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STUDIES DIRECTED TOWARDS THE TOTAL SYNTHESIS OF DICYCLOPENTA[a,d]CYCLOOCTANE TERPENOIDS.

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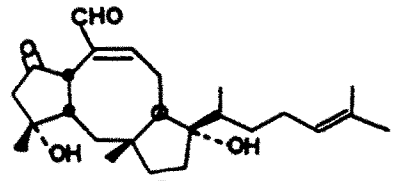
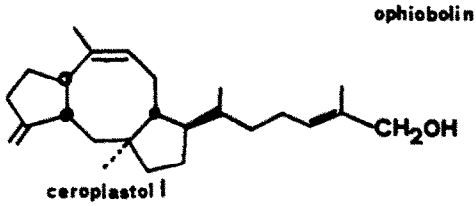
Abstract: A general strategy for the synthesis of dicyclopenta[a,d]cyclooctane terpenoids is reported. Compound 1 was synthesized from 3-methoxycarbonyl-2-cyclopentenone; its [2+2] photocycloaddition led to four diastereoisomeric photoadducts whose structures were determined by X-ray analysis, ^{1}H-NMR data and chemical transformations.

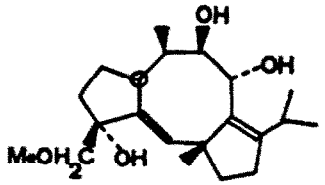
Ophiobolins (e.g. ophiobolin B [1]) and ceroplastins (e.g. ceroplastol I [2]) are naturally occurring sesterterpenes possessing the dicyclopenta[a,d]cyclooctane ring system as a characteristic structural element; the tricyclic 5-8-5 nucleus is also found in some diterpenes as fusicoccin (e.g. cotylenol[3]).



ophiobolin B



ceroplastol I



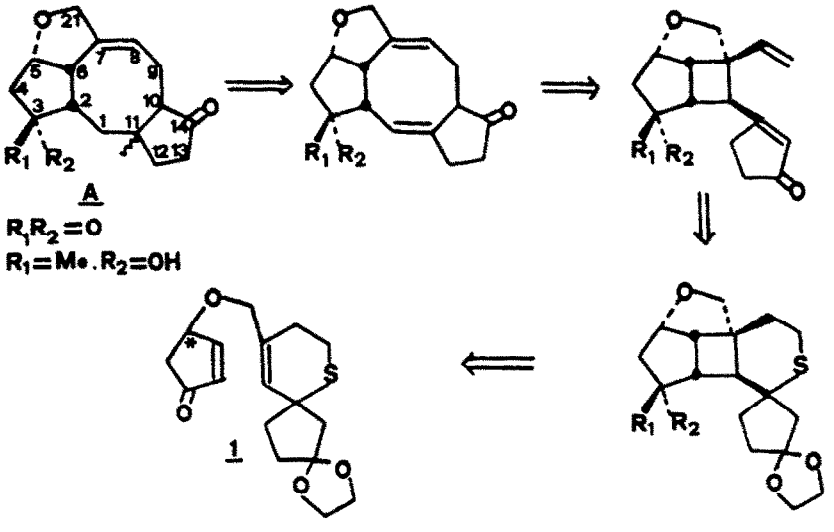
cotylenol

The novel structure, the presence of the uncommon 5-8-5 ring system and the wide ranging biological activity of these terpenoids have stimulated much effort towards their total synthesis[4] . Taking into account that the synthetic problems connected with side chains bound to cyclopentane rings have already been resolved in other approaches to terpenoids and steroids[5], the "key" strategies for the synthesis of the aforementioned compounds are the construction of the trycyclic skeleton, especially the central eight membered ring, the stereochemical control at all ring connections and the presence of correct functionalities suitable for further elaboration to the natural products.

In spite of various approaches to the synthesis of these substances[4] , to date none of them have completely resolved all the abovementioned problems.

For some time our group has been interested in the synthesis of dicyclopenta[a,d]cyclooctane terpenoids and preliminary results have already been reported[6] .

At the beginning of the research a careful retrosynthetic analysis allowed us to envision the strategy reported in Scheme 1. In our opinion, this strategy permits an approach to this class of compounds through intermediates having the characteristics of structure, stereochemistry and functional groups present in natural substances or easily elaborated in them.



Scheme 1

As reported in Scheme 1, the stereochemistry at C-6 and C-2 of the target A(*) could have been determined during the photocycloaddition,the chirality of the two carbons being regulated by the chirality of the starred carbon in 1; continuing a diastereoselective synthesis could have led to both classes of ophiobolins and ceroplastins. An enantioselective synthesis would not have been a problem, due to the fact that optically active derivatives of 2-cyclopenten-1,4-diols[7] are available. Whereas the C-6 stereochemistry could have been maintained during synthesis, that at C-2, like that at C-10, could have been thermodynamically equilibrated by the presence of adjacent carbonyls. The introduction of a methyl at C-11 would presumably not have been influenced by a strong steric induction, thus giving the possibility of constructing the correct stereochemistry for both series. Presumably an organometallic reagent, attacking the carbonyl at C-3, could have occurred with the stereochemistry present in the ophiobolines and similar products.

The atoms of oxygen at C-3, C-5, C-14 and C-21 were considered strategic for the structure elaboration of compounds possessing such functionalization and for the transformation of the intermediates in all the known natural products.

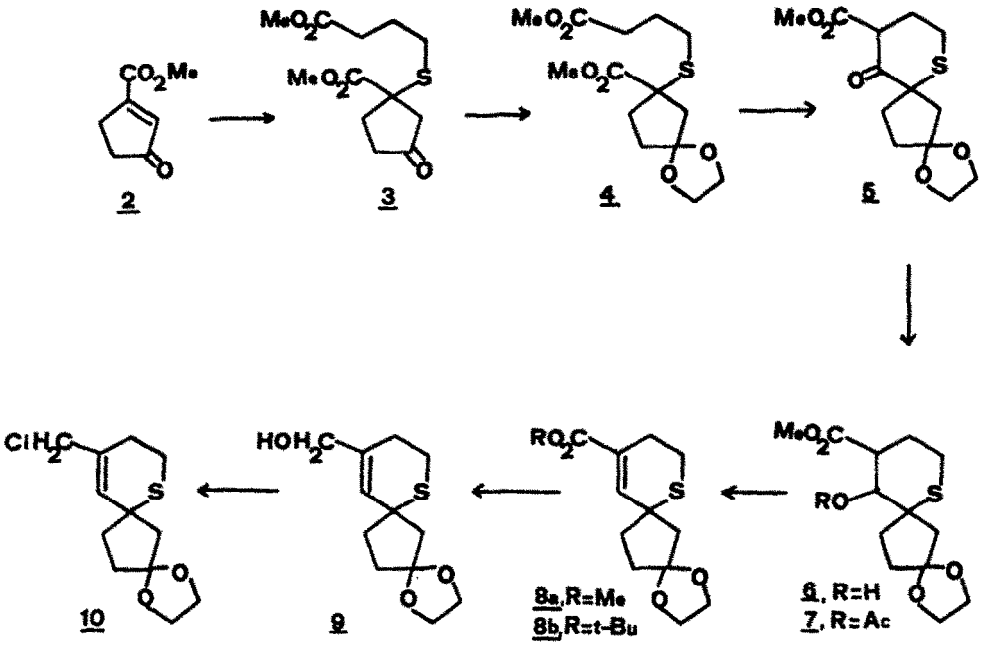
Experimental verification of the discussed strategy proceeded utilizing simple, common synthetic metodologies and the yields were not been optimized.

We report here the synthesis of compound 1 and its photocycloaddition products. Preliminary elaborations of the photoadducts are also described.

Synthesis of the ethylene ketal of 9-chloromethyl-2-oxo-6-thiaspiro[4,5]dec-9-ene 10.

The ethylene ketal of 2-oxo-9-chloromethyl-6-thiaspiro[4,5]dec-9-ene 10 was prepared in few steps from the known ketoester 2[8] as outlined in Scheme 2. Using a less expensive starting product, we took a different approach to the synthesis of 2[9] by oxidizing the corresponding aldheyde but the total yields were comparable to those of previous procedure.

(*) Numbering of ophiobolanes has been adopted in this formula.

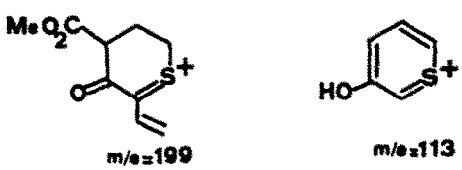


Scheme 2

At room temperature the 3 methoxycarbonyl-2-cyclopentenone 2 reacted smoothly and in good yields with the anion of methyl-4-mercapto-butanoate, with complete regioselectivity as was expected due to the greater withdrawal force of the ketone carbonyl group. By standard procedure, compound 3 was quantitatively transformed into the corresponding ketal 4, the reaction of which with t-BuOK in anhydrous dimethylsulfoxide and benzene gave the spiroderivative 5 in 60% yield. Other bases, like sodium hydride, lithium diisopropylamide or tert-butyl lithium were no better.

The resonances in the ^{1}H-NMR spectrum of compound 5 are quite difficult to interpret, probably due to an extensive overlapping of the signals of the two possible diastereoisomers generated by the cyclization; the presence of the two diastereoisomers agrees with the complete absence of a resonance corresponding to an enolic proton. No attempt was made to identify and separate the diastereoisomers, these not serving our synthetic purposes.

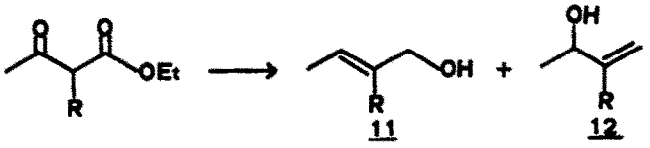
The structure of compound 5 was supported by its IR spectrum (1740,1700 cm^{-1}) and electron impact-induced fragmentation.



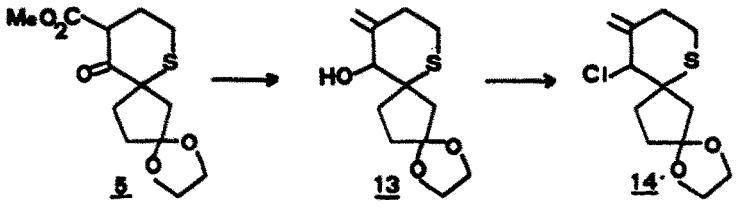
A very rapid reduction of the ketone function in compound 5 occured with sodium boron hydride, as expected for a non enolic carbonyl; the alcohol 6 was then transformed with acetic anhydride into the acetate 7 . Most of the signals in the ^{1}H-NMR spectra of compounds 6 and 7 are difficult to assign as both compounds are a mixture of the four possible diastereoisomers : nevertheless the presence of four isomers is detectable in the ^{1}H-NMR spectrum of 7 where four singlets at δ 2.10-2.20 ($C\underline{H}_3$-CO-) and four singlets at δ 3.60-3.70 (-COOC$\underline{H}_3$) are present as well resolved resonances.

By reacting the acetate 7 with t-BuOK in anhydrous benzene, a mixture of compounds 8a and 8b were obtained in 82% yield. Attempts to employ better leaving groups like mesylate or tosylate in the elimination step, led to a complex reaction mixture, probably due to the formation of cyclic sulphonium salts which can undergo rearrangement. All the resonances in the ^{1}H-NMR spectra of 8a were assigned by double-resonance experiments and fully agree with the proposed structure. Reduction of the mixture of compounds 8a and 8b with $LiAlH_4$, followed by treatment of the alcohol 9 with mesylchloride and lithium chloride[10], gave the ethylene ketal of 2-oxo-9-chloromethyl-6-thiaspiro[4,5]dec-9-ene 10.

It was reported[11] that the reaction of a β-ketoester with sodium hydride and then with lithium aluminum hydride affords a mixture of 11 and 12 in a ratio 20:80.

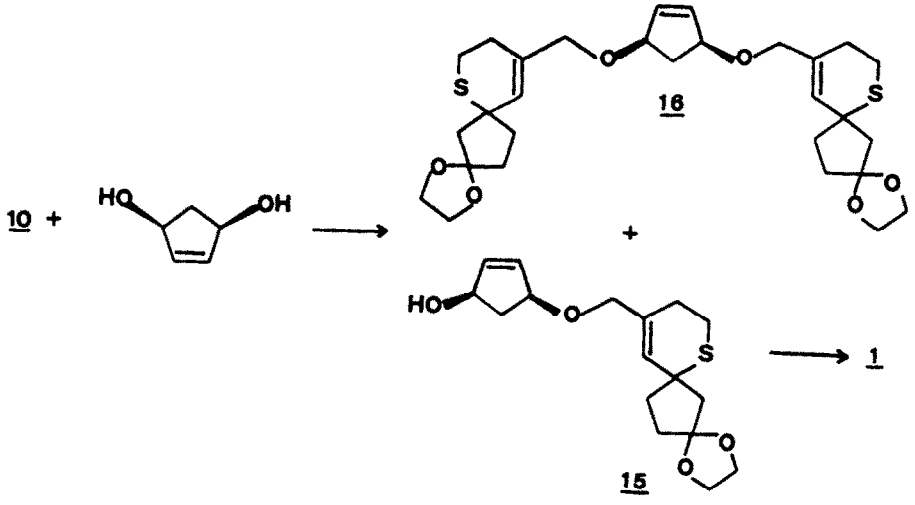


We applied this method to compound 5 in order to shorten the synthetic steps to the chloroderivative 10, and thus we obtained the allylic alcohol 13 in 70% yield; all attempts to isomerize the double bond failed. In fact treatment of 13 with thionyl chloride afforded 14 in low yield with no detectable trace of compound 10. The reaction of 13 with acids, carried out to shift the double bond, led to tarry materials even at low temperatures.



Synthesis of the ethylene ketal of 2-oxo-6-thiaspiro[4,5]dec-9-enylmethyl 4-oxo-2-cyclopentenyl ether (1), its [2+2] photocycloaddition and elaborations of the photoadducts.

The ethylene ketal of 2-oxo-6-thiaspiro[4,5]dec-9-enylmethyl 4-oxo-2-cyclopentenyl ether was synthesized in two steps according to Scheme 3:



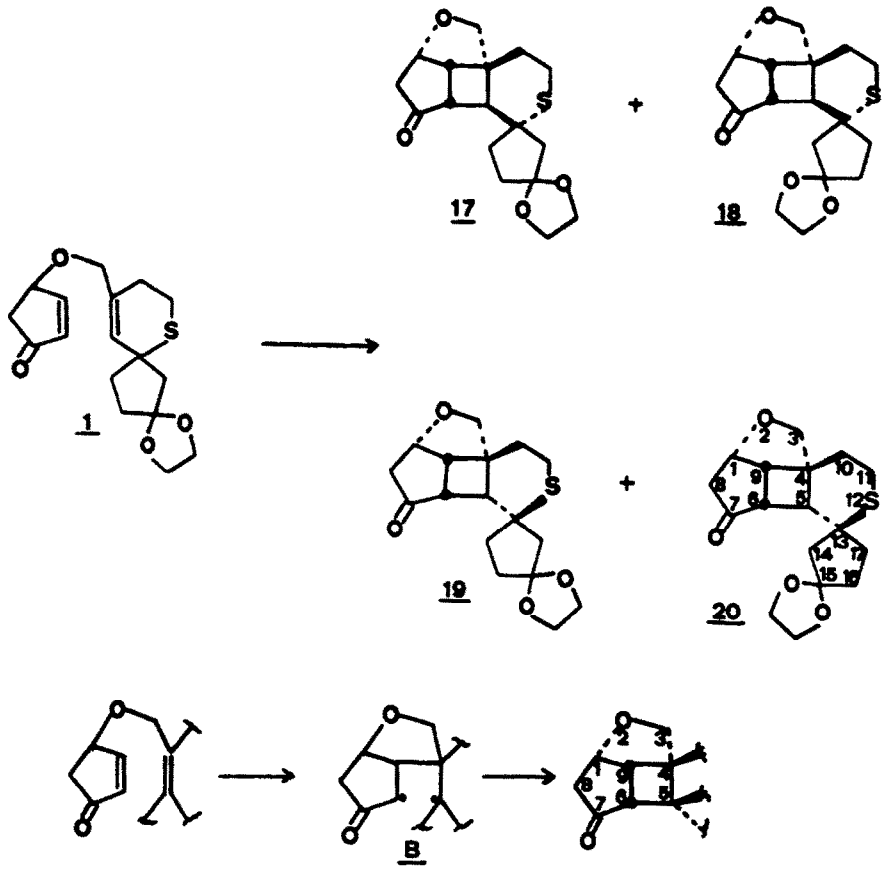
Scheme 3

The cis-2-cyclopentene-1,4-diol was transformed into the monosodium salt and reacted with the halogenoderivative 10: the best experimental conditions consisted in treating 1.5 mmoles of the diol with 1.5 mmole of sodium hydride followed by the reaction with 1.0 mmole of 10. On varying the molar ratios or changing the counterion, (i.e. Li^+) the yields were lower and we noticed an increase in the formation of the diether 16. Alternative routes to diallyl ethers, as we reported[12], were not suitable for the synthesis of 15 owing to the functionalities present in compound 10.

Mild oxidation of 15 with pyridinium chlorochromate (PCC) in the presence of sodium acetate afforded the ethylene ketal of 2-oxo-6-thiaspiro[4,5]dec-9-enylmethyl 4-oxo-2-cyclopentenyl ether 1 as a diastereoisomeric mixture which, even with various eluants, appears as a single spot in TLC. The presence of two diastereoisomers in 1 was never ascertained by analytical methods but was evident from the formation of four diastereoisomeric products by photocycloaddition as described hereunder.

Compound 1 shows an absorption due to the n,π* transition at 314 nm; irradiation of a 10^{-2} M toluene solution of 1 at -25°C with an HP-400 W mercury lamp effected smooth [2+2] cycloaddition to a mixture of the four photoadducts 17, 18, 19, 20 in the ratio 17 + 18: 19 + 20 = 3:7 as evaluated in the ^{1}H-NMR spectra by the integration of the H-1 proton which resonates at the same value of chemical shift in deuterochloroform for each couple.

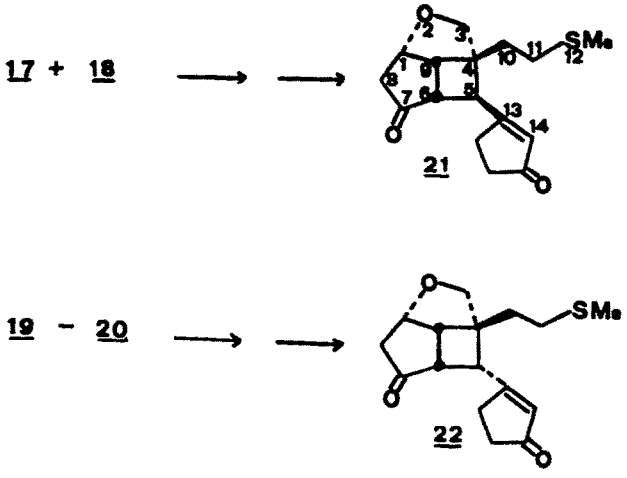
For clarity when comparing the reactivity and spectral data, we adopt here the same numbering of the photoadducts derived from the photocycloadditions of diallyl ethers in the model studies previously reported[12] and summarized in Scheme 4; this numbering does not follow IUPAC rules.



Scheme 4

The photocycloaddition of compound 1, led to four photoadducts: in fact, as we have already demonstrated[12], the reaction is fully regioselective in accordance with the "empirical rule of five" and stereoselective only in the formation of the chiral centres in positions 4, 6, 9, the chirality of these centres being determined by the chirality of C-1. A two-step mechanism through the diradical intermediate B, and the rates ratio of spin inversion and diradical collapsing, justify the lack of a steric control at position 5. As described before a fully stereoselective cycloaddition is only possible when a five-membered ring is fused to a cyclobutane in the product; in this case, in fact, the rotation of the side chain in the intermediate diradical B is structurally forbidden.

It is noteworthy that, in the following elaboration to the target molecule A, as depicted in Scheme 1, the chirality due to the spirane moiety would be destroyed so the two couples 17-18 and 19-20 should give only the two products 21 and 22. In fact on treatment with aqueous acetic acid to remove the ketal, followed by reaction with methyl iodide and sodium hydride, the two diastereoisomeric couples gave, respectively, compounds 21 and 22.



Due to the stronger steric compression of 19-20 with respect to 17-18, as shown by Dreiding model inspection and X-Ray data of 20, the ring opening reaction of 17-18 took place in three days, whereas it was quite fast for 19-20.

Furthermore, microscale experiments demonstrated that compound 22 could be trasformed, by strong bases (i.e. NaH) and prolonged reaction times (24 h) into 21 which possesses the correct stereochemistry at C-5 and C-4 for continuing the synthetic strategy.

Structure of the photoadducts

The crude reaction mixture from the photocycloaddition was first purified by flash chromatography on silica gel in order to eliminate the starting material 1. A careful analysis on TLC showed three main products, their separation being achieved by medium pressure column chromatography on silica gel. While compounds 19 and 20 could be isolated in pure form, a subsequent reversed phase column chromatography was necessary for the purification of the mixture 17-18 from small amounts of the other two diastereoisomers 19 and 20. This mixture showed two partially resolved peaks in HPLC, but we could not separate them by preparative chromatographic systems.

To assign the structure of compound 20, an X-ray crystallographic study was undertaken(*). The derived molecular model is illustrated in Fig. 1 , that shows also the numbering scheme adopted in the X-ray analysis.

(*) Lists of atomic coordinates for H atoms, displacement parameters, together with a table of distances and angles and a list of observed and calculated structure factors have been deposited with Cambridge Crystallographic Data Centre, Lensfield Road, Cambridge CB2 1EW, UK.

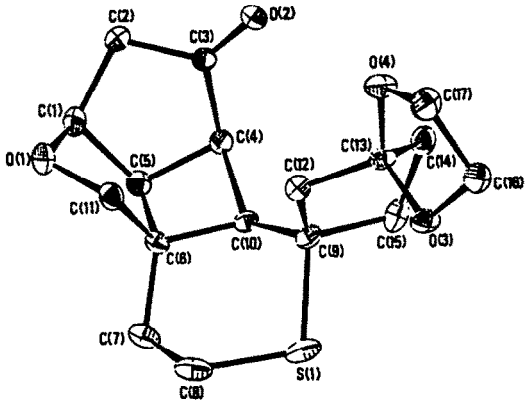


Figure 1

The X-ray structural analysis confirm that 20 is an hexacyclic molecule with a four-fused-ring system to which a spiro-decane derivative is bonded through a spiro-junction. As previously found for 26[13], the furanoid and the cyclopentanone rings are cis-fused, while the junction between the cyclobutane and the six-membered rings is trans.

The six-membered ring shows a slightly distorted chair conformation, with torsion angles across the six bonds ranging from 47.1(2) to 69.4(2)° (average absolute value 58.4°). The puckering parameters θ = 1.4(2)°, close to one of the two values (0 and 180°) describing an ideal chair conformation, and ϕ = -170(7)° indicate that the distorsion is small and occurs in the direction of a boat conformation. The comparison of the total puckering amplitude Q = 0.627(2) Å, with the value, 0.665 Å, of an ideal cyclohexane chair with equal bond length[14], suggests that there is only a slight flattening of the chair.

Two out of the four five-membered rings, the cyclopentane and the furanoid rings, are in an almost perfect twisted conformation with twist axes through the atoms C(9) and C(5), respectively. The puckering parameters are q_2 = 0.404(2) Å, ϕ_2 = - 88.5(3)° for the first ring and q_2= 0.394(2) Å, ϕ_2= -87.5(3)° for the second one. The T conformation of the cyclopentanone ring, with twist axis through atom C(5), is distorted with puckering parameters q_2 = 0.214(2) Å and ϕ_2= 84.4(5)° (to be compared with 72 and 90°, the closest values for pure envelope and twist forms, respectively). The remaining ring is in a distorted envelope conformation, with puckering amplitude q_2= 0.346(2) Å and phase angle ϕ_2= 101.3(3)°, (to be compared with 90 and 108°, typical values of pure T and E forms, respectively). In the cyclobutane ring, the four C atoms are displaced by ± 0.133(1) Å from the mean plane, and the resulting puckering parameter is q = ±0.266(1) Å. The

dihedral angle between the plane defined by the atoms C(5), C(4) and C(10) and that defined by C(5), C(6) and C(10) is 152.5(1)°, well within the range of values reported for non-planar substituted cyclobutanes (145-160°)[15,16].

20 is a highly strained molecule that shows large angular distorsions, the bond angles involving sp^3 C atoms ranging from 87.2(1) to 132.5(2)°, and several short intramolecular contacts that involve mainly the methylene group at C(11) [the shortest distance involving non-H atoms is C(4)...C(11), 2.940(3) Å].

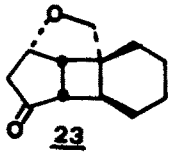
The trans-junction between the four and six-membered rings and the insertion in this bicyclic system of the two fused five-membered rings, as reported also for 26[13], give rise to the following effects: (i) very large angular deformations at the atoms C(6) and C(10), the largest angles of the molecule being C(5)-C(6)-C(7) and C(4)-C(10)-C(9), 127.2(2) and 132.5(2)°, respectively. (ii) the bonds C(6)-C(7) and C(9)-C(10), whose lengths are 1.518(3) and 1.517(3) Å respectively, are the shortest C-C bonds involving sp^3 carbon atoms of the fused-ring system; (iii) the need of avoiding too short interatomic contacts between the carbon atom C(3) and the methylene group at C(11) results in the large values of the angles C(3)-C(4)-C(10) and C(10)-C(6)-C(11), 121.5(2) and 118.5(2)° respectively.

There are only a few intermolecular contacts shorter than the sum of van der Waals radii, the shortest being: O(4)...H(8)B (at x, y, 1+z), 2.48(2) Å.
A visual inspection of the molecule suggests that 20 does not behave, as a whole, as a rigid-body. An analysis of the thermal motion, following the least-squares treatement proposed by Schomaker and Trueblood[17], was then applied only to the molecular moiety including the cyclobutane, the cyclopentanone and the furanoid rings. The value obtained for the RMS residue $\Delta U_{RMS} = \langle (U_{obs}-U_{calc})^2 \rangle^{1/2}$, $20.6\ 10^{-4}$ $Å^2$, to be compared with $\sigma_{RMS}(U_{obs}) = 9.3\ 10^{-4}$ Å , shows that indeed this portion of the molecule behaves, at least to a first approximation, as a rigid body. The resulting corrections to the interatomic distances are in the range 0.005-0.008 Å.

The most significant ^{1}H-NMR resonances were assigned by analysis of a resolution enhanced spectrum of compound 20 and of a COSY spectrum to check proton connectivities. The latter technique was used for most of the compounds discussed in this section owing to the extensive overlapping of signals which prevents usual double resonance experiments. The data are reported in table 1. A discussion of the coupling pattern among the most significant protons has already been presented in a preceeding paper[12].

The COSY spectrum of 20, run in C_6D_6, showed a better signal separation than the one in $CDCl_3$. In some other cases (e.g. compound 22) the opposite phenomenon could be observed, thus indicating a remarkable ASIS effect on these ring systems as we had already observed on simpler models[12].

In table 2 the ASIS effect displayed by H-8 and H-3 protons in compounds 17, 18, 19, 20 are reported in comparison with the formerly synthesized compounds 23, 24, 25, 26.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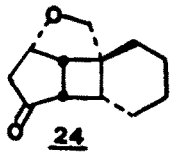
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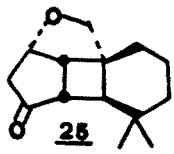
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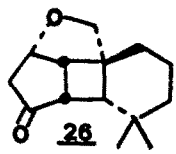
26

It can be observed that a homogeneous set of values of $\Delta\delta$ ($\delta_{CDCl_3}-\delta_{C_6D_6}$) is displayed by compounds with the same stereochemistry at C-4 and C-5. As previously noted[12], such unusually strong ASIS effects are not easy to rationalize owing to the presence of several permanent dipoles, but could be empirically utilized for structure assignments of the molecules on study.

The resolution enhanced ^{1}H-NMR and COSY spectra in C_6D_6 allowed assignments and coupling patterns of the most relevant protons of compound 19 (Table 1). The close similarity of ^{1}H-NMR parameters of compounds 19 and 20 suggested that the only structural difference could be inferred from the configuration of the C-13 spiro carbon atom.

Acid-catalyzed hydrolysis of compounds 19 and 20 followed by ring opening with sodium hydride in the presence of methyl iodide afforded the same compound illustrated by formula 22.

High resolution 1-D and 2-D ^{1}H-NMR of the mixture of compounds 17 + 18 did not allow the straightforward assignment of all the resonances corresponding to each isomer owing to the extensive overlapping of signals. Hence, they were not further characterized but were converted into compound 21 through the above described procedure.

^{1}H-NMR assignments of compounds 21 and 22 were done in the usual manner and the data are reported in Table 3. The proton H-5 resonates as a doublet and displays a vicinal coupling constant with H-6 of 6.6 Hz in compound 21 and of 11.9 Hz in compound 22. Such values could be in agreement with a torsion angle of about 130° and 15° according to Karplus equations suggesting a cis relationship between the two side chains in compound 21 and a trans relationship in compound 22.

The relative stereochemistry of the two side chains was further confirmed by measuring whether cross-relaxation, i.e. N.O.E., was operating between H-5 and H-6. In compound 21 no NOE effect is detectable while in compound 22 the saturation of proton H-5 induces a 14% enhancement of the signal corresponding to H-6, thus indicating their spatial proximity and hence a trans relationship between the side chains.

These spectroscopic evidences indicate that, during chemical transformations, no stereochemical inversions occur on both compounds. These conclusions found a further experimental support by base catalyzed equilibration on compound 22. After 24 h at room temperature in the presence of NaH or t-BuOK in tetrahydrofuran, compound 22 quantitatively affords compound 21. Indeed Dreiding models of 21 show a less severe steric hindrance between the tricyclic

bridgehead system and the bulky cyclopentenone side chain.

Further elaboration of compound 21 to the target molecule A is under investigation and will be a subject of a later communication. Actually a very mild procedure of elimination of methanethiol to the terminal olefin has been performed and the method will be applied to the molecules on study.

Table 1. ^{1}H-NMR Chemical shifts of compounds 19 and 20 in $CDCl_3$ and C_6D_6.(*)

H	20 (C_6D_6)	20 ($CDCl_3$)	19 (C_6D_6)	19 ($CDCl_3$)
H-1	4.27 (m, 6.6)	4.75 (t, 6.7)	4.29 (m, 6.6)	4.75 (t, 6.7)
H-3A	3.95 (dd, 10.5, 1.5)	3.90 (d, 11.0)	3.88 (d, 11)	3.90 (d, 11)
H-3B	3.61 (d, 10.5)	3.79 (d, 11.0)	3.64 (d, 11)	3.80 (d, 11)
$O(CH_2)_2O$	3.65-3.55 (m)	3.95-3.72 (m)	3.70-3.55 (m)	4.00-3.80 (m)
H-5	2.86 (d, 9.5)	3.15-3.26 (m)	3.00 (d, 8.8)	3.30-3.17 (m)
H-14A	2.83 (d, 13.5)	2.42 (d, 15.0)		
H-6	2.70-2.60 (m)	3.15-3.90 (m)	2.65-2.60 (m)	3.30-3.17 (m)
H-9	2.70-2.60 (m)	3.42 (t, 6.7)	2.65-2.60 (m)	3.40 (t, 6.7)
H-14B	2.35 (d, 13.5)	2.07 (d, 15.0)		
H-8A	2.30 (m)	2.46 (d, 17.7)	2.24 (dd, 17.5, 2.2)	2.44 (d, 18.0)
H-8B	1.97 (dd, 17.6, 6.6)	2.65 (dd, 6.7, 17.7)	1.96 (dd, 17.5, 6.6)	2.62 (dd, 6.7, 18.0)
H-17A			2.72 (d, 16.6)	2.35 (d, 14.5)
H-17B			2.25 (d, 16.6)	2.10 (d, 14.5)

(*) Chemical shifts are shown by δ values from TMS. Coupling constants [Hz] are shown in parentheses.

Table 2. ASIS effect ($\Delta\delta=\delta_{CDCl_3} - \delta_{C_6D_6}$) displayed by H-8 and H-3 protons.

	17 + 18	23	25	19	20	24	26
H-8A	0.06	0.05	-0.06	0.20	0.16	0.13	0.14
H-8B	0.51	0.51	0.46	0.66	0.68	0.66	0.66
H-3A	0.23	0.27	0.19	0.02	-0.05	+0.05	0.05
H-3B	0.38	0.33	0.29	0.16	0.18	+0.19	0.15

Table 3. ^{1}H-NMR Chemical shifts of compounds 21 and 22 in $CDCl_3$ and C_6D_6.(*)

H	21 (C_6D_6)	21 ($CDCl_3$)	22 (C_6D_6)	22 ($CDCl_3$)
H-1	4.07 (t, 5.3)	4.70 (t, 5.4)	4.07 (t, 5.6)	4.71 (t, 5.2)
H-3A	3.28 (d, 10.2)	3.77 (d, 9.8)	3.48 (d, 10.5)	3.86 (d, 10.5)
H-3B	3.13 (d, 10.2)	3.65 (d, 9.8)	3.03 (d, 10.5)	3.55 (d, 10.5)
H-5	2.73 (d, 6.6)	3.17 (d, 7.0)	2.65 (d, 11.9)	3.45 (d, 11.4)
H-14	5.89 (m)	6.12 (m)	6.09 (m)	6.01 (m)
H-6	2.12 (dd, 6.6, 6.3)	2.82 (dd, 7.6, 7.0)	2.36 (dd, 11.9, 7.2)	3.07 (dd, 11.4, 7.3)
H-9	2.22 (t, 6.3)	3.09 (dd, 5.4, 7.6)	2.18 (dd, 5.6, 7.2)	3.14 (dd, 7.3, 5.2)
H-8A	2.57 (d, 17.2)	2.74 (d, 17.5)	2.28 (d, 17.5)	2.60 (d, 17.0)
H-8B	1.87 (dd, 17.2, 5.3)	2.52 (dd, 17.5, 5.4)	1.78 (dd, 17.5, 5.6)	2.48 (dd, 17.0, 5.2)
S-CH_3	1.72 (s)	2.07 (s)	1.78 (s)	2.12 (s)

(*) Chemical shifts are shown by δ values from TMS. Coupling constants [Hz] are shown in parentheses.

EXPERIMENTAL

IR spectra were recorded on a Perkin Elmer 457 spectrophotometer and UV spectra with a Perkin Elmer UV-VIS 552. ^{1}H-NMR spectra were measured in deutorochloroform with a Varian XL-200 (200 MHz). COSY spectra were run both on 0.04 M $CDCl_3$ and C_6D_6 solutions. A spectral window of 1400 Hz and an acquisition time of 0.365s were chosen leading to a digital resolution of 2.7 Hz/point. A relaxation delay of 2s was used and 40 scans accumulated for the 256 traces. The pseudo-echo Gaussian shaping function available in the XL-200 software were applied in both dimensions. N.O.E. enhancement experiments were run on properly degassed 0.04 M $CDCl_3$ solutions of compounds 21 and 22 using the pulse sequence 180° (decoupler; 5.10^{-2} s)-mixing time (0.7 s) -90° (observe pulse) - acquisition. During 16 transients the decoupling frequency was set on H-5 resonance while during the following 16 transients it was set off resonance. The cycle was repeated 64 times; the off-resonance FID was then substracted from the on-resonance one. After Fourier transformation the intensity of signal related to H-6 was compared with that in the off-resonance spectrum and the NOE enhancement calculated.
Mass spectra were obtained with a Varian MAT-112 spectrometer (direct inlet 70 eV). Microanalyses were carried out in the microanalytical laboratory of our Department using a Perkin-Elmer 240 instrument. Flash chromatography was carried out with Merck Kieselgel 60 (0.040 - 0.063 mm., 230-400 mesh ASTM) and analytical thin-layer chromatography (TLC) on Merck Kieselgel 60 F254. Tetrahydrofuran (THF) and diethyl ether were distilled under nitrogen from lithium aluminum hydride; hexamethyl phosphoric triammide (HMPA) was distilled from calcium hydride and stored under dry nitrogen. Light petroleum refers to the fraction of b.p. 40-60°C. Organic solutions were dried over Na_2SO_4 and the product isolated by filtration and evaporation of the filtrate using a rotary evaporator operating at 15 torr. Boiling points refer to bulb-to-bulb distillation using a Buchi GKR-50 apparatus. Melting points were determined with a Büchi 510 apparatus and are uncorrected.

3-methoxycarbonyl-3-(3-methoxycarbonyl-propylthio)-cyclopentanone (3): γ-Thiobutyrolactone (35.0 g, 0.343 mol) was dissolved in methanol (1500 ml); anhydrous triethylamine (79.3 ml) was added and the solution refluxed for 24 h. The methanol and triethylammine were evaporated under vacuo and the crude methyl-4-thio-butanoate was utilized without purification.
Methyl-4-thio-butanoate (30.9 g, 0.220 mol) was added to a solution of 3-methoxycarbonyl-2-cyclopentenone (32.1 g, 0.229 mol) buffered at pH 9 with sodium tetraborate solution (0.1 M). After 5 h at room temperature (TLC: light petroleum/ethyl acetate 7:3) tetrahydrofurane was evaporated and the residue extracted several times with diethyl ether. The organic layer was washed with water and dried over Na_2SO_4. Evaporation of the solvent gave 59.2 g of crude 3. By eliminating the volatile fractions at 40°C (0,6 torr), 46.3 g (74%) of pure 3 were obtained; b.p. = 160° C ($3.7.10^{-4}$ torr); IR ($CHCl_3$): ν = 1752, 1740, 1730 cm^{-1} ^{1}H-NMR: δ = 2.41 (2H, t, ^{3}J = 7.0 Hz, $C\underline{H}_2$-CO_2Me), 2.65 (2H, t, ^{3}J = 7.0 Hz, S-$C\underline{H}_2$), 2.84-2.50 (2H, AB system, ^{2}J = 19.0 Hz, $C\underline{H}_2CO$), 3.66 (3H, s, $CO_2C\underline{H}_3$), 3.77 (3H, s, $CO_2C\underline{H}_3$); MS: m/e: 274 (M^+, 9), 243 (13), 215 (28), 142 (92), 141 (90), 133 (57), 114 (100), 81 (57). Anal. calc. for $C_{12}H_{18}O_5S$: C, 52.55; H, 6.57; Found: C, 52.67; H, 6.63.

Ethylene ketal of 3-methoxycarbonyl-3-(3-methoxycarbonyl-propylthio)-cyclopentanone (4): To a solution of compound 3 (46.3 g, 0.169 mol) in benzene (1500 ml) ethylene glycol (30 ml) and a catalytic amount of p-toluen sulphonic acid were added and the mixture refluxed with the azeotropical removal of water. After 5 h (TLC: light petroleum/ethyl acetate 7:3), water was added, the layers separated, and the aqueous one extracted with diethyl ether. The combined extracts were washed with aqueous $NaHCO_3$ (5%), water and brine and then dried.
Filtration and concentration afforded 53.2 g of 4 (98%) pure enough for the next step; b.p. = 170°C (37.10^{-4} torr); I.R. ($CHCl_3$): ν = 1740, 1729 cm^{-1}; ^{1}H-NMR: δ = 2.39 (2H, t, ^{3}J = 7.0 Hz, $C\underline{H}_2$-CO_2Me), 2.50 (2H, t, ^{3}J = 7.0 Hz, S-$C\underline{H}_2$) 2.61-2.07 (2H, AB system, ^{2}J = 15.0 Hz, $C\underline{H}_2CO$), 3.65 (3H, s, $CO_2C\underline{H}_3$), 3.73 (3H, s,

$CO_2\underline{CH_3}$), 3.88 (4H, m, O-$\underline{CH_2}$-$\underline{CH_2}$-O); MS: m/e (%)= 318 (M^+, 2), 259 (5), 186 (36), 185 (100), 171 (5), 99 (58). Anal. calc. for $C_{14}H_{22}O_6S$: C, 52.83; H, 6.92; Found: C, 52.91; H, 6.85.

2-Ethylene ketal of 2,10-dioxo-9-methoxycarbonyl-6-thiaspiro[4,5]decane (5): A solution of compound 4 (6.36 g, 0.020 mol) in benzene (30 ml) was dropped, under argon atmosphere, into a solution of freshly sublimed potassium t-butoxide (6.8 g, 0.060 mol) in anhydrous benzene (72 ml) and anhydrous dimethylsulphoxide (13 ml) at 0°C . At the termination of the dropping the transformation was complete (TLC: light petroleum/ethyl acetate 1:1). An 1 N aqueous HCl was added until pH 7. The layers were separated, the aqueous phase extracted exaustively with diethyl ether. The combined extracts were washed with brine, water and dried. By evaporating the solvents under reduced pressure, an oily residue was obtained; treatment with methanol afforded 3.3 g of pure 5 (60%) as a powder; IR ($CHCl_3$):ν = 1740, 1700 cm^{-1}; MS: m/e (%)= 286 (M^+, 20), 258 (11), 199 (13), 172 (17), 153 (11), 127 (23), 113 (34), 99 (30), 86 (100).

Ethylene ketal of 2-oxo-10-hydroxy-9-methoxycarbonyl-6-thiaspiro[4,5]decane (6): Commercially available sodium borohydride was purified, before use, as follows: it is treated with ethyl acetate under stirring for 12 h, filtered, washed with diethyl ether and dried under vacuo at 50°C. Sodium borohydride (2.43 g, 0.065 mol) was added to a solution of 5 (18.5 g, 0.065 mol) in methanol (550 ml). After a few minutes, the reaction was over (TLC: light petroleum/ethyl acetate 1:1). The solvent was evaporated under vacuo, the residue taken up with water and a 1 N aqueous HCl solution added until neutrality. The aqueous phase was extracted five times with diethyl ether. The combined extracts were dried over Na_2SO_4. Filtration and concentration gave 17.9 g of 6 (96%) pure enough for the following reaction; powder; IR ($CDCl_3$):ν= 3500, 1740 cm^{-1}; MS: m/e (%) = 288 (M^+, 2), 260 (25), 242 (29), 229 (14), 199 (12), 159 (18), 127 (54), 99 (56), 86 (100).

Ethylene ketal of 2-oxo-10-acetoxy-9-methoxycarbonyl-6-thiaspiro[4,5]decane (7): Freshly distilled acetic anhydride (90 ml) was added to a solution of 6 (17.9 g, 0.062 mol) in anhydrous pyridine (45 ml). The reaction mixture was warmed at 75°C for 15 h (TLC: light petroleum/ethyl acetate 1:1) and then poured into ice. A 1 N aqueous HCl was added until pH 5 and the aqueous mixture was extracted several times with diethyl ether. The combined extracts were washed with a 1 N aqueous HCl, with water, with aqueous $NaHCO_3$ (5%) and finally with brine. After drying over Na_2SO_4 and evaporating under reduced pressure, 19.4 g of pure 7 (94%) were obtained; oil; IR ($CHCl_3$): ν = 1753, 1745 cm^{-1}; MS: m/e (%)= 330 (M^+, 9), 285 (48), 243 (36), 226 (86), 167 (90), 129 (100), 86 (76).

Compounds (8): Freshly sublimed potassium t-butoxide (13.4 g, 0.12 mol) was added to a solution of 7 (19.4 g, 0.058 mol) in anhydrous benzene (450 ml) at room temperature and under argon atmosphere. After 90 min., the reaction was over (TLC: light petroleum/ethyl acetate 1:1). The reaction mixture was poured into water and an 1 N HCl was added until neutrality. The organic layer was separated and the aqueous one extracted with diethyl ether. The combined extract were washed with water, dried and evaporated under vacuo. The crude product was purified by "flash" chromatography and 10.0 g of 8a and 3.4 g of 8b were obtained (overall yield 82%).

Ethylene ketal of 2-oxo-9-methoxycarbonyl-6-thiaspiro[4,5]dec-9-ene (8a): oil; IR ($CHCl_3$): ν = 1721 cm^{-1}; ^{1}H-NMR: δ = 2.22-2.11 (2H, AB system ^2J = 12.0 Hz, H-1), 2.55 (2H, m, H-8), 2.73 (2H, m, H-7), 3.73 (3H, s, $COOCH_3$), 3.91 (4H, m, O-CH_2-CH_2O), 6.94 (1H, t, ^4J = 1.8 Hz, H-10); MS: m/e (%) = 270 (M^+, 28), 242 (3), 238 (5), 211 (17), 170 (9), 99 (51), 86 (100). Anal. calc. for $C_{13}H_{18}O_4S$: C, 57.78;

H, 6.67. Found: C 57.69; H, 6.52.

Ethylene ketal of 2-oxo-9-tert-butoxycarbonyl-6-thiaspiro[4,5]dec-9-ene (8b): oil; IR ($CHCl_3$): ν = 1720 cm^{-1}; ^{1}H-NMR: δ = 1.45 (9H, s, $C(CH_3)_3$), 2.10-2.20 (2H, AB system, ^2J = 12.4 Hz, H-1), 2.40 (2H, m, H-8), 2.70 (2H, m, H-7), 3.90 (4H, m, $O-CH_2-CH_2-O$), 6.80 (1H, t, ^4J = 1.7 Hz, H-10); MS: m/e (%) = 312 (M^+, 13), 256 (61), 211 (30), 170 (22), 156 (15), 100 (60), 99 (56), 85 (100).

Ethylene ketal of 2-oxo-9-hydroxymethyl-6-thiaspiro[4,5]dec-9-ene (9): To a suspension of lithium aluminum hydride (1.76 g, 0.046 mol) in anhydrous diethyl ether (200 ml) a solution of 8a (10 g, 0.037 mol) and 8b (3.4 g, 0.011 mol) in diethyl ether (42 ml) was dropped at 0°C, under stirring. After 15 min., the reaction was complete (TLC, light petroleum/ethyl acetate 1:1). The reaction mixture was poured into iced water, 1 N hydrochloric acid was added until pH 6 and the layers separated. The aqueous layer was extracted several times with diethyl ether. The combined organic extracts were washed with water and dried. Filtration and evaporation gave crude 9 which was purified by "flash chromatography". By eluting with light petroleum/ethyl acetate 8:2) 11.3 g of 9 (97%) were obtained; oil; IR ($CHCl_3$): ν = 3400 cm^{-1}; ^{1}H-NMR: δ = 1.59 (1H, bs, OH), 2.16-20.6 (2H, AB system, ^2J = 14 Hz, H-1), 2.75 (2H, m, H-7), 3.86 (4H, m, $O-CH_2-CH_2-O$), 3.99 (2H, bs, CH_2OH), 5.69 (1H, m, H-10); MS: m/e(%) = 242 (M^+, 45), 211 (24), 156 (20), 127 (18), 100 (95), 99 (78), 86 (100). Anal. calc. for $C_{12}H_{18}O_3S$: C, 59.50; H, 7.44; Found: C, 59,38; H, 7.35.

Ethylene ketal of 2-oxo-9-chloromethyl-6-thiaspiro[4,5]dec-9-ene (10): To a solution of 9 (3.25 g, 0.0134 mol) in anhydrous dimethylformammide (14 ml), sym-collidine (1.96 ml, 0.0147 mol), lithium chloride (0.57 g, 0.0134 mol) mesyl chloride (1.14 ml) were added, at 0°C, under stirring and argon atmosphere. After 8 h (TLC, light petroleum/ethyl acetate 1:1), the reaction mixture was poured into iced water and extracted with diethyl ether. The combined extracts were washed with a saturated aqueous copper (II) nitrate solution, water and dried. Filtration and evaporation afforded crude 10 which was purified by "flash chromatography". By eluting with light petroleum/ethyl acetate 8.5/1.5, 2.79 of 10 (80%) were obtained; oil; ^{1}H-NMR: δ = 2.07-2.18 (2H, AB system, ^2J = 12.0 Hz, H-1), 2.35 (2H, m, H-8), 2.75 (2H, m, H-7), 3.90 (4H, m, $O-CH_2-CH_2-O$), 3.97 (2H, bs, $-CH_2Cl$), 5.81 (1H, m, H-10); MS: m/e (%)= 262 (M^+, 8), 260 (M^+, 24), 225 (53), 197 (17), 99 (100), 86 (92). Anal. calc. for $C_{12}H_{17}ClO_2S$: C, 55.28; H, 6.52. Found: C, 55.15; H, 6.40.

Ethylene ketal of 2-oxo-10-hydroxy-9-methylene-6-thiaspiro[4,5]decane (13): To a suspension of sodium hydride (14 mg, 60% dispersion in oil, 0.35 mmol) in anhydrous tetrahydrofuran a solution of 5 (0.100 g, 0.35 mmol) in tetrahydrofurane (1 ml) was added, at room temperature, under stirring and argon atmosphere. The reaction mixture was refluxed for 1 h, then cooled to room temperature; lithium aluminum hydride (0.027 g, 0.7 mmol) was added. After 2 h (TLC light petroleum/ethylacetate 1:1), ethyl formate (0.14 ml) was added and the mixture refluxed for 15'. The solvents were evaporated and the residue taken up with water and exhaustively extracted with diethyl ether. The combined extracts were washed with water and dried. The drying agent was removed by filtration and the solvent distilled under reduced pressure. The residue was purified by "flash chromatography". By eluting with light petroleum/ethyl acetate 1:1, 59.3 mg. of pure 13 (70%) were obtained; oil; IR ($CHCl_3$): ν = 3450 cm^{-1}; ^{1}H-NMR: δ = 1.60 (1H, m, OH), 3.90 (4H, m, $O-CH_2-CH_2O$), 3.96 (1H, m, H-10), 4.90 (1H, m, $C=CH_2$), 4.95 (1H, m, $C=CH_2$); MS: m/e (%) = 242 (M^+, 60), 213 (26), 198 (42), 128 (53), 127 (38), 115 (77), 99 (98), 86 (100).

Ethylene ketal of 2-oxo-6-thiaspiro[4,5]dec-9-enylmethyl 4-hydroxy-2-cyclopentenyl ether (15): Sodium hydride (0.173 g, 4.32 mol from a 60% suspension in oil by washing with n-pentane) was added to a magnetically stirred solution of cis-2-cyclopentene-1,4-diol (0.432 g, 4.32 mmol) in anhydrous tetrahydrofurane (40 ml) under argon atmosphere. After 20', compound 10 (0.749 g, 2.88 mmol) was added followed by anhydrous HMPT (3 ml). The mixture was refluxed for 8 h and then left overnight under stirring at room temperature (TLC, light petroleum ether/ethyl acetate 1:1). The solvents were evaporated, the residue was treated with a NaCl aqueous solution (5%) and extracted with diethyl ether. The organic phase was dried and evaporated to give crude 15 which was purified by "flash chromatography". By eluting with light petroleum ether/ethyl acetate 4:6, 0.513 g of 15, 0.095 g of 10 (overall yield 68%) and 0.136 g of 16 were obtained.

15: oil; IR ($CHCl_3$): ν = 3420 cm^{-1}; ^{1}H-NMR: δ = 3.94-3.86 (6H, m, O-C$\underline{H}_2$-C$\underline{H}_2$O and -OC$\underline{H}_2$), 4.32 (1H, m, HO-C$\underline{H}$), 4.63 (1H, m, -O-C$\underline{H}$), 5.71 (1H, m, C$\underline{H}$=C), 6.05 (2H, m, C$\underline{H}$=C$\underline{H}$); MS: m/e (%) = 324 (M^+, 28), 305 (5), 241 (33), 225 (24), 224 (27), 211 (86), 100 (100), 99 (100).

16: oil; MS: m/e (%)= 548 (M^+, 5), 307 (48), 241 (85), 225 (100), 224 (100), 211 (100), 181 (100), 167 (75), 139 (74), 125 (75), 100 (100), 99 (100).

Ethylene ketal of 2-oxo-6-thiaspiro[4,5]dec-9-enylmethyl 4-oxo-2-cyclopentenyl ether (1): A solution of 15 (1.13 g, 3.5 mmol) in anhydrous dichloromethane (100 ml) was treated with pyridinium chlorochromate (PCC, 1.13 g, 5.24 mmol) and anhydrous sodium acetate (0.287 g, 3.5 mmol). The mixture was stirred at room temperature for 3 h (TLC light petroleum/ethyl acetate 1:1), then was diluted with anhydrous diethyl ether and filtered through Florisil. Evaporation of the solvents afforded the crude product 1 which was purified by "flash chromatography". By eluting with light petroleum/ethyl acetate 1:1, 0.789 g of 1 (70%) were obtained; oil; IR ($CHCl_3$): ν = 1720 cm^{-1}; UV (EtOH): λ_{max} = 210 nm (ε = 13700), λ_{max} = 314 nm (ε = 41); ^{1}H-NMR: δ = 3.97-3.83 (6H, m, OC$\underline{H}_2$-C$\underline{H}_2$O and O-C$\underline{H}_2$), 4.66 (1H, m, O-C$\underline{H}$), 5.75 (1H, m, C$\underline{H}$=C), 6.24 (1H, dd, ^3J = 1.5Hz, ^3J = 5.8Hz, CH=C$\underline{H}$), 7.58 (1H, dd, ^3J = 2.2Hz, ^3J = 5.8Hz); MS: m/e (%) = 322 (M^+, 20), 211 (21), 100 (84), 99 (100).

Photocycloaddition of (1): A solution of compound 1 (1.43 g, 4.44 mmol) in toluene (440 ml) was irradiated through Pyrex using a 400 W Philips high-pressure lamp at -25°C under argon atmosphere. After 8 h the reaction was complete (TLC light petroleum/ethyl acetate 4:6). The solution was evaporated to dryness and the crude products were first purified by "flash chromatography" (light petroleum/ethyl acetate 1:1) to give 1.02 g of the photoadducts (71%). The diastereoisomers were separated by medium pressure column chromatography (MPLC) on silica gel (40-63 nm) (Büchi B-685 column 36x460 mm, flow = 10 ml/min). By eluting with cyclohexane/ethyl acetate 6:4, 0.202 g of 19, 0.165 g of 20, 0.110 g of 19 + 20 and 0.290 g of 19 + 17 + 18 were obtained. The mixture 19 + 17 + 18 was separated by medium pressure column chromatography on silica gel (LiChroprep RP 18 40-63 µm, flow 20 ml/min). By eluting with methanol/water 6:4, 0.120 g of 17 + 18, 0.050 g of 19 and 0.080 g of 19 + 17 + 18 were obtained.

9-oxa-4-thia-tetracyclo[5.5.1.0 ^{2,7}.0^{10,13}]tridecan-12-one-3-spiro-1'-cyclopentan-3'-ones(3'-ethylene ketals) (17) +(18). oil; IR ($CHCl_3$): ν = 1740 cm^{-1}; ^{1}H-NMR: δ = 2.45 (1H, dd ^2J = 18.0 Hz, ^3J = 5.0 Hz, H-8B), 2.66 (1H, d, ^2J = 18.0 Hz, H-8A), 3.38 (1H, d, ^2J = 9.5 Hz, H-3B), 3.71 (1H, d, ^2J = 9.5 Hz, H-3A), 4.65 (1H, t, ^3J = 5.0 Hz, H-1); MS: m/e (%)= 322 (M^+, 100), 293 (9), 289 (7), 241 (16), 100 (30), 99 (100).

9-oxa-4-thia-tetracyclo[5.5.1.0^{2,7}.0^{10,13}]tridecan-12-one-3-spiro-1'-cyclopentan-3'-one(3'-ethylene ketal) (19): m.p.(methanol) = 144-146°C; IR ($CHCl_3$):ν= 1745 cm^{-1}; MS: m/e (%) = 322 (M , 23), 236 (14), 180 (17), 100 (24), 99 (100), 87 (34), 86 (92). Anal. calc. for $C_{17}H_{22}O_4S$: C, 63.35; H, 6.83. Found: C, 63.28; H, 6.75.

9-oxa-4-thia-tetracyclo[5.5.1.$0^{2,7}$.$0^{10,13}$]tridecan-12-one-3-spiro-1'-cyclopentan-3'-one(3'-ethylene ketal) (20): m.p. (Ethyl acetate/diisopropyl ether) = 160°C; IR ($CHCl_3$): ν = 1740 cm^{-1}; MS: m/e (%)= 322 (28), 262 (10), 236 (17), 180 (23), 100 (38), 99 (100), 87 (44), 86 (100). Anal. calc. for $C_{17}H_{22}O_4S$: C, 63.35; H, 6.83. Found: C, 63.30; H, 6.78.

4-(2-Methylthio-ethyl)-5-(3-oxo-1-cyclopentenyl)-2-oxatricyclo[4.2.1.$0^{4,9}$]nonan-7-one (21): A solution of the mixture 17 + 18 (0.020 g, 0.06 mmol) in water (2.5 ml) and acetic acid (2.5 ml) was stirred at room temperature for 4 h (cyclohexane/ethyl acetate 6:4, triple development); it was then poured into aqueous $NaHCO_3$ (5%) and extracted with chloroform several times. The combined extracts were washed with water and dried. By evaporating the solvent under reduced pressure, 0.016 g (92%) of an oily residue was obtained pure enough for the next step (the MS spectrum revealed the molecular peak at m/e = 278).
To a solution of the product derived from hydrolysis (0.014 g, 0.05 mmol) in anhydrous tetrahydrofurane (5 ml) sodium hydride (0.002 g, 0.05 mmol from a 60% suspension in oil) and methyl iodide (0.005 ml, 0.08 mmol) were added at room temperature, under argon atmosphere.
The reaction mixture was stirred for 72 h (light petroleum/ethyl acetate 3:7); then it was diluted with ethyl acetate and water. The organic layers were separated and the aqueous one extracted with ethyl acetate. The combined extracts were washed with water and dried. Filtration and evaporation afforded a residue which was purified by "flash chromatography". By eluting with light petroleum/ethyl acetate 3/7, 0.011 g of pure 21 (75%) were obtained; oil; IR (CCl_4): ν = 1744, 1715 cm^{-1}; MS m/e (%) 292 (M^+, 32), 278 (100), 221 (19), 142 (47), 136 (68), 135 (30), 95 (65). Anal. calc. for $C_{16}H_{20}O_3S$: C, 65.75; H, 6.85. Found: C, 65.68; H, 6.78

4-(2-Methylthio-ethyl)-5-(3-oxo-1-cyclopentenyl)-2-oxatricyclo[4.2.1.$0^{4,9}$]nonan-7-one (22): The procedure was the same as that used for the preparation of 21. The hydrolysis of the ketal group was complete in 4 h, both for 19 and 20.
The ring opening with sodium hydride and methyl iodide took place, for both compounds, in 4 h giving a crude product which was purified by "flash chromatography" (light petroleum/ethyl acetate 25:75).
From 19 (0.020 g, 0.06 mmol) we obtained 0.017 g of hydrolized product (100%) and 0.014 g of 22 (78%). From 20 (0.020 g, 0.06 mmol) we obtained 0.017 g of hydrolized product (100%) and 0.013 g of 22 (73%). 22: oil; IR (CCl_4): ν = 1745, 1715 cm^{-1}. MS: m/e (%)= 292 (M^+, 30), 278 (12), 277 (14), 211 (12), 142 (21), 136 (48), 135 (20), 95 (43), 84 (100). Anal. calc. for $C_{16}H_{20}O_3S$: C, 65.75; H, 6.85. Found: C, 65.68; H, 6.78

X-ray analysis of compound 20: Data for the substance under study were $C_{17}H_{22}SO_4$, M_r= 322.43; crystal of approximate dimensions 0.30 x 0.25 x 0.20 mm, monoclinic, space group $P2_1/c$, a = 9.640(2), b = 19.195(4), c = 8.614(2) Å, β = 104.75(2)°, V = 1541.4(6) $Å^3$, Z = 4, D_{calc}= 1.389 g/cm^3, μ(MoKα) = 0.215 mm^{-1}, F(000) = 688.
The intensity data were collected at room temperature on an Enraf-Nonius CAD-4 diffractometer, using graphite-monochromated MoKα radiation (λ = 0.71073 Å). The lattice parameters were derived from a least-squares treatment of 25 reflections with $11.6° \leq \theta \leq 12.9°$ and the intensity measurements were carried out up to 2θ = 55° by variable-rate ω-scan technique. Out of the 3510 independent reflections collected, 3185 with I>0 were considered observed and were assigned variances $\sigma^2(I)$ estimated including counting statistics for the scans and the additional term $(0.03I)^2$. Three standard reflections were periodically checked and no significant variation of the intensities was observed. The data were corrected for Lorentz and polarization, but not for absorption effects.
The structure was solved by direct methods using program MULTAN[18]. Preliminary positions for the 22 H atoms were derived from a difference map after a few cycles of anisotropic refinement of the 22 non-H atoms. The Full matrix least-squares refinement was based on F with weights $w = 4F_o^2/\sigma^2(F_o^2)$. In the final

cycles 288 variables were simultaneously adjusted: coordinates and anisotropic temperature parameters for the C,O and S atoms, coordinates and isotropic B's for the H atoms, a scale factor and a secondary extinction coefficient [final value = $1.8(6)\times10^{-7}$]. Convergence was reached at R = 0.067, wR = 0.051 for 3185 reflections with I>0 [R = 0.046 and wR = 0.048 for 2407 reflections with I>2 $\sigma(I)$]; maximum $\Delta/\sigma = 0.03$. Scattering factors and real and imaginary anomalous-dispersion corrections for neutral S, O and C atoms were taken from Ref. 19,for H atoms from Ref. 20. No residual peaks higher than 0.26 e/Å^3 were found on the final difference map.
The final atomic coordinates and the equivalent isotropic thermal parameters are listed in Table 4.

Table 4. Positional parameters and equivalent isotropic thermal parameters with e.s.d.'s in parentheses.

$$B_{eq} = 4/3 \sum_{ij} \beta_{ij} a_i a_j$$

Atom	x	y	z	B_{eq}(Å^2)
S(1)	0.31939(5)	0.09309(3)	0.14103(7)	4.53(1)
O(1)	-0.1939(2)	0.20781(8)	0.1038(2)	4.43(3)
O(2)	-0.0304(2)	0.11257(8)	0.5497(2)	4.21(3)
O(3)	0.5116(1)	0.14312(8)	0.5434(2)	3.87(3)
O(4)	0.3670(1)	0.18331(8)	0.6954(2)	4.09(3)
C(1)	-0.2486(2)	0.1450(1)	0.1552(2)	3.80(5)
C(2)	-0.2356(2)	0.1447(1)	0.3350(2)	3.75(5)
C(3)	-0.0974(2)	0.1077(1)	0.4115(2)	3.01(4)
C(4)	-0.0582(2)	0.06099(9)	0.2875(2)	2.67(4)
C(5)	-0.1495(2)	0.0878(1)	0.1236(2)	3.15(4)
C(6)	-0.0130(2)	0.1249(1)	0.0967(2)	2.82(4)
C(7)	0.0399(2)	0.1246(1)	-0.0549(2)	4.14(5)
C(8)	0.1964(2)	0.1473(1)	-0.0089(3)	4.77(5)
C(9)	0.2314(2)	0.0917(1)	0.3084(2)	2.86(4)
C(10)	0.0765(2)	0.07553(9)	0.2240(2)	2.45(3)
C(11)	-0.0411(2)	0.1994(1)	0.1475(2)	3.49(4)
C(12)	0.2605(2)	0.1585(1)	0.4113(2)	2.95(4)
C(13)	0.3704(2)	0.1382(1)	0.5653(2)	3.04(4)
C(14)	0.3326(2)	0.0637(1)	0.5930(3)	3.84(5)
C(15)	0.3021(2)	0.0324(1)	0.4257(3)	4.03(5)
C(16)	0.6017(2)	0.1622(1)	0.6965(3)	4.16(5)
C(17)	0.5062(3)	0.2106(1)	0.7584(3)	5.04(6)

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