PREPARATION OF γ-HETEROSUBSTITUTED α,β-HEXENOLIDES AND THEIR 1,3-DIPOLAR CYCLOADDITION TO 2,3,4,5-TETRAHYDROPYRIDINE 1-OXIDE§

Félix Busqué, Pau Cid, Pedro de March,* Marta Figueredo,* and Josep Font

Departament de Química, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain

§*Dedicated to Prof. Rolf Huisgen on occasion of his 75th birthday*

Abstract - This paper describes the preparation of several γ-heterosubstituted α,β-hexenolides and their 1,3-dipolar cycloaddition to 2,3,4,5-tetrahydropyridine 1-oxide. In all these reactions the formed tricyclic cycloadducts arise exclusively from an *exo* transition state and the antifacial approach of the reactants is preferred.

Among many different strategies used in the synthesis of the indolizidine class of alkaloids,[1] one involving the intermediacy of a perhydroisoxazolo[2,3-*a*]pyridine system has found remarkable success in some cases.[2] When using this approach, the features of the target molecule may require that this heterocyclic system incorporates multiple stereocenters in a precise relative configuration and, therefore, it may be quite convenient to generate it in a stereospecific fashion. The 1,3-dipolar cycloaddition reaction of 2,3,4,5-tetrahydropyridine 1-oxide (**1**) to alkenes has proven to be very effective to this end and, for that reason, we have dedicated many efforts to fully understand the stereochemical course of this reaction. Our studies indicated that five, six, and seven membered α,β-unsaturated lactones add regiospecifically to nitrone (**1**) affording isoxazolidines with the electron-withdrawing group attached to the 4-position and we were able to conclude also that in all cases an *exo* approach of the reactants in the transition state is preferred.[3]

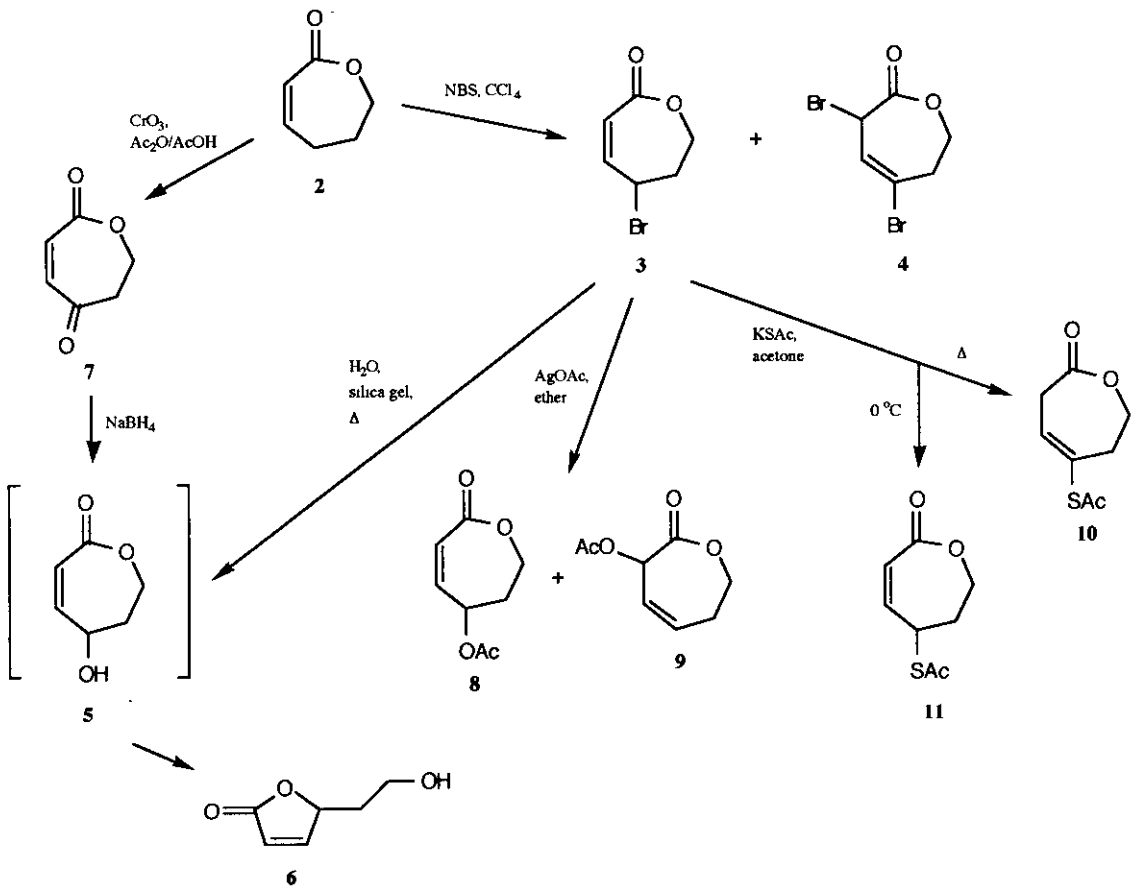
In order to apply the results of these studies to the synthesis of some interesting alkaloids, we have prepared several γ-substituted α,β-hexenolides and performed their cycloadditions to nitrone (**1**). In this paper we wish to describe the results of these experiments.

RESULTS AND DISCUSSION

For our synthetic purposes, the nature of the group at the γ-position of the α,β-hexenolide should make it susceptible of nucleophilic displacement in a later stage of the synthetic pathway: bromine, oxygen, and sulfur were considered appropriate atoms meeting this requirement. The preparation of the selected lactones is showed in Scheme 1. Allylic bromination of 6,7-dihydro-2(5*H*)-oxepinone (**2**)[4] with NBS in refluxing carbon tetrachloride afforded in 96% yield the corresponding 3-bromo derivative (**3**), which was fully characterized according to its spectroscopic properties. In the ^{1}H nmr spectrum of this compound, the signal corresponding to the allylic hydrogen atom appears at δ 4.95 as a quadruple triplet with J values of ≈ 4.5 Hz for the three vicinal couplings and ≈ 0.9 Hz for the two long distance couplings. In this reaction a 3% yield of a dibrominated compound was also isolated. The ^{1}H nmr spectrum of this minor product presents only one ethylenic hydrogen atom at δ 6.24 as a ddd with coupling constant values of 8.4, 2.5, and 0.9 Hz, corresponding to one vicinal and two allylic couplings; this signal and another one at δ 4.94 with a single J value of 8.4 Hz are diagnostic for the structure depicted in **4** and discard other possible dibrominated products. The formation of compound (**4**) may be explained through a second allylic bromination followed by 1,3-bromine rearrangement, which is consistent with the occasional isolation of small quantities of 5,5-dibromo-6,7-dihydro-2(5*H*)-oxepinone from this reaction.

All attempts to synthesize the γ-hydroxy-α,β-hexenolide (**5**) from the brominated precursor (**3**) were unsuccessful: sodium bicarbonate in acetone,[5] silver nitrate in THF-water,[6] potassium superoxide in a two phase solvent system,[7] all led to unidentifiable decomposition products; when the substitution reaction was tried with silica gel in refluxing water, instead of the expected lactone, we isolated the known 5-(2-hydroxyethyl)-2(5*H*)-furanone (**6**)[8] in 75% yield. Our observations seem to indicate that the hydroxyhexenolide (**5**) spontaneously isomerizes to the correspondig butenolide (**6**). Molecular mechanic calculations performed with the MacroModel program[9] gave relative steric energies of 38.1 and 23.0 kcal/mol for lactones (**5**) and (**6**) respectively. In fact, observation of molecular models shows that lactone (**5**) can not exist in an unstrained conformation with both the carbonyl group and the double bond located on the same plane. The synthesis of compound (**5**) was alternatively tried by sodium borohydride reduction of 6,7-dihydro-5-oxo-2(5*H*)-oxepinone (**7**) which had in turn been prepared from **2** by allylic oxidation with chromium oxide in a mixture of acetic anhydride/acetic acid[10] in 62% yield. The reduction of **7** afforded butenolide (**6**) as the only isolable compound in 46% yield. Considering these results we turned out our attention to the acetate (**8**), which was obtained through treatment of bromide (**3**) with silver acetate in refluxing ether[11] in 51% yield

after purification by flash chromatography. Another less polar compound could be also isolated in 16% yield, which was fully characterized as the regioisomer (**9**).

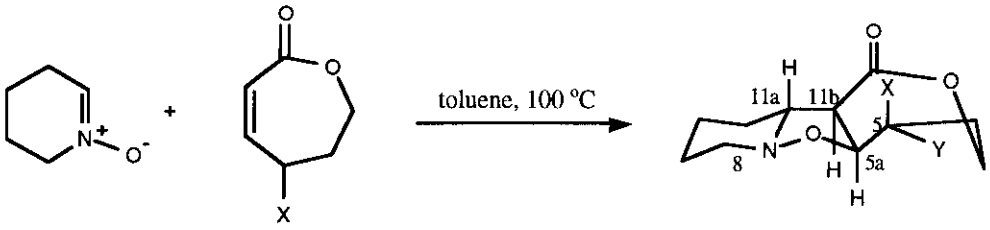


Scheme 1

In order to introduce the sulfur substituent, bromide (**3**) was heated in acetone in the presence of potassium thioacetate for 10 minutes.[12] This reaction afforded 70% yield of 5-acetylthio-6,7-dihydro-2(3*H*)-oxepinone (**10**) instead of the desired isomer (**11**). Deconjugation of the double bond was avoided by performing the reaction at 0 °C in the same solvent. In these conditions the expected thioacetate (**11**) was obtained in 98% yield. A perfect matching between the spectroscopic data of compounds (**3**, **8**, and **11**) is observed (see experimental section).

In the previously studied 1,3-dipolar cycloaddition of nitrone (**1**) to 6,7-dihydro-2(5*H*)-oxepinone (**2**) we had observed that in order to get a good degree of conversion in a reasonable time the temperatures required were

higher than those for the additions to six and five membered lactones. Nevertheless the stereoselectivity of the reaction was not affected by the increase of the temperature and only one cycloadduct (**12**) was always isolated whose *exo* stereochemistry was unequivocally established through NOE and HetNOE experiments.[3,13] In view of this precedent, the cycloaddition reactions of nitrone (**1**) to hexenolides (**3**, **8**, and **11**) were performed in toluene at 100 °C with an excess of nitrone (**1**), they were monitored by tlc and stopped when the starting lactone disappeared; all crude products were purified by flash chromatography. In the case of hexenolide (**3**), after 5 hours of reaction, a single adduct was isolated in 70% yield, while hexenolides (**8**) and (**11**) required shorter reaction times of 2 and 1.5 hours respectively and, in both cases, two isomeric products were obtained with overall yields of 98% for **8** and 92% for **11** (Scheme 2).



1 X=H, **2** X=Y=H, **12**, 79%

X=Br, **3** X=H, Y=Br, **13**, 70%

X=OAc, **8** X=H, Y=OAc, **14**, 72% X=OAc, Y=H, **15**, 26%

X=SAc, **11** X=H, Y=SAc, **16**, 75% X=SAc, Y=H, **17**, 17%

Scheme 2

As in the unsubstituted previously described parent compound (**12**), the cycloadducts formed in these reactions present in solution a nitrogen inversion process slow enough to allow the observation of the *trans* and *cis* invertomers as separate sets of signals in the ^{1}H nmr spectra at room temperature.[3,13] Although the ratio between both invertomers is solvent dependent, in all the isolated cycloadducts the *trans* fused conformer always predominates, as it can be deduced from the chemical shift differences between the two protons attached to the methylenic carbon atom α to the nitrogen.[14] Selected nmr data for the *trans* invertomer of compounds (**12-17**) are collected in Table 1. Thus, for the major invertomer of all the cycloadducts prepared the equatorial α-nitrogen proton at C_8 resonates around 1 ppm downfield with respect to its geminal axial proton. For all the new compounds obtained (**13-17**) the pattern of the ^{1}H nmr spectra corresponding to their

trans invertomers is quite similar to that observed for the previously described unsubstituted cycloadduct (**12**), with the value of the coupling constant between protons H_{11a} and H_{11b} always in the range 9.5-10.0 Hz. Therefore we assign a *trans* relationship to these protons according with the expected *exo* stereochemistry of the transition state. In the major adducts (**13**, **14**, and **16**) the observed J value of at least 11 Hz between protons H_5 and H_{5a} is characteristic of a *trans* stereochemistry, while in the minor isomers (**15** and **17**) the smaller values observed for $J_{5,5a}$ denote that these protons are *cis* to each other. These results are in agreement with a predominance of an antifacial approach of the reactants in the transition state. Although efforts were made to either isolate or detect the *exo-syn* adduct corresponding to the reaction of the bromohexenolide (**3**), this isomer could never be observed.

Table 1. Selected ^{1}H nmr data (400 MHz, d_6-acetone) for the *trans*-invertomer of compounds (**11-17**).

Compoud	δH_{8eq}	δH_{8ax}	$J_{11a,11b}$	$^{trans}J_{5,5a}$	$^{cis}J_{5,5a}$
12	3.27	2.37	9.5	12.5	2.9
13	3.39	2.43	9.5	11.7	
14	3.34	2.39	9.6	11.0	
15	3.29	2.35	9.9		1.7
16	3.32	2.38	9.5	12.1	
17	3.27	2.36	9.9		3.4

In conclusion, we have synthesized several new heterosubstituted hexenolides that are useful multifunctionalized synthons. Their 1,3-dipolar cycloaddition reactions to nitrone (**1**) have occurred with the expected *exo* stereochemistry and antifacial selectivity. Through these reactions we have prepared a series of perhydrooxepino[3',4':4,5]isoxazolo[2,3-*a*]pyridin-1-ones. The conversion of all these cycloadducts in more elaborated valuable synthetic intermediates is currently being investigated.

EXPERIMENTAL

Commercial grade solvents were used without further purification. Reaction mixtures were stirred magnetically. The organic extracts were dried over anhydrous sodium sulfate. The reaction course was monitored by tlc using hexane-ethyl acetate 1/1 as eluent. Reaction times were prolonged until disappearance

of the starting materials. Reaction solutions were concentrated using a rotary evaporator at 15-20 Torr. Flash column chromatographies were performed by using silica gel (230-400 mesh). Melting points have been determined on a Kofler hot stage and are corrected. The ir spectra were recorded on a Nicolet 5 ZDX spectrophotometer. The 400 MHz pmr and 100 MHz cmr spectra were recorded on Bruker AM-400-WB or AC-400-NB instruments. Mass spectra and gc-ms analyses at 70 eV were recorded on a Hewlett-Packard 5985B gc-ms system; only peaks with higher intensity than 20% are reported, unless they belong to molecular ions or to significant fragments.

2,3,4,5-Tetrahydropyridine 1-oxide (1)

This nitrone was prepared in chloroform immediately before use according to the described method[15] and the solvent was exchanged through evaporation under reduced pressure followed by addition of toluene.

6,7-Dihydro-2(5*H*)-oxepinone (2)

This lactone was synthesized by the previously reported method.[4]

Allylic bromination of 2

A stirred solution of 1.47 g (13.1 mmol) of **2** and 2.33 g (13.1 mmol) of *N*-bromosuccinimide in 100 ml of carbon tetrachloride was heated at the reflux temperature. After 5 min, 0.075 g (0.31 mmol) of dibenzoyl peroxide were added and the mixture was kept on refluxing for 45 min. The cooled reaction mixture was filtered and the solvent removed to obtain 2.59 g of a red oil, which after purification by flash column chromatography afforded by elution order 102 mg (3%) of *3,5-dibromo-6,7-dihydro-2(3*H*)-oxepinone* (**4**) and 2.39 g (96%) of *5-bromo-6,7-dihydro-2(5*H*)-oxepinone* (**3**).

*3,5-Dibromo-6,7-dihydro-2(3*H*)-oxepinone* (**4**): ^{1}H Nmr (250 MHz, $CDCl_3$) δ 2.95 (dddd, $J_{6,6'}$=19.6 Hz, $J_{6,7}$≈3.5 Hz, $J_{6,7'}$≈1.4 Hz, $J_{6,4}$≈0.9 Hz, 1H: H_6), 3.33 (ddddd, $J_{6',6}$=19.6 Hz, $J_{6',7'}$=12.1 Hz, $J_{6',7}$=3.6 Hz, $J_{6',4}$=2.5 Hz, $J_{6',3}$=1.2 Hz, 1H: $H_{6'}$), 4.26 (dt, $J_{7,7'}$=13.2 Hz, $J_{7,6}$=$J_{7,6'}$=3.6 Hz, 1H: H_7), 4.94 (br d, $J_{3,4}$=8.4 Hz, 1H: H_3), 5.21 (ddd, $J_{7',7}$=13.2 Hz, $J_{7',6'}$=12.1 Hz, $J_{7',6}$=1.4 Hz, 1H: $H_{7'}$), 6.24 (ddd, $J_{4,3}$=8.4 Hz, $J_{4,6'}$=2.5 Hz, $J_{4,6}$=0.9 Hz, 1H: H_4); ^{13}C nmr (62.5 MHz, $CDCl_3$) δ 38.9 (C_3, DEPT), 40.4 (C_6, DEPT), 65 2 (C_7), 124.1 (C_4, DEPT), 130.3 (C_5, DEPT), 166.1 (C_2); ir (film) 2923 (w), 1736 (s), 1641 (m), 1458 (w), 1282 (s), 1241 (s), 1076 (s) cm^{-1}; ms (*m/z*) 272-270-268 (M^+, 1, 2, 1), 191 (12), 189 (13), 163 (25), 161 (40), 147 (25), 145 (28), 133 (40), 131 (35), 67 (86), 51 (100). Anal. Calcd for $C_6H_6O_2Br_2$: C, 26.70; H, 2.24; Br, 59.21. Found: C, 26.76; H, 2.23; Br, 59.56.

*5-Bromo-6,7-dihydro-2(5*H*)-oxepinone* (**3**): ^{1}H Nmr (400 MHz, $CDCl_3$) δ 2.63 (m, 2H: H_6, $H_{6'}$), 4.28 (dddd, $J_{7,7'}$=13.0 Hz, J=4.5 Hz, J'=3.4 Hz, $J_{7,5}$=0.9 Hz, 1H: H_7), 4.52 (ddd, $J_{7,7'}$=13.0 Hz, J=5.3 Hz, J'=4.0 Hz, 1H:

$H_{7'}$), 4.95 (qt, 3xJ≈4.5 Hz, $J_{5,3}$≈$J_{5,7}$≈0.9 Hz, 1H: H_5), 5.93 (dd, $J_{3,4}$=12.5 Hz, $J_{3,5}$=1.0 Hz, 1H: H_3), 6.43 (dd, $J_{4,3}$=12.5 Hz, $J_{4,5}$≈4.3 Hz, 1H: H_4); ^{13}C nmr (62.5 MHz, $CDCl_3$) δ 37.0 (C_6), 47.2 (C_5), 63.7 (C_7), 120.8 (C_3), 140.9 (C_4), 166.3 (C_2); ir (film) 2979 (w), 2954 (w), 1704 (s), 1468 (m), 1406 (s), 1294 (s), 1219 (s), 1199 (s), 1073 (s), 840 (s) cm^{-1}; ms (*m/z*) 192-190 (M^+, 1, 1), 111 (45), 83 (69), 81 (69), 53 (100). Anal. Calcd for $C_6H_7O_2Br$: C, 37.90; H, 3.71; Br, 41.54. Found: C, 37.68; H, 3.78; Br, 41.53.

6,7-Dihydro-5-oxo-2(5*H*)-oxepinone (7)

To a mixture of 30 ml of acetic anhydride and 50 ml of glacial acetic acid, 4.0 g (40.0 mmol) of chromium(III) oxide were added in small portions and the resulting mixture was diluted with 50 ml of benzene under ice-cooling and vigorous stirring. Then a solution of lactone (**2**) (0.9 g, 8.0 mmol) in 5 ml of benzene was added dropwise and stirring was followed under 15 °C for 2 h. The reaction mixture was treated with water (100 ml) and the aqueous phase extracted with ether (3 x 50 ml). The combined organic extracts were dried, filtered, and the solvent was evaporated to give a solid residue which after purification by flash chromatography (ether-ethyl acetate 1/1) yielded 630 mg (62%) of *6,7-dihydro-5-oxo-2(5H)-oxepinone* (**7**) as a white solid: mp 79-80 °C (crystallized from hexane). ^{1}H Nmr (250 MHz, $CDCl_3$) δ 2.95 (t, J=5.1 Hz, 2H: H_6), 4.52 (t, J=5.1 Hz, 2H: H_7), 6.40 (d, J=12.4 Hz, 1H), 6.56 (d, J=12.4 Hz, 1H); ^{13}C nmr (62.5 MHz, $CDCl_3$) δ 43.3 (C_6), 63.6 (C_7), 130.1 (C_3), 136.2 (C_4), 165.2 (C_2), 198.0 (C_5); ir (film) 3360 (m), 3044 (m), 1715 (s), 1694 (s), 1609 (m), 1314 (s), 1159 (s), 1040 (s), 850 (s) cm^{-1}; ms (*m/z*) 126 (M^+, 39), 99 (100), 98 (62), 82 (48), 54 (88), 53 (20), 42 (39). Anal. Calcd for $C_6H_6O_3$: C, 57.14; H, 4.80. Found: C, 57.28; H, 4.80.

Reaction of 3 with silver acetate

To a solution of 0.5 g (2.62 mmol) of **3** in 50 ml of ether, 656 mg (3.93 mmol) of silver acetate were added and the mixture stirred in the dark for 4 h. Then a second addition of 437 mg (2.62 mmol) of silver acetate was done and heating prolonged for another additional 4 h. The solid residue was filtered through *celite* and the solvent evaporated to obtain 380 mg of an oily product. Purification by flash chromatography (hexane-ethyl acetate 3/1) produced by elution order 70 mg (16%) of *3-acetoxy-6,7-dihydro-2(3H)-oxepinone* (**9**) and 226 mg (51%) of *5-acetoxy-6,7-dihydro-2(5H)-oxepinone* (**8**).

3-Acetoxy-6,7-dihydro-2(3H)-oxepinone (**9**): ^{1}H Nmr (250 MHz, $CDCl_3$) δ 2.17 (s, 3H: CH_3COO), 2.45 (m, 1H: H_6), 2.62 (m, 1H: H_6), 4.33 (dddd, $J_{7,7'}$=13.0 Hz, $J_{7,6}$=4.4 and 2.8 Hz, $J_{7,5}$=1.6 Hz, 1H: H_7), 4.61 (td, $J_{7',7}$=13.0 Hz, $J_{7',6}$=13.0 and 2.2 Hz, 1H: $H_{7'}$), 5.52 (dq, $J_{4,5}$≈11.7 Hz, $J_{4,3}$≈$J_{4,6}$=$J_{4,6}$=2.2 Hz, 1H: H_4), 5.78 (ddddd, $J_{5,4}$=11.7 Hz, $J_{5,3}$=4.5 Hz, $J_{5,6}$≈$J_{5,6}$≈2.9 Hz, $J_{5,7}$=1.6 Hz, 1H: H_5), 6.32 (dddd, $J_{3,5}$=4.5 Hz, $J_{3,6}$≈3.0 and 1 6 Hz, $J_{3,4}$=2.2 Hz, 1H: H_3); ^{13}C nmr (62.5 MHz, $CDCl_3$) δ 20.6 (CH_3COO), 29.7 (C_6), 64.8 (C_7), 68.4

(C_3), 122.9 (C_4), 128.8 (C_5), 168.8 (C_2), 169.8 (CH_3COO); ir (film) 2922 (w), 1743 (s), 1658 (w), 1481 (w), 1373 (s), 1236 (s), 1226 (s), 1174 (s), 1070 (s), 1056 (s) cm^{-1}; ms (*m/z*) 171 (M^++1, 0.3), 128 (17), 110 (2), 84 (38), 83 (22), 43 (100). Anal. Calcd for $C_8H_{10}O_4$: C, 56.45; H, 5.93. Found: C, 56.54; H, 5.94.

5-Acetoxy-6,7-dihydro-2(5H)-oxepinone (**8**): ^1H Nmr (250 MHz, $CDCl_3$) δ 2.05 (s, 3H: CH_3COO), 2.18 (ddddd, $J_{6,6'}$=16.1 Hz, $J_{6,7}$=6.2 Hz, $J_{6,5}$=5.2 Hz, $J_{6,7'}$=2.1 Hz, $J_{6,4}$=1.0 Hz, 1H: H_6), 2.41 (dddd, $J_{6',6}$=16.1 Hz, $J_{6',7'}$=8.7 Hz, $J_{6',5}$=6.0 Hz, $J_{6',7}$=2.4 Hz, 1H: $H_{6'}$), 4.22 (ddd, $J_{7,7'}$=12.7 Hz, $J_{7,6}$=6.2 Hz, $J_{7,6'}$=2.4 Hz, 1H: H_7), 4.34 (ddd, $J_{7',7}$=12.7 Hz, $J_{7',6'}$=8.7 Hz, $J_{7',6}$=2.1 Hz, 1H: $H_{7'}$), 5.53 (dddd, $J_{5,6'}$=6.0 Hz, $J_{5,6}$=5.2 Hz, $J_{5,4}$=3.9 Hz, $J_{5,3}$=1.4 Hz, 1H: H_5), 6.04 (dd, $J_{3,4}$=12.4 Hz, $J_{3,5}$=1.4 Hz, 1H: H_3), 6.28 (ddd, $J_{4,3}$=12.4 Hz, $J_{4,5}$=3.8 Hz, $J_{4,6}$=1.0 Hz, 1H: H_4); ^{13}C nmr (62.5 MHz, $CDCl_3$) δ 20.8 (CH_3COO), 33.1 (C_6), 63.7 (C_7), 69.5 (C_5), 122.9 (C_3), 139.8 (C_4), 167.0 (C_2), 169.7 (CH_3COO); ir (film) 2931 (w), 1735 (s), 1709 (s), 1643 (w), 1471 (w), 1234 (s), 1219 (s), 1055 (s) cm^{-1}; ms (*m/z*) 128 (M^+, 27), 110 (17), 53 (25), 43 (100). Anal. Calcd for $C_8H_{10}O_4$: C, 56.45; H, 5.93. Found: C, 56.22; H, 5.93.

Reaction of 3 with potassium thioacetate

To a solution of 112 mg (0.59 mmol) of **3** in 10 ml of freshly distilled acetone at 0 °C under argon, 67 mg (0.59 mmol) of potassium thioacetate were added in small portions, and the mixture stirred at 0 °C for 1 h. The solid residue was filtered and the solvent evaporated. The oily residue obtained was purified by flash column chromatography to yield 107 mg (98%) of *5-acetylthio-6,7-dihydro-2(5H)-oxepinone* (**11**): ^1H Nmr (250 MHz, $CDCl_3$) δ 2.17 (m, 1H: H_6), 2.31 (s, 3H: CH_3COS), 2.47 (m, 1H: $H_{6'}$), 4.26 (m, 2H: H_7, $H_{7'}$), 4 43 (dddd, J=7.1 Hz, J'=6.2 Hz, $J_{5,4}$=4.4 Hz, $J_{5,3}$=1.9 Hz, 1H: H_5), 5.96 (dd, $J_{3,4}$=12.4 Hz, $J_{3,5}$=1.9 Hz, 1H: H_3), 6.21 (dd, $J_{4,3}$=12.4 Hz, $J_{4,5}$=4.4 Hz, 1H: H_4); ^{13}C nmr (62.5 MHz, $CDCl_3$) δ 30.3 (CH_3COS), 34.0 (C_6), 43.4 (C_5), 65.4 (C_7), 122.2 (C_3), 141.5 (C_4), 167.2 (C_2), 193.4 (CH_3COS); ir (film) 2922 (w), 1697 (s), 1632 (w), 1468 (w), 1203 (s), 1126 (s), 1076 (s) cm^{-1}; ms (*m/z*) 186 (M^+, 1), 144 (100), 111 (15), 43 (57). Anal. Calcd for $C_8H_{10}O_3S$: C, 51.60; H, 5.41; S, 17.22. Found C, 51.50; H, 5.49; S, 17.12.

When the same reaction was performed at the reflux temperature for 10 min, we obtained 70% yield of *5-acetylthio-6,7-dihydro-2(3H)-oxepinone* (**10**): ^1H Nmr (250 MHz, $CDCl_3$) δ 2.30 (s, 3H: CH_3COS), 2.76 (m, 2H: H_6, $H_{6'}$), 3.49 (dt, $J_{3,4}$=5.8 Hz, $J_{3,6}$=$J_{3,6'}$ =2.4 Hz, 2H: H_3, $H_{3'}$), 4.44 (dd, J=6.2 Hz, J'=4.6 Hz, 2H: H_7, $H_{7'}$), 5.96 (tt, $J_{4,3}$=$J_{4,3'}$=5.8 Hz, $J_{4,6}$=$J_{4,6'}$=1.7 Hz, 1H: H_4); ^{13}C nmr (62.5 MHz, $CDCl_3$) δ 30.0 (CH_3COS), 34.1 (C_6), 35.7 (C_3), 65.2 (C_7), 129.2 (C_4), 130.4 (C_5), 171.3 (C_2), 194.5 (CH_3COS); ir (film) 2982 (w), 2921 (w), 1736 (s), 1696 (s), 1639 (w), 1480 (w), 1120 (s), 1079 (s) cm^{-1}; ms (*m/z*) 186 (M^+, 2), 144 (51), 43 (100). Anal. Calcd for $C_8H_{10}O_3S$: C, 51.60; H, 5.41; S, 17.22. Found: C, 51.66; H, 5.47; S, 17.19.

1,3-Dipolar cycloaddition of nitrone (1) to lactone (3)

A solution of **1**, prepared from 794 mg (7.86 mmol) of *N*-hydroxypiperidine and 5.11 g (23.6 mmol) of yellow HgO, in 70 ml of toluene was treated with a solution of **3** (500 mg, 2.62 mmol) for 5 h at 100 °C. After cooling and removal of the solvent, 1.03 g of crude product was obtained as an oil. Purification by flash column chromatography (CH_2Cl_2-ether 9/1) yielded 530 mg (70%) of pure *(5*RS,*5a*RS,*11a*SR,*11b*SR)-*5-bromodecahydro-1H-oxepino[3',4':4,5]isoxazolo[2,3-a]pyridin-1-one* (**13**), as a viscous oil, which solidified on standing: mp 149-150 °C (crystallized from acetone-pentane). ^{1}H Nmr (400 MHz, acetone-d_6) [*trans*-invertomer] δ 1.30 (qt, $J_{10ax,10eq}\approx J_{10ax,9ax}\approx J_{10ax,11ax}\approx$12.8 Hz, $J_{10ax,9eq}\approx J_{10ax,11eq}\approx$3.8 Hz, 1H: H_{10ax}), 1.38 (m, 1H: H_{11ax}), 1.58 (qt, $J_{9ax,9eq}\approx J_{9ax,10ax}\approx J_{9ax,8ax}\approx$13.0 Hz, $J_{9ax,10eq}\approx J_{9ax,8eq}\approx$4.1 Hz, 1H: H_{9ax}) 1.71 (m, 1H: H_{10eq}), 1.80 (m, 1H: H_{9eq}), 2.02 (m, 1H: H_{11eq}), 2.23 (ddd, $J_{4,4}$=14.3 Hz, $^{trans}J_{4,5}$=10.5 Hz, $^{cis}J_{4,3}$=4.0 Hz, 1H: H_4), 2.43 (ddd, $J_{8ax,9ax}$=12.1 Hz, $J_{8ax,8eq}$=9.0 Hz, $J_{8ax,9eq}$=3.1 Hz, 1H: H_{8ax}), 2.61 (ddd, $J_{11a,11ax}\approx$12.0 Hz, $J_{11a,11b}$=9.5 Hz, $J_{11a,11eq}$=2.4 Hz, 1H: H_{11a}), 2.73 (tt, $J_{4,4}\approx{}^{trans}J_{4,3}\approx$13.7 Hz, $^{cis}J_{4,3}\approx{}^{cis}J_{4,5}\approx$6.7 Hz, 1H: H_4), 3.39 (dt, $J_{8eq,8ax}$=9.0 Hz, $J_{8eq,9ax}\approx J_{8eq,9eq}\approx$3.7 Hz, 1H: H_{8eq}), 3.67 (t, $J_{11b,11a}=J_{11b,5a}$=9.5 Hz, 1H: H_{11b}), 3.90 (ddd, $J_{5,5a}$=11.7 Hz, $^{trans}J_{5,4}$=10.5 Hz, $^{cis}J_{5,4}$=6.7 Hz, 1H: H_5), 4.19 (dd, $J_{3,3}$=13.3 Hz, $^{cis}J_{3,4}$=6.8 Hz, 1H: H_3), 4.33 (dd, $J_{5a,5}$=11.7 Hz, $J_{5a,11b}$=9.5 Hz, 1H: H_{5a}), 4.50 (td, $J_{3,3}=^{trans}J_{3,4}\approx$13.3 Hz, $^{cis}J_{3,4}\approx$4.0 Hz, 1H: H_3), [*cis*-invertomer] observed absorptions δ 2.79 (m, 1H), 3.00 (m, 1H), 3.78 (m, 1H), 4.09 (t, $J_{11b,11a}\approx J_{11b,5a}\approx$9.3 Hz, 1H: H_{11b}), 4.19 (m, 1H: H_3), 4.58 (td, $J_{3,3}$=13.4 Hz, $J_{3,4}$=13.4 and 3.8 Hz, 1H: H_3), 4.87 (dd, $J_{5a,5}$=11.4 Hz, $J_{5a,11b}$=9.8 Hz, 1H: H_{5a}), relative area *trans*/*cis*= 85/15; ^{13}C nmr (100 MHz, acetone-d_6) [*trans*-invertomer] δ 24.1 (C_{10}), 25.2 (C_9), 29.9 (C_{11}), 36.5 (C_4), 46.8 (C_5), 55.1 (C_{11b}), 55.6 (C_8), 64.3 (C_3), 70.9 (C_{11a}), 77.5 (C_{5a}), 171.6 (C_1), [*cis*-invertomer] observed absorptions δ 19.4, 24.4, 25.9, 37.0, 47.7, 50.3, 51.3, 64.2, 77.2; ir (KBr) 2966 (m), 2945 (s), 2939 (s), 2920 (m), 2886 (m), 2855 (s), 2845 (s), 1717 (s), 1482 (m), 1392 (s), 1287 (s), 1212 (s), 1183 (s), 1158 (s), 1085 (s), 1056 (s) cm^{-1}; ms (*m/z*) 291-289 (M^+, 12, 12), 210 (9), 182 (20), 142 (20), 124 (100), 99 (50), 97 (56), 82 (34), 69 (40), 41 (64). Anal. Calcd for $C_{11}H_{16}NO_3Br$: C, 45.53; H, 5.56; Br, 27.54; N, 4.83. Found: C, 45.48; H, 5.58; Br, 27.55; N, 4.70.

1,3-Dipolar cycloaddition of nitrone (1) to lactone (8)

A solution of **1**, prepared from 588 mg (5.82 mmol) of *N*-hydroxypiperidine and 3.78 g (17.5 mmol) of yellow HgO, in 40 ml of toluene was treated with a solution of **8** (330 mg, 1.94 mmol) for 2 h at 100 °C. After cooling and removal of the solvent, 1.11 g of crude product was obtained as a solid. This crude material was purified by flash column chromatography (ethyl acetate), affording the following fractions:

-380 mg (72%) of *(5*RS,*5a*RS,*11a*SR,*11b*SR*)-5-acetoxydecahydro-1*H*-oxepino[3',4':4,5]isoxazolo[2,3-*a*]-pyridin-1-one* (**14**) as a white solid.

-135 mg (26%) of *(5*RS,*5a*SR,*11a*RS,*11b*RS*)-5-acetoxydecahydro-1*H*-oxepino[3',4':4,5]isoxazolo[2,3-*a*]-pyridin-1-one* (**15**) as a white solid.

14: mp 114-115°C(crystallized from acetone-pentane). ^{1}H Nmr (400 MHz, acetone-d_6) [*trans*-invertomer] δ 1.29 (qt, $J_{10ax,10eq}\approx J_{10ax,9ax}\approx J_{10ax,11ax}\approx$13.0 Hz, $J_{10ax,9eq}\approx J_{10ax,11eq}\approx$4.0 Hz, 1H: H_{10ax}), 1.39 (m, 1H: H_{11ax}), 1.56 (qt, $J_{9ax,9eq}\approx J_{9ax,10ax}\approx J_{9ax,8ax}\approx$12.5 Hz, $J_{9ax,10eq}\approx J_{9ax,8eq}\approx$3.5 Hz, 1H: H_{9ax}) 1.70 (m, 2H: H_{10eq},H_{4a}), 1.77 (m, 1H: H_{9eq}), 2.00 (s, 3H: CH_3COO), 2.04 (m, 1H: H_{11eq}), 2.39 (ddd, $J_{8ax,9ax}$=12.1 Hz, $J_{8ax,8eq}$=9.0 Hz, $J_{8ax,9eq}$=3.0 Hz, 1H: H_{8ax}), 2.51 (tt, $J_{4,4}\approx{}^{trans}J_{4,3}\approx$13.7 Hz, ${}^{cis}J_{4,3}\approx J_{4,5}\approx$6.9 Hz, 1H, H_4), 2.54 (m, 1H: H_{11a}), 3.34 (m, $J_{8eq,8ax}$=8.9 Hz, 1H: H_{8eq}), 3.59 (t, $J_{11b,11a}=J_{11b,5a}$=9.6 Hz, 1H: H_{11b}), 4.24 (dd, $J_{3,3}$=13.2 Hz, ${}^{cis}J_{3,4}$=6.5 Hz, 1H: H_3), 4.35 (dd, $J_{5a,5}$=10.9 Hz, $J_{5a,11b}$=9.8 Hz, 1H: H_{5a}), 4.48 (td, $J_{3,3}={}^{trans}J_{3,4}$ =13.3 Hz, ${}^{cis}J_{3,4}$=3.8 Hz, 1H: H_3), 4.81 (ddd, $J_{5,5a}$ =11.0 Hz, ${}^{trans}J_{5,4}$=9.4 Hz, ${}^{cis}J_{5,4}$=7.2 Hz, 1H: H_5), [*cis*-invertomer] observed absorptions δ 2.90 (m, 1H), 3.75 (m, 1H: H_8), 3.97 (br t, $J_{11b,11a}\approx J_{11b,5a}\approx$9 Hz, 1H: H_{11b}), 4.57 (br dt, $J_{3,3}\approx$13.0 Hz, $J_{3,4}\approx$13.0 and 5.0 Hz, 1H: H_3), relative area *trans*/*cis*= 78/22; ^{13}C nmr (100 MHz, acetone-d_6) [*trans*-invertomer] δ 20.8 (CH_3COO), 24.1 (C_{10}), 25.3 (C_9), 29.7 (C_{11}), 30.7 (C_4), 53.5 (C_{11b}), 55.6 (C_8), 63.1 (C_3), 70.3 (C_{11a}), 70.9 (C_5), 75.7 (C_{5a}), 169.9/172.0 (C_1/CH_3COO), [*cis*-invertomer] observed absorptions δ 19.5, 24.4, 25.7, 31.1, 49.7, 50.4, 63.0, 63.8, 70.7, 75.4; ir (KBr) 2955 (s), 2947 (s), 2927 (s), 2855 (s), 2828 (s), 1732 (s), 1720 (s), 1448 (m), 1397 (s), 1371 (s), 1336 (s), 1295 (s), 1252 (s), 1254 (s), 1224 (s), 1217 (s), 1191 (s), 1159 (s), 1088 (s), 1058 (s), 1020 (s), 979 (s), 955 (s), 639 (s) cm^{-1}; ms (*m/z*) 269 (M^+, 10), 226 (3), 210 (5), 124 (100), 99 (33), 69 (20), 43 (81). Anal. Calcd for $C_{13}H_{19}NO_5$: C, 57.98; H, 7.12; N, 5.20. Found: C, 58.04; H, 7.16; N, 5.20.

15: mp 145-146°C(crystallized from acetone-pentane). ^{1}H Nmr (400 MHz, acetone-d_6) [*trans*-invertomer] δ 1.30 (m, 2H: H_{10ax},H_{11ax}), 1.56 (br qt, $J_{9ax,9eq}\approx J_{9ax,10ax}\approx J_{9ax,8ax}\approx$12.5 Hz, $J_{9ax,10eq}\approx J_{9ax,8eq}\approx$4.0 Hz, 1H: H_{9ax}), 1.69 (m, 1H: H_{10eq}), 1.76 (m, 1H: H_{9eq}), 1.92 (s, 3H: CH_3COO), 2.10 (m, 3H: $2H_4$, H_{11eq}), 2.35 (ddd, $J_{8ax,9ax}$=12.2 Hz, $J_{8ax,8eq}$=9.0 Hz, $J_{8ax,9eq}$=3.1 Hz, 1H: H_{8ax}) 2.44 (br td, $J_{11a,11b}\approx J_{11a,11ax}\approx$10.2 Hz, $J_{11a,11eq}\approx$2.4 Hz, 1H: H_{11a}), 3.29 (dddd, $J_{8eq,8ax}\approx$8.9 Hz, $J_{8eq,9ax}\approx$3.8 and 2.5 Hz, $J_{8eq,10eq}\approx$0.8 Hz, 1H: H_{8eq}), 3.47 (t, $J_{11b,11a}=J_{11b,5a}$=9.9 Hz, 1H: H_{11b}), 4.20 (m, 1H: H_3), 4.44 (dd, $J_{5a,11b}$=10.1 Hz, $J_{5a,5}$=1.7 Hz, 1H: H_{5a}), 4.48 (m, 1H: H_3), 5.34 (m, 1H: H_5), [*cis*-invertomer] observed absorptions δ 1.42 (m), 2.18 (m), 2.68 (m, J≈12.0 Hz, J'≈9.5 Hz, J"=2.5 Hz, 1H: H_8), 2.98 (m, 1H: H_8), 3.64 (ddd, $J_{11a,11b}\approx$10.0 Hz, $J_{11a,11}\approx$5.1 Hz and 1.3 Hz, 1H: H_{11a}), 3.92 (t, $J_{11b,11a}\approx J_{11b,5a}\approx$10.2 Hz, 1H: H_{11b}), 4.93 (dd, $J_{5a,11b}$=10.4 Hz, $J_{5a,5}$=1.7

Hz, 1H: H_{5a}), 5.29 (m, 1H: H_5), relative area *trans/cis*= 70:30; ^{13}C nmr (100 MHz, acetone-d_6) [*trans*-invertomer] δ 20.8 (CH_3COO), 24.1 (C_{10}), 25.4 (C_9), 29.9-30.4 (C_{11}, occult under the solvent signals), 30.7 (C_4), 53.2 (C_{11b}), 55.9 (C_8), 64.1 (C_3), 69.5 (C_5), 70.8 (C_{11a}), 75.4 (C_{5a}), 169.6/172.4 (C_1/CH_3COO), [*cis*-invertomer] observed absorptions δ 18.8, 20.8, 25.3, 25.9, 31.0 (C_4), 47.3 (C_{11b}), 50.7 (C_8), 64.6 (C_{11a}), 70.4 (C_5), 75.6 (C_{5a}); ir (KBr) 2933 (m), 2855 (w), 1745 (s), 1735 (s), 1231 (s) cm^{-1}; ms (*m/z*) 269 (M^+, 15), 226 (5), 210 (5), 124 (100), 99 (33), 43 (67). Anal. Calcd for $C_{13}H_{19}NO_5$: C, 57.98; H, 7.12; N, 5.20. Found: C, 57.97; H, 7.26; N, 5.19.

1,3-Dipolar cycloaddition of nitrone (1) to lactone (11)

A solution of **1**, prepared from 651 mg (6.45 mmol) of *N*-hydroxypiperidine and 5.59 g (25.8 mmol) of yellow HgO, in 40 ml of toluene was treated with a solution of **11** (400 mg, 2.15 mmol) for 1.5 h at 100 °C. After cooling and removal of the solvent, 1.14 g of crude product was obtained as an oil. This material was purified by flash column chromatography (ethyl acetate), affording the following fractions:

-465 mg (75%) of *(5*RS,*5a*RS,*11a*SR,*11b*SR*)-5-acetylthiodecahydro-1*H-*oxepino[3',4':4,5]isoxazolo-[2,3-*a*]-pyridin-1-one* (**16**), as a colorless oil.

-24 mg of a mixture of cycloadducts (**16**) and its epimer *(5*RS,*5a*SR,*11a*RS,*11b*RS*)-5-acetylthio-decahydro-1*H-*oxepino[3',4':4,5]isoxazolo[2,3-*a*]pyridin-1-one* (**17**).

-105 mg (17%) of cycloadduct (**17**), as a white solid.

16: ^1H Nmr (400 MHz, acetone-d_6) [*trans*-invertomer] δ 1.30 (qt, $J_{10ax,10eq}\approx J_{10ax,9ax}\approx J_{10ax,11ax}\approx$12.8 Hz, $J_{10ax,9eq}\approx J_{10ax,11eq}\approx$4.1 Hz, 1H: H_{10ax}), 1.35 (m, 1H: H_{11ax}), 1.55 (qt, $J_{9ax,9eq}\approx J_{9ax,10ax}\approx J_{9ax,8ax}\approx$12.5 Hz, $J_{9ax,10eq}\approx J_{9ax,8eq}\approx$4.1 Hz, 1H: H_{9ax}) 1.69 (m, 1H: H_{10eq}), 1.76 (m, 1H: H_{9eq}), 1.85 (dddd, $J_{4,4}$=14.2 Hz, $^{trans}J_{4,5}$=11.3 Hz, $^{cis}J_{4,3}$=3.8 Hz, $^{trans}J_{4,3}$<1 Hz, 1H: H_4), 2.03 (m, 1H: H_{11eq}), 2.29 (s, 3H: CH_3COS), 2.38 (ddd, $J_{8ax,9ax}$=12.2 Hz, $J_{8ax,8eq}$=9.2 Hz, $J_{8ax,9eq}$=3.1 Hz, 1H: H_{8ax}), 2.41 (tt, $J_{4,4}\approx{}^{trans}J_{4,3}\approx$13.3 Hz, $^{cis}J_{4,3}\approx{}^{cis}J_{4,5}\approx$6.7 Hz, 1H: H_4), 2.57 (ddd, $J_{11a,11ax}\approx$11.4 Hz, $J_{11a,11b}\approx$8.9 Hz, $J_{11a,11eq}$=2.5 Hz, 1H: H_{11a}), 3.32 (br dt, $J_{8eq,8ax}\approx$9.0 Hz, $J_{8eq,9ax}\approx J_{8eq,9eq}\approx$3.0 Hz, 1H: H_{8eq}), 3.45 (ddd, $J_{5,5a}\approx{}^{trans}J_{5,4}\approx$11.7 Hz, $^{cis}J_{5,4}$=6.7 Hz, 1H: H_5), 3.63 (t, $J_{11b,11a}=J_{11b,5a}$=9.5 Hz, 1H: H_{11b}), 4.21 (br dd, $J_{3,3}$=13.3 Hz, $^{cis}J_{3,4}$=6.7 Hz, 1H: H_3), 4.22 (dd, $J_{5a,5}$=12.1 Hz, $J_{5a,11b}$=9.5 Hz, 1H: H_{5a}), 4.43 (td, $J_{3,3}=^{trans}J_{3,4}$=13.3 Hz, $^{cis}J_{3,4}$=3.8 Hz, 1H: H_3), [*cis*-invertomer] observed absorptions δ 2.75 (m, 1H), 2.96 (m, 1H), 3.79 (m, 1H), 4.53 (td, J=J'=13.4 Hz, J''=3.6 Hz, 1 H), 4.72 (dd, J=11.9 Hz, J'=9.8 Hz, 1 H), relative area *trans/cis*= 80:20; ^{13}C nmr (100 MHz, acetone-d_6) [*trans*-invertomer] δ 24.1 (C_{10}), 25.3 (C_9), 29.8 (C_{11}), 30.5 (CH_3COS), 32.5 (C_4), 41.5 (C_5), 55.6 (C_8, C_{11b}), 64.1 (C_3), 70.3 (C_{11a}), 74.9 (C_{5a}), 172.1 (C_1), 194.0 (CH_3COS), [*cis*-invertomer] observed

absorptions δ 19.1, 24.7, 25.9, 32.7, 42.0, 50.3, 51.4, 63.9, 64.0, 74.8, 172.6, 193.9; ir (film) 2930 (s), 3858 (m), 1737 (s), 1691 (s), 1545 (w), 1440 (m), 1188 (s), 1164 (s), 1120 (s), 1107 (s), 1083 (s), 1053 (s) cm^{-1}; ms (*m/z*) 287-285 (M^+, 1, 15), 242 (8), 210 (9), 124 (65), 113 (73), 100 (75), 71 (34), 43 (67). Anal. Calcd for $C_{13}H_{19}NO_4S$: C, 54.72; H, 6.71; N, 4.91; S, 11.24. Found: C, 54.60; H, 6.66; N, 4.78; S, 11.40.

17:mp153-154°C (crystallized from acetone). ^1H Nmr (400 MHz, acetone-d_6) [*trans*-invertomer] δ 1.28 (m, 2H: H_{10ax}, H_{11ax}), 1.55 (qt, $J_{9ax,9eq}\approx J_{9ax,8ax}\approx J_{9ax,10ax}\approx 13.0$ Hz, $J_{9ax,10eq}\approx J_{9ax,8eq}\approx 4.0$ Hz, 1H: H_{9ax}), 1.67 (m, 1H: H_{10eq}), 1.75 (m, 1H: H_{9eq}), 2.15 (m, 2H: H_{11eq}, H_4), 2.29 (s, 3H: CH_3COS), 2.36 (ddd, $J_{8ax,9ax}=12.2$ Hz, $J_{8ax,8eq}=9.1$ Hz, $J_{8ax,9eq}=3.1$ Hz, 1H: H_{8ax}), 2.49 (m, 2H: H_{11a}, H_4), 3.27 (br dt, $J_{8eq,8ax}=9.1$ Hz, $J_{8eq,9ax}\approx J_{8eq,9eq}\approx 2.9$ Hz, 1H: H_{8eq}), 3.50 (t, $J_{11b,5a}=J_{11b,11a}=9.9$ Hz, 1H: H_{11b}), 4.28 (dd, $J_{3,3}\approx 13.1$ Hz, $J_{3,4}\approx 5.8$ Hz, 1H: H_3), 4.28 (dd, $J_{5,4}\approx 7.6$ Hz, $J_{5,5a}\approx 4.1$ Hz, 1H: H_5), 4.45 (td, $J_{3,3}=13.3$ Hz, $J_{3,4}=13.3$ and 3.9 Hz, 1H: H_3), 4.55 (dd, $J_{5a,11b}=9.8$ Hz, $J_{5a,5}=3.4$ Hz, 1H: H_{5a}), [*cis*-invertomer] observed absorptions δ 1.89 (tt, J=J'=14.0 Hz, J''=J'''=5.0 Hz, 1H), 2.68 (ddd, J≈12.5 Hz, J'≈10.0 Hz, J''≈2.5 Hz, 1H: H_8), 2.97 (m, 1H: H_8), 3.67 (ddd, $J_{11a,11b}=9.9$ Hz, $J_{11a,11}=5.3$ and 1.6 Hz, 1H: H_{11a}), 3.95 (t, $J_{11b,5a}=J_{11b,11a}=10.2$ Hz, 1H: H_{11b}), 4.56 (td, J≈J'≈13.2 Hz, J''=4.1 Hz, 1H), 5.07 (dd, $J_{5a,11b}=10.2$ Hz, $J_{5a,5}=3.4$ Hz, 1H: H_{5a}), relative area *trans*/*cis*=73:27; ^{13}C nmr (100 MHz, acetone-d_6) [*trans*-invertomer] δ 24.1 (C_{10}), 25.3 (C_9), 30.0 (C_{11}), 30.5 (CH_3COS), 32.1 (C_4), 40.9 (C_5), 54.7 (C_{11b}), 55.6 (C_8), 64.8 (C_3), 70.6 (C_{11a}), 75.0 (C_{5a}), 172.4 (C_1), 193.3 (CH_3COS), [*cis*-invertomer] observed absorptions δ 18.7, 25.2, 25.8, 32.5, 41.5, 49.0, 50.9, 64.5, 75.0, 173.1, 193.3; ir (KBr) 2937 (m), 2856 (w), 1716 (s), 1702 (s), 1429 (w) cm^{-1}; ms (*m/z*) 287-285 (M^+, 2, 32), 242 (26), 210 (11), 152 (30), 142 (25), 124 (100), 100 (95), 99 (39), 84 (29), 82 (23), 43 (71). Anal. Calcd for $C_{13}H_{19}NO_4S$: C, 54.72; H, 6.71; N, 4.91; S, 11.24. Found: C, 54.85; H, 6.77; N, 4.90; S, 11.28.

ACKNOWLEDGMENTS

We gratefully acknowledge the *Ministerio de Educación y Ciencia* for financial support through *Dirección General de Investigación Científica y Técnica* (project PB92-0605) and for a grant (P. C.) and *Comissió Interdepartamental de Recerca i Innovació Tecnológica* for a grant (F. B.).

REFERENCES

1. For recent examples: J. P. Michael, *Nat. Prod. Rep.*, 1992, **9**, 51.
2. A. J. Blake, A. C. Forsyth, and R. M. Paton, *J. Chem. Soc., Chem. Commun.*, 1988, 440.

3. P. Cid, P. de March, M. Figueredo, J. Font, S. Milán, A. Soria, and A. Virgili, *Tetrahedron*, 1993, **49**, 3857.
4. H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, 1975, **97**, 5434; H. Chow, I. Fleming, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1815.
5 K. Jitsukawa, K. Kameda, and S. Teranishi, *J. Org. Chem.*, 1984, **49**, 199.
6. M. Mitani, H. Takeuchi, and K. Koyama, *Chem. Lett.*, 1987, 333 and 2335.
7. M. A. Brimble, M. K. Edmonds, and G. M. Williams, *Tetrahedron Lett.*, 1990, **31**, 7509.
8. M. Labelle and Y. Guindon, *J. Am. Chem. Soc.*, 1989, **111**, 2204; B. Herradon, *Tetrahedron: Asymmetry*, 1991, **2**, 191.
9. F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, C. Caufield, T. Hendrickson, and W. C. Still, *J. Comp. Chem.*, 1990, **11**, 440.
10. M. Nakayama, S. Shinke, Y. Matsushita, S. Ohira, and S. Hayashi, *Bull. Chem. Soc. Jpn.*, 1979, **52**, 184.
11. N. Finch and E. Schlittler, *Tetrahedron*, 1968, **24**, 5421.
12. R. A. Volkmann, P. R. Kelbaugh, D. M. Nason, and V. J. Jasys, *J. Org. Chem.*, 1992, **57**, 4352.
13. P. Cid, M. Figueredo, J. Font, C. Jaime, P. de March, and A. Virgili, *Magn. Reson. Chem.*, 1990, **28**, 947.
14. L. Banting and T. A. Crabb, *Magn. Reson. Chem.*, 1987, **25**, 696; P. D. Livant and J. A. Beutler, *Tetrahedron*, 1987, **43**, 2915.
15. J. Thesing and W. Sirrenberg, *Chem. Ber.*, 1959, **92**, 1748; W. Sabel, *Chem. Ind. (London)*, 1966, 1216.

Received, 9th May, 1994