic α-diketones with enol ethers have rarely been reported.[12] Also, although there have been several reports on the Paterno–Büchi reactions of carbonyl compounds with acyclic alkoxyethenes [13] and acyloxyethenes,[14] the diastereoselectivity in these reactions has scarcely been reported. [13e,13i,14b,14c] ‡

Isatin (1*H*-indole-2,3-dione) is a heterocyclic α-diketone which has a wide range of biological activities [15] and serves as an important precursor for the synthesis of biologically active indole derivatives and natural products.[16] However, the photochemistry of isatin and its role in the elaboration of the indole structure has not received much attention.[17] We have recently reported the Paterno–Büchi reactions of 1-acetylisatin with styrene derivatives and the regio- and diastereoselectivity in these photocycloadditions.[17] We now report photocycloadditions of 1-acetylisatin **1** with the acyclic and cyclic enol ethers **2**–**7**. These reactions are found to give the corresponding spiro(3*H*-indole-3,2′-oxetane)s in high yield and with high regio- and diastereoselectivity. Factors that influence the regio- and diastereoselectivity are discussed in relation to the reaction mechanisms. We have also investigated the acid catalysed ring opening reactions of the spirooxetanes derived from furan and benzofuran and found that these reactions give the 3-(furan-3-yl)indole and 3-(benzofuran-3-yl)indole derivatives in high yield.



1 **2** **3** X=H **4** X=Ph **5** **6** R=*n*-Bu **7** R=OAc

Results

1 Photoinduced cycloadditions of 1-acetylisatin (1) with alkenes 2–7

Irradiation of a benzene solution of **1** and furan (**2**) with light of $\lambda > 400$ nm where **1** is the only absorbing species gave two 1 : 1 cycloadducts **8** (48%) and **9** (6%) together with a 2 : 1 adduct **10** (30%) after chromatographic separation of the

† Electronic supplementary information (ESI) available: NMR spectra and ORTEP diagrams. Crystallographic data for compounds **10**, **17** and **23** are included in the ESI. CCDC numbers 175732, 175733 and 175736. See http://www.rsc.org/suppdata/p1/b1/b109697d/

‡ Diastereoselectivity in the Paterno–Büchi reaction of carbonyl compounds with acyclic silyl enol ethers has been intensively investigated by Bach and his coworkers.[5b,5c,10]

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reaction mixture. The ratio of **8**–**9** is 8 : 1. Since all the $\Delta\delta$ values for the corresponding protons in **8** and **9** are smaller than 0.12 ppm, and the signals of the minor isomer are partly submerged in that of the major isomer, only a rough estimation of product ratio could be made by comparing the integration of the corresponding signals of the two compounds in the ^{1}H NMR spectrum of the crude product mixture, which is essentially the same as that found in the chromatographic separation. The ^{1}H NMR of the crude 2 : 1 product **10** reveals the presence of at least five minor stereoisomers of **10**, with yields ranging from 5–10% of that of **10**. These stereoisomers could not be separated completely. Products **8** and **9** are diastereomers with an acetal structure. In the ^{1}H NMR spectrum, H(2′a) and H(5′a) in the oxetane ring resonate at 4.1 and 6.8 ppm respectively with a large $\Delta\delta$ value of 2.7 ppm. The assignment of the absorptions of the four protons in the dihydrofuran ring and the measurement of the coupling constants between them, including two 'W' couplings through four bonds, were made by H–H COSY and decoupling experiments (see Experimental section). There is no significant difference in the ^{1}H NMR spectra of **8** and **9** and therefore for their steric configurations to be unambiguously assigned, an X-ray crystallographic analysis of **8** was carried out which indicates that it is the *syn(endo)*- isomer (*syn*- refers here to the *syn*- relationship between the dihydrofuran ring and the isatin benzene ring) (Fig. 1). In the 2 : 1 adduct **10**, the two isatins are added to the

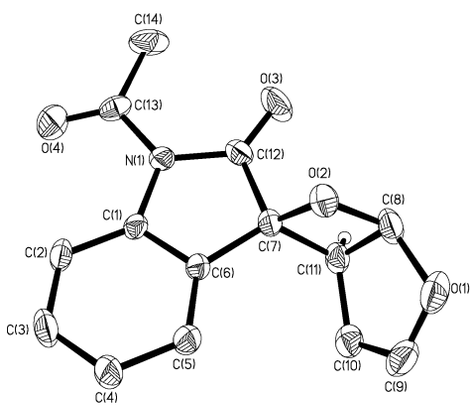
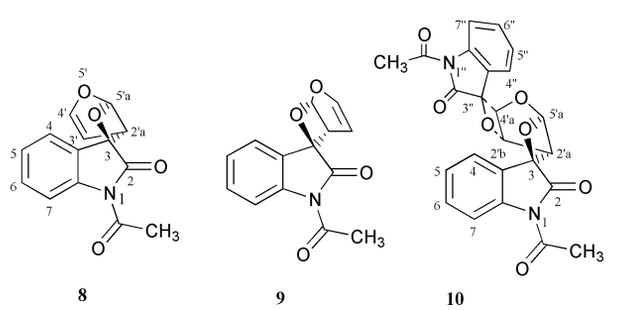


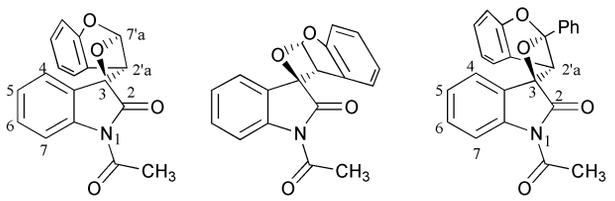
Fig. 1

two C=C bonds in furan with different regioselectivity so that the two isatin carbonyl oxygen atoms are head-to-head and head-to-tail to the furan oxygen atom respectively. The two isatin benzene rings are all *syn* with the tetrahydrofuran ring, and the two oxetane rings at the two sides of the furan ring are *trans* to each other.

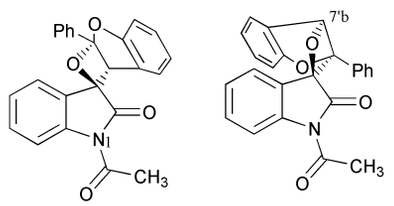


8 **9** **10**

Similar irradiation of a benzene solution of **1** with benzofuran gave the *syn*-(**11**, 76%) and the *anti*-(**12**, 6.5%) spirooxetanes as products after chromatographic separation. The **9**–**10** ratio is 12 : 1, in agreement with that found in the ^{1}H NMR spectrum of the crude reaction mixture. No signals ascribable to other regioisomeric cycloadducts were found in the reaction mixture's spectrum. In the ^{1}H NMR spectra of **11** and **12**, H(2′a) and H(7′a) at the oxetane ring absorb at ~4.7 and ~7 ppm respectively with a $\Delta\delta$ value of 2.3 ppm, indicating their acetal structure. There are two main differences in the ^{1}H NMR spectrum of **11** and **12**. 1. The acetyl methyl protons in the *syn*-isomer **11** absorb at 2.76 ppm, while in the *anti*-isomer **12**, this absorption is shifted upfield to 2.49 ppm due to the shielding effect of the benzofuran benzene ring. 2. H^4 in the *syn*-isomer is shielded by the benzofuran benzene ring and resonates at a much higher field (δ 6.28) than ^{4}H in the *anti*-isomer **12** which absorbs at δ 7.



11 **12** **13**



14 **15**

Photocycloadditions of **1** with **4** under similar conditions furnished **13**(72%), **14**(10%), and **15**(13%). Compounds **13** and **14** are diastereomers with an acetal structure. Again, the acetyl methyl protons in the *syn*-isomer[18] absorb at a lower field (δ 2.72 ppm) than in the *anti*-isomer (δ 2.49 ppm). Also, H^4 in *syn*-**13** resonates at a much higher field at δ 6.47 ppm than the H^4 in *anti*-**14** which absorbs at $\delta > 7$. The *syn*-spirooxetane **15** is regioisomeric to **13** and **14**. The methine proton in the oxetane ring absorbs at δ 7 ppm, and the acetyl methyl proton absorption is at δ 2.73.

Photoinduced [2 +2] cycloadditions of 8-methoxypsoralen (8-methoxy-7*H*-furo[3,2-*g*][1]benzopyran-7-one) (**5**) with alkenes have been widely investigated as a model process to simulate the photochemotherapeutic action of psoralen. It was found that photocycloadditions usually take place at the pyran ring to yield the corresponding cyclobutanes.[19] We have previously shown[20] that under photoinduced electron transfer (PET) conditions, the reaction site in **5** is at the furan ring. Recently, photocycloadditions of **5** with electron acceptor alkenes (such as maleimide) at the furan ring have also been reported.[19d] However, photoinduced cycloadditions of carbonyl compounds with psoralens to give oxetanes have not been investigated. We therefore investigated the photocycloadditions of **1** with **5**. It was found that cycloaddition takes place exclusively at the furan C=C bond to gave the *syn*-spirooxetane **16** as the sole isolated product in 95% yield. The ^{1}H NMR spectrum of the crude reaction mixture reveals the presence of the *anti*-isomer as a minor product in a ratio of *anti–syn* ~3 : 100. In the ^{1}H NMR spectrum, H(9′a) and H(2′a) resonate at δ7 and δ4.69 ppm respectively, indicating that **16** has an acetal structure.

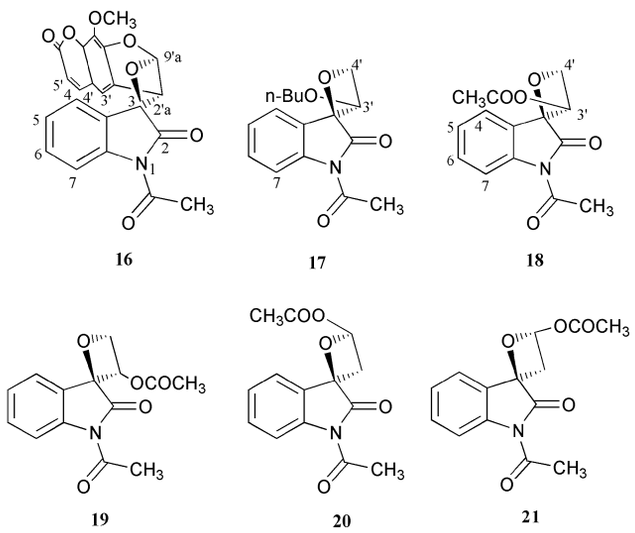
Photolysis of a benzene solution of **1** and *n*-butyl vinyl ether gave the *syn*-spirooxetane **17** in 95% yield after chromatographic separation. The ^{1}H NMR spectrum of the crude reaction mixture after photolysis reveals the presence of the *anti*-isomer in a *anti–syn* ratio of ~5 : 100.

Photoinduced reaction of **1** with vinyl acetate **7** in benzene gives four cycloadducts **18**, **19**, **20** and **21** in a total yield of 94% after chromatographic separation. The ^{1}H NMR spectrum of the crude products shows that the ratio of (**18** + **19**)–(**20** + **21**) is 1.72 : 1, and the diastereoisomeric ratio (**18**–**19**) is 11 : 1

Table 1 Photoinduced reactions of **1** with enol ethers **2**–**7**

	Alkene	Solvent	Products and yield (%)	*syn*–*anti*
	2	PhH	**8** (48), **9** (6), **10** (30)	8 : 1 [a]
	3	PhH	**11** (76), **12** (6.5)	12 : 1 [a]
	4	PhH	**13** (72), **14** (10), **15** (13)	7.2 : 1 [a]
	5	PhH	**16** (95)	~100 : 3 [b]
	6	PhH	**17** (95)	~100 : 5 [b]
	7	PhH	**18** (55), **19** (5), **20** (32), **21** (2.5)	11 : 1(**18**–**19**), 13 : 1 (**20**–**21**) [b]

[a] *syn*–*anti* ratio obtained by chromatographic separation of the reaction mixture after photolysis and by ^{1}H NMR analysis of the reaction mixture. [b] *syn*–*anti* ratio obtained by ^{1}H NMR analysis of the reaction mixture after photolysis.



(Table 1). The *syn*-configuration of **18** is indicated by an X-ray crystallographic analysis (Fig. 2). Diastereomers **20** and **21** are formed in a ratio of 13 : 1, also in favor of the *syn*-isomer. In these two 2-alkoxyoxetanes, the absorption of the two methylene protons in the oxetane ring moves upfield to δ2.7–3.5 ppm from ~δ5 ppm in **18** and **19**, while the methine proton absorption moves downfield by more than 1 ppm from that in **18** and **19** to ~6.75 ppm.

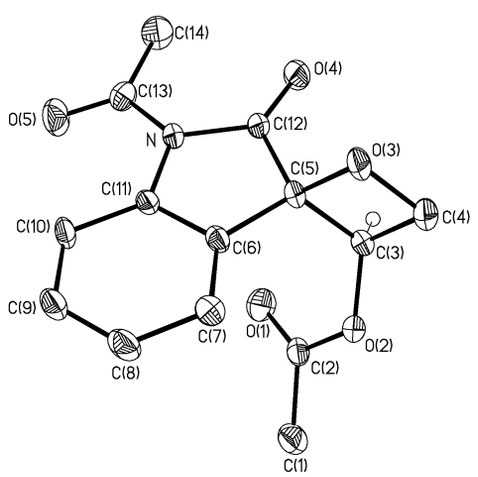


Fig. 2

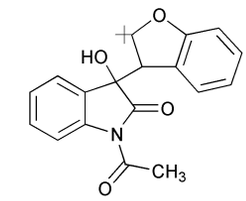
Solvent effects on these photoinduced reactions have been tested. In contrast to the smooth reactions in benzene between **1** and the olefins **2**–**7** yielding the corresponding spirooxetane products, photolysis in acetonitrile resulted in sluggish reactions for all the alkenes except **6**. Preparative photolyses were not carried out for these alkenes since only low conversions were achieved after lengthy irradiation, and unambiguous identification of products and estimation of their ratios by inspection of the ^{1}H NMR spectra of the crude reaction mixture were impeded by the low conversion and the presence of components derived from such side reactions as alkene cation radical polymerization *etc*. In the case of *n*-butyl vinyl ether, although the reaction is still much slower than in benzene, it proceeded to high conversion. The ^{1}H NMR spectrum of the reaction mixture showed that *syn*-**17** is the main product while the *anti*-isomer was formed in a *syn*–*anti* ratio of ~10 : 1. No absorptions for other regioisomers were found in the spectrum. In a preparative photolysis, a significant amount of highly polar tarry materials was also formed in the reaction.

2 Chemical transformations of the spirooxetane products

It is seen that photocycloadditions of **1** with the enol ethers **2**–**5** furnish the 2-alkoxyoxetanes regioselectively. With the aim of exploring synthetic applications of these reactions for indole structure elaboration, we have examined the acid catalysed ring opening reactions of the spirooxetanes derived from furan and benzofuran. Purging dry hydrogen chloride at room temperature into a methanol solution of the spirooxetane **11** gave two oxetane ring cleavage products **22** (41%) and **23** (52%). On the other hand, passing dry hydrogen chloride into a benzene solution at room temperature gave the 3-(benzofuran-3-yl)indol-2-one **24** (36%) and two of its hydrochlorinated products **25** (28%) and **26** (23%) as a pair of diastereomers. Acid catalysed ring opening of **11** at room temperature in THF also gave **24** (43%) and **25** (14%), together with a solvent incorporated product **27** (33%), which is possibly derived from trapping of the carbocation **A** by THF followed by hydrolysis of the oxonium salt by the adventitious water in the solvent. Purging dry hydrogen chloride into a THF solution of the spirooxetane **8** at room temperature gave the 3-(furan-3-yl)indole derivative **28** in 91% yield.

Discussion

Prediction and rationalization of the regioselectivity and diastereoselectivity in view of the reaction mechanism of the cycloadditions have been the main concerns in the studies of the Paterno–Büchi reaction. Our results show that, photoinduced cycloadditions of **1** with the alkenes **2**–**7** from the n–π^* triplet state (T_1) of the isatin take place at the C(3) carbonyl of **1** selectively and furnish the corresponding spiro(3*H*-indole-3,2′-oxetane)s with high regio- and diastereoselectivity. Recent advances in the field of photoinduced electron transfer (PET) reactions have had great impact on our understanding of the mechanism[21–24] and the factors that influence the regio-[13f,13h,21] and diastereoselectivity[6–8,17] in the Paterno–Büchi reaction. Photoinduced cycloadditions of triplet nπ^* carbonyl compounds with electron rich alkenes are initiated by the orbital interaction between the low lying half occupied n orbital of the carbonyl compound and the filled π orbital (HOMO) of the alkene.[25] An electron (charge) transfer interaction between the two addends is therefore involved, and a high lying alkene π orbital with energy higher than or close to the carbonyl singly occupied n orbital can be seen as a prerequisite for these reactions. In accord with this, we have found that **1** cannot take part in photocycloadditions with electron deficient alkenes



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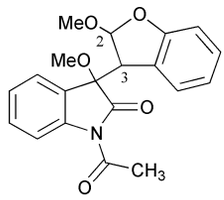

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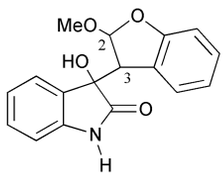

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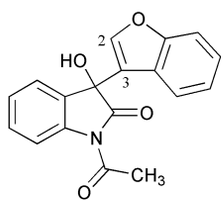

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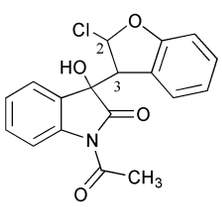

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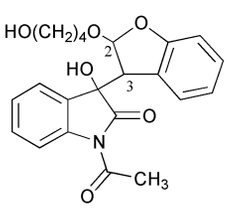

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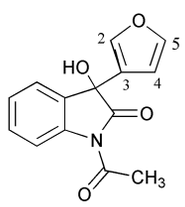


28

such as acrylonitrile (AN), methyl acrylate (MA), and *N*-vinylsuccinimide, all of which have a π orbital with energy much lower than the n orbital of **1**.[26] Alkenes **2**–**6** have HOMOs much higher than the n orbital of **1**.[27] The HOMO energy of **7** is −10.06 eV,[28] a little lower than the n orbital of **1**, but it is still much higher than the HOMO in MA and AN. However, this charge transfer character in the frontier molecular orbital (FMO) interaction responsible for the cycloaddition of triplet nπ* carbonyl with electron-rich alkenes does not necessarily lead to the SET process, and in many cases, full electron transfer is not involved. In this regard, the empirical Weller equation[29] could be used to assess the possibility of the SET involvement in the reaction. A negative ΔG_{ET} for electron transfer suggests that SET is energetically feasible, and *vice versa*. It has been shown that in cycloadditions with and without SET involvement regio- and diastereoselectivity can be determined by different factors.[6,13f,13h]

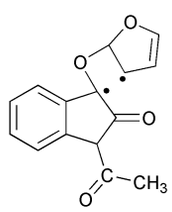
1 Regioselectivity in the cycloadditions

In the Paterno–Büchi reactions without SET involvement, the regioselectivity can be predicted from the most stable 1,4-diradical intermediate[13a,13e,30] and by considering the FMO interactions between the two addends.[31] The oxidation potential and the estimated ΔG_{ET} value from the Weller equation in PhH and in MeCN between ^{3}**1*** and the alkenes are listed in Table 2. All the alkenes **2**–**7** have positive ΔG_{ET} with ^{3}**1*** in PhH, suggesting that SET is unfavorable in this solvent. In the reaction of ^{3}**1*** with furan, benzofuran and psoralen, the products formed (**8**, **9**, **11**, **12** and **16**) are cyclic acetals. This regioselectivity is similar to that found in photocycloadditions of furan with other carbonyl addends (aldehydes and ketones,[3a,6–9]) and can be rationalized by the fact that in the 1,4-diradical intermediates, an allylic radical as in **B** is ~7 kcal mol^{-1} more stable than an α-oxymethylene radical as in **C**.[36] The 2 : 1 adduct **11** formed in a secondary reaction by the addition of ^{3}**1*** with the primary adduct **9** has a head-to-tail structure since an α-oxymethylene radical is ~12 kcal mol^{-1} more stable than a methylene radical.[36] In the photocycloaddition of **1** with 2-phenylbenzofuran, a head-to-tail regioisomer **15** is obtained in 13% yield. Obviously, in the 1,4-diradical leading to **15** (**D**), the phenyl at C(2) in the furan ring renders additional stability to the α-alkoxymethine radical although steric hindrance to the subsequent ring closure is greater here.

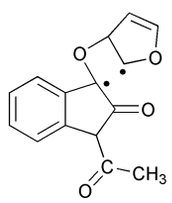
Table 2 ΔG_{ET} for SET between ^{1}**1*** and alkenes

Alkene	E^{ox} (SCE, MeCN)	ΔG_{ET}[a] In PhH	ΔG_{ET}[a] In MeCN
2	1.85[32]	4.7	−5.4
3	1.82[33]	4.0	−6.1
5	1.67[34]	0.6	−9.6
6	1.80[35]	3.6	−6.5
7	2.51[35]	19.9	9.8

[a] Estimated from the Weller equations[29]



B



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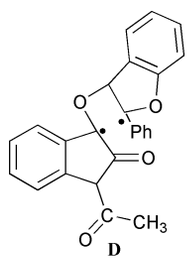


D

Reaction of ^{3}**1*** with vinyl butyl ether **6** gave the head-to-tail adduct **17** exclusively in benzene. This is in contrast with the previously reported photocycloadditions of aldehydes and aliphatic ketones with acyclic vinyl ethers[13a–f] where two regioisomers are formed in comparable yield. It seems that while in the reaction of ^{3}**1*** with **6** in benzene, the formation of the most stable 1,4-diradical determines the regioselectivity, in the reactions of aldehydes and aliphatic ketones with vinyl ethers,[13a–f] charge transfer interaction plays a more important role, and preorientation of the two addends in the exciplex intermediate is responsible for the low regioselectivity since a charge density calculation has shown that in the vinyl alkyl ether cation radical, the two vinyl carbon atoms have comparable positive charge density.[13f] Similar to **6**, in the reactions of ^{3}**1*** with vinyl acetate, the head-to-tail cycloadducts **18** and **19** are formed in preference to the head-to-head products **20** and **21** with a (**18** + **19**)–(**20** + **21**) ratio of 1.72 : 1.

2 Diastereoselectivity in the cycloadditions of 1 with 2–7

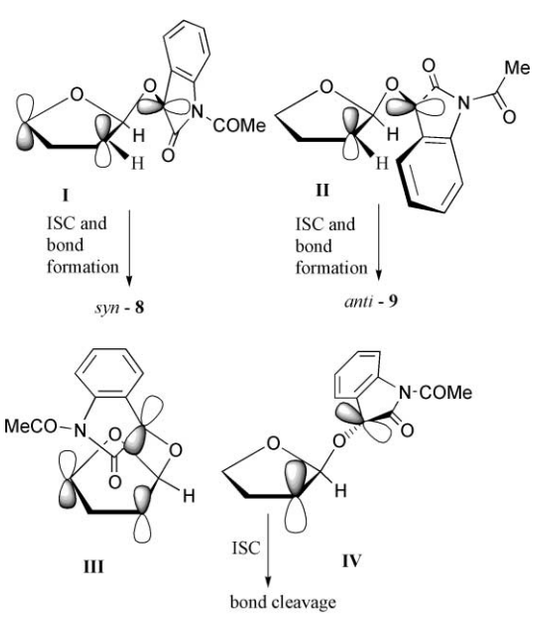
The mechanistic and structural factors that decide the diastereoselectivity in the Paterno–Büchi reaction have not been as extensively studied as for regioselectivity. However, recent studies have shown that the possibility of SET involvement is also an important factor in the rationalization of the diastereoselectivity.[6,17] In cases where SET is not involved, Griesbeck and coworkers have recently suggested the application of the Salem–Rowland rules[37] on diradical intersystem crossing (ISC) by the spin-orbit coupling (SOC) mechanism to the preoxetane 1,4-diradical intermediate in the Paterno–Büchi reaction to rationalize the cycloaddition diastereoselectivity.[6,38] These considerations based on the conformational influence on ISC rate have been successfully applied to rationalize the *endo*-selectivity in the photocycloadditions of aldehyde and ketones with cyclic monoalkenes.[6,7a] We also found that, the preferential *syn*-(*endo*)-selectivity in the cycloadditions of the triplet 1-acetylisatin (**1**)

with styrene derivatives could be rationalized by this model.[17] A recent high level *ab initio* calculation on the conformational dependence of SOC and singlet–triplet separation in the Paterno–Büchi diradical intermediate provided computational support for this model.[39]

To account for the *exo*-selectivity in the photocycloadditions of aldehyde and ketones with furan, Griesbeck and coworkers further postulated that[6c] secondary orbital interactions in the diradical intermediate between the exocyclic radical and the allyl radical play an important role in determining the relative contribution of the diradical conformers with the two spin-bearing p orbitals orthogonal to each other. This idea has also been used to account for the diastereoselectivity in the cycloaddition of carbonyl compounds with 2-siloxyfuran.[8]

Diastereoselectivity in the Paterno–Büchi reactions of carbonyl compounds with acyclic enol ethers such as vinyl alkyl ether[13d,13i] and vinyl acetate[14c] have scarcely been reported. Also, diastereoselectivity in the reactions of excited cyclic α-diketo-compounds with furan derivatives have not been investigated. We have shown that, although the quantitative diastereomeric ratios are different, depending on the structures of the alkenes, photocycloadditions of **1** with all the enol ethers **2**–**7** gave the thermodynamically less stable *syn*-spirooxetanes with high selectivity.

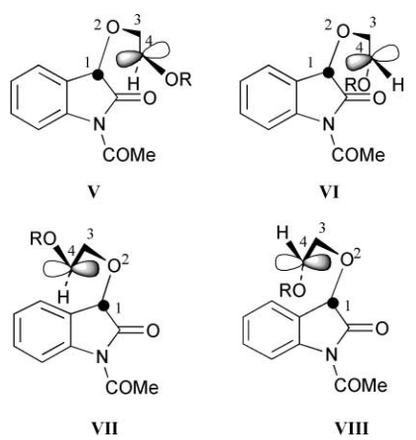
The *syn–anti*- ratio is 8 : 1 in the reaction of ^{3}**1*** with furan. In this case, four conformations which have the two spin-bearing p-orbitals orthogonal and close in space to each other are suitable for efficient ISC and C=C bond formation. In two of these (**I** and **II**), the isatin C(3) p orbital approaches the furan C(3) p orbital from outside of the furan ring. It is obvious that **I** is sterically more favorable because of the absence of the severe *gauche* hindrance between the furan C(3)–H bond and the isatin benzene ring in **II**. C–O bond rotation leading to ISC in **I** gives the major diastereomer *syn*-**8**, while ISC from the sterically less favored **II** furnishes the minor isomer **9**. In the two other conformers with the isatin C(3) p orbital approaching the furan C(3) p orbital from the inner side of the furan ring, only **III** needs to be considered since the other conformation with the isatin phenyl pointing to the furan ring suffers from extreme steric congestion. ISC from **III** leads to the minor *anti*-**9**. The possible benefit achieved in conformation **III** through secondary orbital interaction between the isatin C(3) p-orbital and the allyl orbital must have been overridden by the unfavorable steric interaction between the furan ring and the isatin ring. A similar situation was found for the photocycloaddition of phenylglyoxylate with furan[6c,7a] where the *exo–endo* ratio tends to increase as the carbonyl α-substituent becomes bulkier.



The *syn-trans-syn*-configuration in the 2 : 1 adduct **10** shows that the two sequential cycloadditions of ^{3}**1*** with furan all proceed with *syn*-selectivity, which is in accord with the above analysis on the formation of the 1 : 1 adducts. The *trans*-configuration around the furan ring minimizes the steric strain between the two isatins.

The preferential *syn*-selectivity in the cycloadditions with **3**, **4** and **5** can be rationalized likewise by considering the sterically more favorable ISC conformers similar to **I–III**. Benzannelation of the furan ring has no significant influence on the steric situation around the 1,4-diradical.

As an acyclic enol ether, *n*-butyl vinyl ether also displays an overwhelming *syn*-preference in cycloadditions with **1**. Four ISC conformations are to be considered here. In **V** and **VI**, where the alkene C(2) p-orbital approaches the isatin C(3) p-orbital from outside of the isatin framework, the sterically more favorable **V** gives the major *syn*-adduct **17**. In **VII** and **VIII** where the alkene C(1) p orbital approaches the isatin C(3) p orbital from the inner side, ISC from **VII** gives the *anti*-isomer, while **VIII** gives the *syn*-adduct. However, the Paterno–Büchi 1,4-diradicals are known to be sufficiently long-lived (τ typically in the range of ~1–7 ns[38,40]) to allow C–O and C–C bond free rotation. These C(3)–O(2) and C(4)–O(R) bond rotations and the chain motion caused by C–C bond rotation in the butyl would prevent the 1,4-diradical from reaching the 'inward' conformations (**VII** and **VIII**) due to the large steric hindrance between the butyloxy group and the isatin benzene ring. As a result, conformers **VII** and **VIII** would be difficult to achieve, and **V** and **VI** are the main conformers responsible for ISC with the diastereomer ratio reflecting their relative contribution to the ISC.



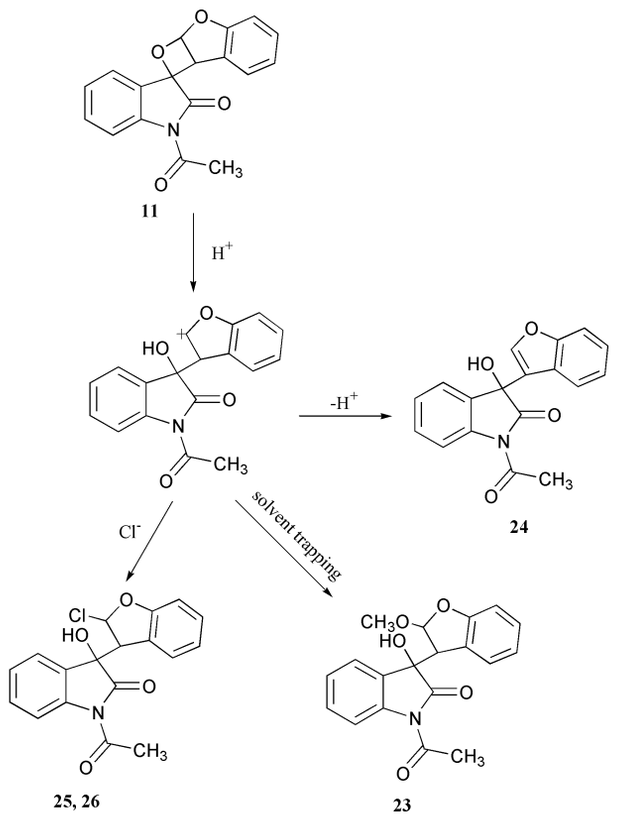
This analysis also applies to the photocycloaddition of **1** with vinyl acetate, where in the two pairs of cycloadducts with different regioselectivity, the *syn–anti* ratio is 13 : 1 and 11 : 1 respectively, and the *syn*-diastereomers predominate.

Solvent polarity has a profound effect on the reactions. For alkenes **2**–**6** with low E^{ox}, the ΔG_{ET}s in MeCN are significantly negative, indicating that SET is energetically feasible in this polar solvent. In these cases, triplet ion radical pairs are formed, which tend to dissociate further. In cage ion-radical pair combination leading to cycloadducts is therefore largely suppressed, resulting in severely retarded reaction rates. Also, side reactions induced by the alkene cation radicals which have escaped out of solvent cages such as polymerization, oxygenation, *etc*., arise and give significant amounts of tarry materials.

3 Acid catalysed ring opening reactions of the spirooxetanes

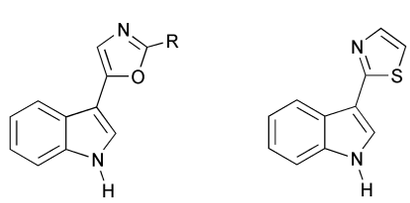
Photocycloadditions of **1** with **2**–**7** provide a convenient and high yielding access to a novel class of spiro(3*H*-indole-3,2′-oxetane)s with additional diverse structural features. Many of them are polycyclic and have a cyclic acetal structure. Although spirooxetanes have been found in a few natural products[41] and

have biological effects of practical interest such as antitumor activity,[42] their main merit from a synthetic point of view is that they are apt to undergo further transformations under various conditions and can be used as a useful synthon in the synthesis of compounds with delicate structures.[3,4,5] The acid catalysed transformations of the furan series spirooxetanes **8** and **11** furnish the 3-(furan-3-yl)indole and 3-(benzofuran-3-yl)indole derivatives respectively in high yield. The reaction mechanism is postulated in Scheme 1 with the reactions of **11** as an example.



Scheme 1

It is known that many biologically active indole derivatives are C(3) substituted.[43] C(3) spiroindoles are of considerable recent interest due to their various biological activities.[44] Several 3-(heteroaryl)indoles such as 3-(oxazol-5-yl)indoles (**29**) and 3-(thiazol-2-yl)indoles (**30**) are naturally occurring alkaloids.[45] Our results show that acid catalysed ring opening of the spirooxetanes derived from photocycloadditions of isatin with enol ethers provides a general and versatile method for C(3) derivatization of indole derivatives, and also easily furnishes in high yields the 3-(furan-3-yl)indole derivatives which are otherwise difficult to access.[46]



In summary, photocycloadditions of 1-acetylisatin with enol ethers **2**–**7** give spiroindole[3,2′]oxetanes in high yield and with high regio- and diastereoselectivity. Regioselectivity in these cycloadditions is determined by the formation of the most stable 1,4-diradical intermediate. The application of the Salem–Rowland rule in the rationalization of the diastereoselectivity in the photocycloadditions of cyclic ketones with cyclic and acyclic enol ethers has been examined and the results show that the predominate *syn*-selectivity in these reactions can be rationalized by the conformational dependence of the ISC efficiency in the 1,4-diradical intermediate as required by the Salem–Rowland rule. Acid-catalysed oxetane ring opening reactions of the spiro[3*H*-indole[3,2′]oxeto[2,3-*b*]furan(benzofuran)]s provide a straightforward and efficient access to the 3-(furan-3-yl)indole and 3-(benzofuran-3-yl)indole derivatives. Therefore, the Paterno–Büchi reaction of isatin with enol ethers and subsequent chemical transformations of the spirooxetanes may serve as an efficient and versatile synthetic approach for indole derivatization at C(3).

Experimental

Melting points are uncorrected. ^{1}H NMR were recorded at 300 MHz on a Bruker spectrometer with $CDCl_3$ as solvent. *J* Values are given in Hz. ^{13}C NMR were recorded with a Bruker Ac 500 MHz spectrometer at 125 MHz. IR spectra were taken with a Shimadzu IR 440 spectrometer in KBr pellets. Mass spectra were recorded with a VG ZAB-HS spectrometer. Elemental analyses were obtained using a Perkin-Elmer-240 C analyser. Benzene (AR grade) and tetrahydrofuran (AR grade) were dried with sodium and distilled before use. Acetonitrile was dried with P_2O_5 and distilled before use. Other reagents were CP or AR grade and were used as received without further purification.

General procedures for the preparative photolyses of 1-acetylisatin with alkenes

The light source was a medium-pressure mercury lamp (500 W) in a cooling water jacket which was further surrounded by a layer of filter solution (10% aq. sodium nitrite, 1 cm thickness, $\lambda > 400$ nm). The solution of 1-acetylisatin (0.05 M) and an excess amount of alkene in benzene was placed in glass tubes and purged with dry nitrogen for 30 min. The solutions were then irradiated at room temperature under continuous nitrogen purging. At the end of the reaction (TLC monitoring), the solvent was removed *in vacuo*. ^{1}H NMR spectra of the crude reaction mixture were measured for the estimation of product ratio. The reaction mixture was then separated by flash chromatography on a silica gel column with petroleum ether (bp 60–90 °C)–ethyl acetate as eluent to afford the cycloadducts. The diastereomers were either separated by column chromatography or by fractional crystallization when the two isomers could not be separated by column chromatography.

General procedures for the acid catalysed ring cleavage of the oxetanes

The oxetanes were dissolved in the corresponding solvent (0.05 M). Hydrochloride gas was purged into the solution through a drying tube filled with $CaCl_2$. When the reaction was completed (TLC monitoring), the solution was washed twice with aqueous Na_2CO_3 and extracted with ether, the ether solution was then dried and concentrated *in vacuo*. The residue was separated by flash chromatography on a silica gel column with petroleum ether (bp 60–90 °C)–ethyl acetate as eluent.

Photolysis of 1 with furan 2

A solution of **1** (0.05 M) and **2** (0.5 M) in benzene was photolysed for 48 h to reach a complete conversion of **1**. Work-up as before gave the products **8**, **9** and **10**.

***syn*-1-Acetyl-2′a,5′a-dihydrospiro[indole-3,2′-oxeto[2,3-*b*]-furan]-2(1*H*)-one 8.** Colorless blocks from petroleum ether–acetone, mp 155–157 °C; ν_{max}/cm^{-1} 3000, 1760, 1710, 1600, 760; δ_H (300 MHz, H–H COSY) 2.73 (3H, s, CH_3), 4.17 (1H, ddd, *J* 4.1, 2.9, 1.0, H$^{2'a}$), 5.12 (1H, t, *J* 2.9, H$^{3'}$), 6.77 (1H, d, *J* 4.1, H$^{5'a}$), 6.85 (1H, dd, *J* 2.9, 1.0, H$^{4'}$), 7.24 (1H, td, *J* 7.5, 1.0,

ArH), 7.45 (1H, td, *J* 8.1, 1.0, ArH), 7.85 (1H, d, *J* 7.5, ArH), 8.23 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 257 (M^+, 2), 146 (76), 43 (100) (Found: C, 65.39; H, 4.39; N, 5.48. $C_{14}H_{11}NO_4$ requires C, 65.37; H, 4.28; N, 5.45%).

***anti*-1-Acetyl-2′a,5′a-dihydrospiro[indole-3,2′-oxeto[2,3-*b*]-furan]-2(1*H*)-one 9.** Colorless needles from petroleum ether–acetone, mp 129–130 °C; ν_{max}/cm^{-1} 3016, 2995, 1777, 1769, 1607, 759; δ_H (300 MHz) 2.67 (s, 3H, CH_3), 4.12 (1H, dd, *J* 4.1, 1.0, $H^{2'a}$), 5.14 (1H, t, *J* 2.9, $H^{3'}$), 6.74 (1H, d, *J* 4.0, $H^{5'a}$), 6.84 (1H, dd, *J* 2.9, 1.0, $H^{4'}$), 7.33 (1H, t, *J* 7.5, ArH), 7.44 (1H, td, *J* 8.1, 1.0, ArH), 7.71 (1H, dd, *J* 7.5, 1.0, ArH), 8.24 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 257 (M^+, 3), 43 (100) (Found: C, 65.51; H, 4.38; N, 5.47. $C_{14}H_{11}NO_4$ requires C, 65.37; H, 4.28; N, 5.45%).

***syn-trans-syn*-1,1″-Diacetyl-2,2″-dioxodispiro[indole-3,9′-[3,6,8]trioxatricyclo[5,2,0,$0^{2,5}$]nonane-4′,3″-indole] 10.** Colorless needles from MeCN, mp 157–159 °C; ν_{max}/cm^{-1} 3010, 1760, 1730, 1720, 1610, 1465, 1180, 980, 780; δ_H (300 MHz) 2.73 (3H, s, CH_3), 2.74 (3H, s, CH_3), 3.99 (1H, d, *J* 3.6, $H^{2'a}$), 5.61 (1H, d, *J* 3.6, $H^{2'b}$ or $H^{4'a}$), 5.91 (1H, d, *J* 3.6, $H^{2'b}$ or $H^{4'a}$), 6.85 (1H, d, *J* 3.6, $H^{5'a}$), 7.27–7.53 (6H, m, ArH), 8.25 (1H, d, *J* 8.2, H^7 or $H^{7'}$), 8.30 (1H, d, *J* 8.2, H^7 or $H^{7'}$); *m*/*z* (%) 257 (M^+, 2), 173 (10), 161 (50), 133 (15), 43 (100) (Found: C, 64.66; H, 4.11; N, 6.16. $C_{24}H_{18}N_2O_7$ requires C, 64.57; H, 4.04; N, 6.28%).

Photolysis of 1 with 3

A benzene solution of **1** (0.05 M) and **3** (0.1 M) was photolysed for 24 h (total conversion of **1**). Work up as before gave **11** and **12**.

***syn*-1-Acetyl-2′a,7′a-dihydrospiro[indole-3,2′-oxeto[2,3-*b*]-benzofuran]-2(1*H*)-one 11.** Colorless prisms from petroleum ether–acetone, mp 177–178 °C; ν_{max}/cm^{-1} 3000, 1760, 1710, 1600, 1460, 1172, 760; δ_H (300 MHz) 2.76 (3H, s, CH_3), 4.67 (1H, d, *J* 3.9, $H^{2'a}$), 6.28 (1H, d, *J* 7.5, ArH), 6.81 (1H, d, *J* 7.5, ArH), 6.91–6.99 (3H, m, $H^{7'a}$ and ArH), 7.15 (1H, d, *J* 8.1, ArH), 7.37–7.42 (2H, m, ArH), 8.21 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 307 (4, M^+), 118 (100), 90 (27) (Found: C, 70.26; H, 5.34; N, 4.49. $C_{18}H_{13}NO_4$ requires C, 70.36; H, 5.54; N, 4.56%).

***anti*-1-Acetyl-2′a,7′a-dihydrospiro[indole-3,2′-oxeto[2,3-*b*]-benzofuran]-2(1*H*)-one 12.** Colorless needles from petroleum ether–acetone, mp 198–200 °C; ν_{max}/cm^{-1} 3000, 1770, 1712, 1650, 1600, 960, 761, 752; δ_H (300 MHz) 2.49 (3H, s, CH_3), 4.67 (1H, d, *J* 4.3, $H^{2'a}$), 6.91 (1H, d, *J* 4.3, $H^{7'a}$), 7.00–7.43 (5H, m, ArH), 7.49 (1H, td, *J* 7.8, 1.4, ArH), 7.79 (1H, dd, *J* 7.4, 1.4, ArH), 8.28 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 307 (M^+, 12), 221 (56), 118 (100) (Found: C, 70.53; H, 5.64; N, 4.67. $C_{18}H_{13}NO_4$ requires C, 70.36; H, 5.54; N, 4.56%).

Photolysis of 1 with 4

A benzene solution of **1** (0.05 M) and **4** (0.1 M) was photolysed for 24 h (total conversion of **1**). Work-up as before gave **13**, **14** and **15**.

***syn*-1-Acetyl-7′a-phenyl-2′a,7′a-dihydrospiro[indole-3,2′-oxeto[2,3-*b*]benzofuran]-2(1*H*)-one 13.** Colorless prisms from petroleum ether–acetone, mp 203–204 °C; ν_{max}/cm^{-1} 1770, 1710, 1600, 1176, 750, 700; δ_H (300 MHz) 2.72 (3H, s, CH_3), 4.82 (1H, s, $H^{2'a}$), 6.47 (1H, dd, *J* 7.6, 0.9, ArH), 6.81 (1H, d, *J* 7.4, ArH), 6.91–7.89 (10H, m, ArH), 8.22 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 383 (1, M^+), 194 (100), 165 (58), 105 (47) (Found: C, 75.14; H, 4.55; N, 3.82. $C_{24}H_{17}NO_4$ requires C, 75.20; H, 4.44; N, 3.66%).

***anti*-1-Acetyl-7′a-phenyl-2′a,7′a-dihydrospiro[indole-3,2′-oxeto[2,3-*b*]benzofuran]-2(1*H*)-one 14.** Colorless needles (petroleum ether–acetone), mp 215–216 °C; ν_{max}/cm^{-1} 3050, 1770, 1710, 1600, 968, 750, 700; δ_H (300 MHz) 2.49 (3H, s, CH_3), 4.72 (1H, s, $H^{2'a}$), 7.03–7.77 (12H, m, ArH), 8.27 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 383 (M^+, 0.1), 194 (100), 165 (62), 105 (32) (Found: C, 75.23; H, 4.74; N, 3.78. $C_{24}H_{17}NO_4$ requires C, 75.20; H, 4.44; N, 3.66%).

***syn*-1-Acetyl-2′a-phenyl-2′a,7′b-dihydrospiro[indole-3,2′-oxeto[3,2-*b*]benzofuran]-2(1*H*)-one 15.** Colorless prisms (petroleum ether–acetone), mp 185–188 °C; ν_{max}/cm^{-1} 1740, 1710, 1600, 1280, 760, 700; δ_H (300 MHz) 2.77 (3H, s, CH_3), 7.02 (1H, s, $H^{8'a}$), 7.24–7.59 (8H, m, ArH), 7.68–7.77 (2H, m, ArH), 7.87 (2H, d, *J* 7.3, ArH), 8.41 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 383 (M^+, 1.3), 194 (100), 165 (58), 146 (53) (Found: C, 75.32; H, 4.68; N, 3.59. $C_{24}H_{17}NO_4$ requires C, 75.20; H, 4.44; N, 3.66%).

Photolysis of 1 with 5

A benzene solution of **1** (0.05 M) and **5** (0.1 M) was photolysed for 36 h (total conversion of **1**). Work-up as before gave the product **16**.

***syn*-1-Acetyl-9′a*H*-8′-methoxyspiro[indole-3,2′-oxeto[3′,2′:4,5]furo[3,2-*g*][1]benzopyran]-2,6′-dione 16.** Colorless needles, mp 240 °C (decomposed); ν_{max}/cm^{-1} 3050, 3000, 2950, 1780, 1720, 1700, 1620, 1582, 1021, 760; δ_H (500 MHz) 2.76 (3H, s, $-COCH_3$), 4.21 (3H, s, $-OCH_3$), 4.70 (1H, d, *J* 3.7, $H^{2'a}$), 6.30 (1H, d, *J* 9.5, $H^{4'}$), 6.36 (1H, d, *J* 7.6, ArH), 6.62 (1H, s, H^3), 6.97 (1H, t, *J* 7.6, ArH), 7.03 (1H, d, *J* 3.7, $H^{9'a}$), 7.39 (1H, t, *J* 7.8, ArH), 7.49 (1H, d, *J* 9.5, $H^{5'}$), 8.22 (1H, d, *J* 8.2, H^7); δ_C (125 MHz) 26.6, 53.5, 61.4, 86.4, 107.6, 114.2, 115.0, 116.7, 119.4, 121.1, 122.4, 125.2, 125.9, 132.2, 133.2, 140.5, 143.4, 148.4, 153.9, 160.0, 170.2, 175.7; *m*/*z* (%) 405 (M^+, 1.5), 377 (42), 335 (100), 216 (66) (Found: C, 64.97; H, 3.76; N, 3.38. $C_{22}H_{15}NO_7$ requires C, 65.19; H, 3.70; N, 3.46%).

Photolysis of 1 with 6

A benzene solution of **1** (0.05 M) and **6** (0.5 M) was photolysed for 4 h (total conversion of **1**). Work-up as before gave the product **17**.

***syn*-1-Acetyl-3′-*n*-butyl-1,2-dihydrospiro[indole-3,2′-oxetane] 17.** Colorless blocks (petroleum ether–acetone), mp 89 °C; ν_{max}/cm^{-1} 2950, 1777, 1710, 1610, 1280, 760; δ_H 0.74 (3H, t, *J* 7.2, CH_3 in n-Bu), 1.08–1.35 (4H, m, $-OCH_2CH_2CH_2CH_3$), 2.71 (3H, s, $COCH_3$), 2.76 (1H, dt, *J* 9.0, 6.4, 1/2 OCH_2–), 3.13 (1H, dt, *J* 9.0, 6.4, 1/2 OCH_2–), 4.69 (1H, dd, *J* 6.7, 1.7, 1/2$H^{4'}$), 4.76 (1H, dd, *J* 6.7, 1.7, 1/2$H^{4'}$), 5.10 (1H, t, *J* 6.7, $H^{3'}$), 7.32 (1H, d, *J* 7.5, ArH), 7.44 (1H, dd, *J* 7.8, 1.2, ArH), 7.81 (1H, dd, *J* 7.5, 1.2, ArH), 8.23 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 259 (14), 161 (100), 146 (15) (Found: C, 66.25; H, 6.58; N, 4.94. $C_{16}H_{19}NO_4$ requires C, 66.44; H, 6.57; N, 4.84%).

Photolysis of 1 with vinyl acetate 7

A solution of **1** (0.05 M) and **7** (0.5 M) in benzene was photolysed for 4 h for the total conversion of **1**. Work-up as before gave the product **18** and three not fully separated products **19**, **20** and **21**.

***syn*-1-Acetyl-3′-acetyloxy-2-oxo-1,2-dihydrospiro[indole-3,2′-oxetane] 18[47].** Colorless needles (petroleum ether (bp 60–90 °C)–ethyl acetate), mp 113–115 °C; ν_{max}/cm^{-1} 2950, 1750, 1710, 1600, 1462, 1375, 1176, 762; δ_H (300 MHz) 1.88 (3H, s, CH_3), 2.74 (3H, s, CH_3), 4.94 (1H, dd, *J* 5.6, 7.1, $H^{3'}$), 5.16 (1H, t, *J* 7.1, 1/2$H^{4'}$), 5.62 (1H, dd, *J* 5.6, 7.1, 1/2$H^{4'}$), 7.29 (1H, td, *J* 7.5, 0.9, ArH), 7.43–7.71 (2H, m, ArH), 8.25 (1H, d, *J* 8.1, H^7); *m*/*z* (%) 275 (M^+, 1.7), 148 (79), 132 (37), 43 (100) (Found: C, 61.02; H, 4.81; N, 5.22. $C_{14}H_{13}NO_5$ requires C, 61.09; H, 4.73; N, 5.09%).

***anti*-1-Acetyl-3′-acetyloxy-2-oxo-1,2-dihydrospiro[indole-3,2′-oxetane] 19.** Not fully separated from other isomers;

δ_H (300 MHz) 2.05 (3H, s, CH_3), 2.67 (3H, s, CH_3), 4.91 (1H, t, *J* 11.5, $H^{3'}$), 5.03 (1H, t, *J* 11.5, 1/2$H^{4'}$), 5.45 (1H, t, *J* 11.5, 1/2$H^{4'}$), 7.25–8.21 (4H, m, ArH).

***syn*-1-Acetyl-4′-acetyloxy-2-oxo-1,2-dihydrospiro[indole-3,2′-oxetane] 20.** Not fully separated from other isomers; δ_H (300 MHz) 2.21 (3H, s, CH_3), 2.66 (3H, s, CH_3), 2.89 (1H, dd, *J* 4.1, 12.6, $H^{3'}$), 3.39 (1H, dd, *J* 5.5, 12.6, 1/2$H^{4'}$), 6.76 (1H, dd, *J* 4.1, 5.5, 1/2$H^{4'}$), 7.23–7.65 (3H, m, ArH), 8.18 (1H, d, *J* 7.8, H^7).

***anti*-1-Acetyl-4′-acetyloxy-2-oxo-1,2-dihydrospiro[indole-3,2′-oxetane] 21.** Not fully separated from other isomers; δ_H (300 MHz) 2.27 (3H, s, CH_3), 2.64 (3H, s, CH_3), 2.73 (1H, m, $H^{3'}$), 3.17 (1H, m, $H^{3'}$), 6.88 (1H, m, $H^{4'}$), 7.25–8.21 (4H, m, ArH).

Acid treatment of the spirooxetanes 8 and 11

Acid treatment of **11** in MeOH gave **22** and **23**, in PhH gave **24**, **25** and **26**, in THF gave **24**, **25** and **27** respectively. Similar treatment of **8** in THF gave **28**.

(±)-Acetyl-2-oxo-3-methoxy-3-(2-methoxy-2,3-dihydrobenzofuran-3-yl)-1,2-dihydro-3*H*-indole 22. Colorless prisms (petroleum ether–acetone), mp 110–111 °C; ν_{max}/cm^{-1} 2950, 1742, 1650, 1600, 1480, 1240, 1190, 776, 760; δ_H (300 MHz) 1.86 (3H, s, CH_3), 3.55 (3H, s, CH_3), 3.86 (3H, s, CH_3), 4.19 (1H, d, *J* 1.8, H^3), 5.50 (1H, d, *J* 1.8, H^2), 6.19 (1H, d, *J* 7.5, ArH), 6.63 (1H, td, *J* 7.5, 0.8, ArH), 6.82–7.39 (5H, m, ArH), 7.43 (1H, dd, *J* 7.5, 1.5, ArH); *m*/*z* (%) 353 (1), 204 (100), 144 (30), 118 (7) (Found: C, 67.79; H, 5.44; N, 3.98. $C_{20}H_{19}NO_5$ requires C, 67.99; H, 5.38; N, 3.97%).

(*3R,2′S,3′R*)-2-Oxo-3-hydroxy-3-(2-methoxy-2,3-dihydrobenzofuran-3-yl)-1,2-dihydro-(3*H*)-indole 23. Colorless blocks (petroleum ether–acetone), mp 180–182 °C; ν_{max}/cm^{-1} 3400, 3200, 1750, 1700, 1620, 1600, 1480, 750; δ_H (300 MHz) 3.58 (3H, s, CH_3), 3.79 (1H, d, *J* 0.5, H^3), 6.02 (1H, d, *J* 0.5, H^2), 6.67–7.21 (7H, m, ArH), 7.41 (1H, d, *J* 7.5, ArH), 8.00 (1H, br); *m*/*z* (%) 265 (9), 149 (100), 118 (58) (Found: C, 68.83; H, 5.34; N, 4.43. $C_{17}H_{15}NO_4$ requires C, 68.69; H, 5.05; N, 4.71%).

(±)-1-Acetyl-2-oxo-3-hydroxy-3-(benzofuran-3-yl)-1,2-dihydro-(3*H*)-indole 24[46]. Colorless prisms (petroleum ether–acetone), mp 158–159 °C; ν_{max}/cm^{-1} 3500, 1778, 1690, 1610, 1280, 1160, 770, 750; δ_H (300 MHz) 2.64 (3H, s, CH_3), 7.22–7.36 (3H, m, ArH), 7.44 (1H, s, H^2), 7.49–7.55 (3H, m, ArH), 7.60 (1H, d, *J* 7.7, ArH), 8.35 (1H, d, *J* 8.2, ArH); *m*/*z* (%) 307 (M^+, 28), 220 (55), 146 (100) (Found: C, 70.47; H, 4.37; N, 4.43. $C_{18}H_{13}NO_4$ requires C, 70.36; H, 4.23; N, 4.43%).

(*3R,2′R,3′R*)-1-Acetyl-2-oxo-3-hydroxy-3-(2-chloro-2,3-dihydrobenzofuran-3-yl)-1,2-dihydro-(3*H*)-indole 25. Colorless prisms (petroleum ether–acetone), mp 132–133 °C; ν_{max}/cm^{-1} 3500, 1772, 1700, 1600, 1460, 1276, 760; δ_H (300 MHz) 2.70 (3H, s, CH_3), 4.22 (1H, s, H^3), 6.78 (1H, d, *J* 7.8, ArH), 6.91 (1H, t, *J* 7.5, ArH), 7.01 (1H, s, H^2), 7.07 (1H, d, *J* 7.5, ArH), 7.13–7.21 (2H, m, ArH), 7.28 (1H, td, *J* 7.8, 1.4, ArH), 7.44 (1H, dd, *J* 7.5, 1.4, ArH), 8.01 (1H, d, *J* 8.0, ArH); *m*/*z* (%) 307 (22), 237 (18), 220 (39), 146 (100), 118 (45), 90 (23) (Found: C, 62.69; H, 4.19; N, 4.18. $C_{18}H_{14}NO_4Cl$ requires C, 62.88; H, 4.08; N, 4.08%).

1-Acetyl-2-oxo-3-hydroxy-3-(2-chloro-2,3-dihydrobenzofuran-3-yl)-1,2-dihydro-(3*H*)-indole (configuration not determined) 26. White powder (petroleum ether–acetone), mp 127–128 °C; ν_{max}/cm^{-1} 3368, 1779, 1681, 1476, 761; δ_H (300 MHz) 2.55 (3H, s, CH_3), 4.85 (1H, d, *J* 5.5, H^3), 6.19 (1H, d, *J* 5.5, H^2), 7.02 (1H, d, *J* 8.0, ArH), 7.22 (1H, t, *J* 7.5, ArH), 7.30–7.41 (2H, m, ArH), 7.54 (1H, td, *J* 8.0, 1.2, ArH), 7.61 (1H, d, *J* 7.5, ArH), 8.05 (1H, d, *J* 7.5, ArH), 8.30 (1H, d, *J* 8.0, ArH); *m*/*z* (%) 307 (4), 220 (13), 146 (93), 118 (100), 90 (65) (Found: C, 62.77; H, 4.28; N, 3.92. $C_{18}H_{14}NO_4Cl$ requires C, 62.88; H, 4.08; N, 4.08%).

(*3R,2′S,3′R*)-1-Acetyl-2-oxo-3-hydroxy-3-[2-(4-hydroxybutyloxy)-2,3-dihydrobenzofuran-3-yl]-1,2-dihydro-(3*H*)-indole 27. Colorless blocks (petroleum ether–acetone), mp 150–151 °C; ν_{max}/cm^{-1} 3500, 2900, 1780, 1700, 1600, 1480, 760; δ_H (300 MHz) 1.69–1.84 (4H, m, –OCH_2 CH_2 CH_2 CH_2–OH), 2.69 (3H, s, CH_3), 3.52 (2H, t, *J* 6.2, –OCH_2 CH_2 CH_2 CH_2–OH), 3.65 (1H, dt, *J* 10.0, 6.0, 1/2-OCH_2 CH_2 CH_2 CH_2–OH), 3.82 (1H, s, H^3), 3.90 (1H, dt, *J* 10.0, 6.0, 1/2-OCH_2 CH_2 CH_2 CH_2–OH), 5.87 (1H, s, H^2), 6.69 (1H, d, *J* 8.0, ArH), 6.79 (1H, t, *J* 7.5, ArH), 6.99 (1H, d, *J* 7.5, ArH), 7.09 (1H, t, *J* 8.1, ArH), 7.18 (1H, t, *J* 7.5, ArH), 7.29 (1H, t, *J* 8.1, ArH), 7.46 (1H, d, *J* 7.5, ArH), 8.05 (1H, d, *J* 8.1, ArH); *m*/*z* (%) 307 (1), 146 (15), 118 (27), 90 (100) (Found: C, 66.40; H, 6.01; N, 3.49. $C_{22}H_{23}NO_6$ requires C, 66.50; H, 5.79; N, 3.53%).

(±)-1-Acetyl-3-hydroxy-3-(furan-3-yl)-1,2-dihydro-(3*H*)-indole 28. Colorless prisms (petroleum ether–acetone), mp 109–110 °C; ν_{max}/cm^{-1} 3455, 1777, 1692, 1604, 814, 769, 737; δ_H 2.56 (3H, s, CH_3), 6.50 (1H, dd, *J* 1.6, 1.0, H^4), 7.15 (1H, dd, *J* 1.6, 1.0, H^5), 7.22 (1H, td, *J* 7.5, 1.0, ArH), 7.33–7.36 (2H, m, ArH and H^3), 7.43 (1H, dd, *J* 7.5, 1.0, ArH), 8.17 (1H, d, *J* 8.2, ArH); *m*/*z* (%) 257 (10), 146 (81), 90 (28), 43 (100) (Found: C, 65.30; H, 4.51; N, 5.60. $C_{14}H_{11}NO_4$ requires C, 65.37; H, 4.28; N, 5.45%).

Crystal structure of compound 8§

$C_{14}H_{11}NO_4$, *M* = 257.24. monoclinic, space group *C*2/*c*, *Z* = 8, *a* = 19.2158(1), *b* = 9.2422(2), *c* = 15.6965(3) Å, *α* = 90.00°, *β* = 121.111(1)°, *γ* = 90.00°, *V* = 2386.69(7) $Å^3$, D_c = 1.432 g cm^{-3}. Data were collected on a Siemens SMART CCD area detector diffractometer equipped with graphite-monochromatized Mo-Kα in the range of *θ* = 2.48–28.30°. A total of 2893 independent reflections [*R*(int) = 0.1312] were used in the refinement which converged with *R* = 0.0789 and *ωR* = 0.1902.

Crystal structure of compound 18§

$C_{14}H_{13}NO_5$, *M* = 275.25. Triclinic, space group *P*-1, *Z* = 2, *a* = 8.3660(17), *b* = 9.6653(19), *c* = 9.7304(19) Å, *α* = 68.82(3)°, *β* = 68.35(3)°, *γ* = 68.44(3)°, *V* = 656.5(2) $Å^3$, D_c = 1.392 g cm^{-3}. Data were collected on a AFC5R (RIGAKU) area detector diffractometer equipped with graphite-monochromatized Mo-Kα in the range of *θ* = 2.33–26.01°. A total of 2099 independent reflections [*R*(int) = 0.0880] were used in the refinement which converged with *R* = 0.0742 and *ωR* = 0.1933.

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§ CCDC reference number(s) 173803 and 175734. See http://www.rsc.org/suppdata/p1/b1/b109697d/ for crystallographic files in .cif or other electronic format.

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