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Highly Efficient and Diastereoselective Approaches to (+)- and (-)-Grandisol

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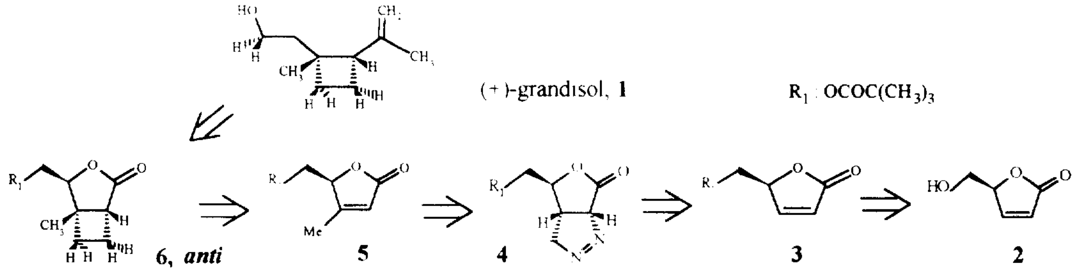
Abstract Two new routes to (+)-grandisol and three new routes to (-)-grandisol are described. All of them are highly efficient and diastereoselective. The common starting material is an easily available homochiral butenolide.

INTRODUCTION

(−)-Grandisol, (−)-**1**, was isolated for the first time in 1969 by Gueldner *et al.*[1] It is the most important constituent of the aggregation male-produced pheromone of the cotton boll weevil, *Anthonomous grandis* Boheman, a Curculionidae being an important pest of the cotton boll.[2] Morever, (+)-grandisol is also released by females of the ambrosia beetle *Trypodendron signatum* L.,[3] by males of bark beetles *Pityophthorus pityographus*,[4] and other insects like *Pityogenes quadridens*,[5] *Pityogenes calcaratus*[5] and also by the genus *Pissodes*.[6]



Scheme 1

Due to its singular structure and to its use as alternative to classical pesticides, this monoterpene has attracted the attention of many synthetic chemists. Rather large number of racemic[7] and enantiopure[8-10] (dextrorotatory as well as levorotatory isomers) grandisol syntheses have been described up to date. Almost all of them have the inconvenience of large synthetic sequences (10 to 18 steps) and/or very low total yields (0.5% to 9%). Only recently a very long (17 steps), but surprisingly very high yielding (23%), synthesis[9] and a short (20%) overall yield synthesis[10] have been reported for (+)-grandisol.

One of the crucial steps in the construction of the molecule of grandisol, apart from the creation of the right configuration in its chiral centers, is the formation of the cyclobutane ring. A [2+2] cycloaddition, either promoted photochemically or by thermal addition of an olefin to a ketene is the most popular approach, although intramolecular alkylation through an iodine derivative has also been described.[8]

In 1993 and 1994 we reported in two letters short and high yielding syntheses of (+)- and (-)-grandisol[11] starting from an homochiral butenolide **2**, commercially available or easily obtained from D-mannitol[12] or D-ribonolactone.[13] The latter chiral building block has been widely used in the last decade in organic synthesis not only by our group but also in many other laboratories.[14] We wish to present now the complete features of these syntheses.

SYNTHESIS OF THE COMMON INTERMEDIATE FOR (+)- AND (-)-GRANDISOL

A retrosynthetic analysis of (+)-grandisol is shown in Scheme 1, and direct us to (*S*)-(-)-5-hydroxymethyl-2(*5H*)-furanone **2** as starting material. A [2+2] cycloaddition of ethylene to a derivative of this butenolide, bearing the stereogenic centre, is the crucial diastereoselective step. This centre, that ensures the creation of the new chiral carbon atoms by internal assymmetric induction, must be sacrificed later on, e.g. with a Barton regiochemical reduction of the secondary hydroxyl group.

Following this strategy (see precedent paper), **2** was converted to its 5-pivalate ester **3** by reaction with pivaloyl chloride in the presence of pyridine and dimethylaminopyridine (89% yield). **3** was treated with an excess of diazomethane in ether-THF for 48 hours giving in 98% yield pyrazoline **4** as a white crystalline solid, that under pyrolysis in boiling dioxane led to (*S*)-(-)-4-methyl-5-pivaloyloxymethyl-2(*5H*)-furanone **5** in 75% yield.[15]

SYNTHESIS OF CYCLOBUTANE DERIVATIVES

The photocycloaddition of olefins to cycloalkenones is well documented and we[11,15] and others[16] have studied the same reaction to α,β-butenolides.

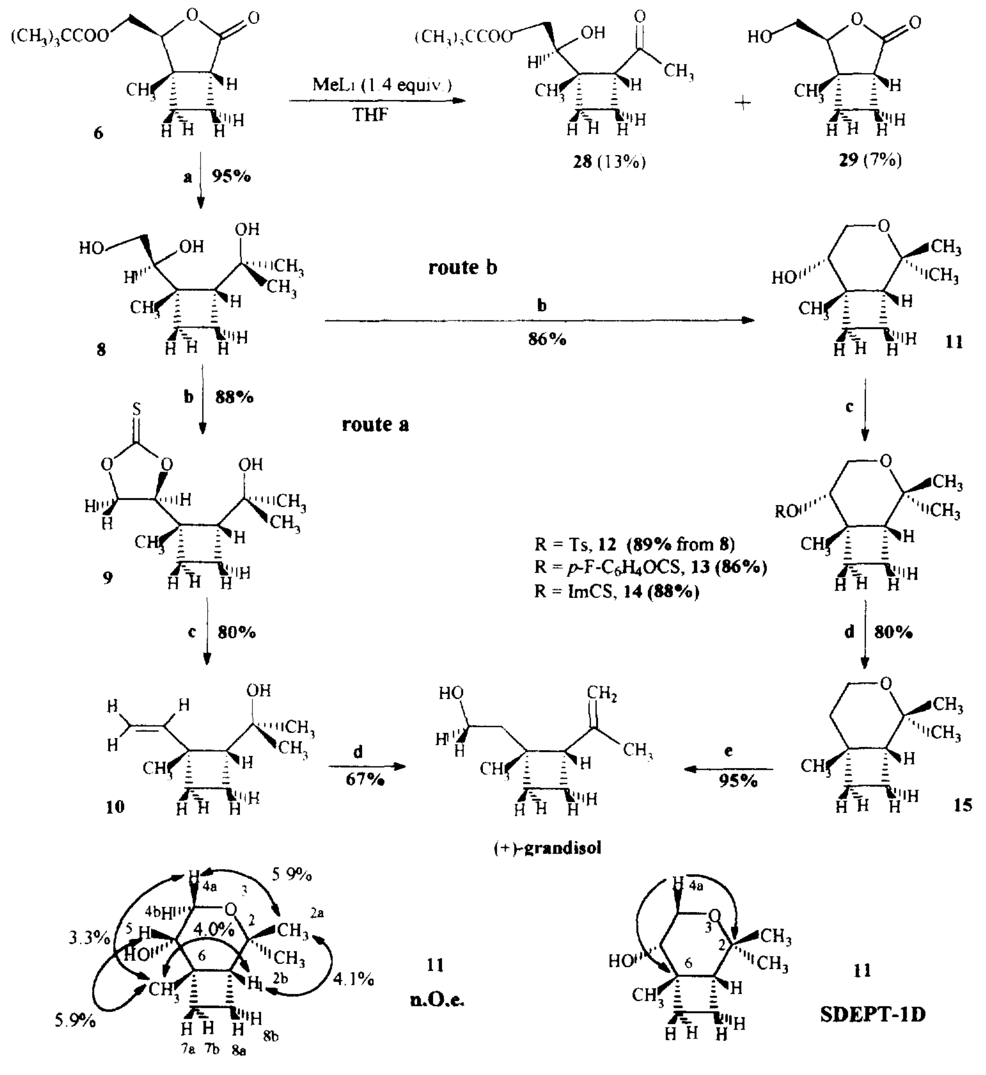
Irradiation of **5** (see precedent paper) in an ethylene saturated acetone solution with a 125W medium pressure mercury lamp at low temperature (-45 °C) for 3 hours led in 70% yield to a 62:38 mixture of (1*R*,4*S*,5*S*)-(-)-5-methyl-4-pivaloyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-one, **6** (*anti* cycloadduct) and (1*S*,4*S*,5*R*)-(+)-5-methyl-4-pivaloyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-one, **7** (*syn* cycloadduct) that could be separated easily by flash chromatography. The pivaloyl group guarantees the largest *anti:syn* cycloadducts ratio since other groups attached to position 5 of the α,β-butenolide gave lower diastereomeric excesses (see preceding paper). The *anti* cycloadduct has the correct configurations at the cyclobutane carbon atoms as needed in (+)-grandisol. The relative stereochemistry of these adducts was elucidated through their ^{13}C NMR spectra.[15]

SYNTHESIS OF (+)-GRANDISOL

Once with the appropriate cyclobutane derivative in our hands we developed a synthetic sequence to (+)-grandisol with two alternative routes showed in Scheme 2. Lactone **6** opens to the triol **8** when an excess (5.8 equivalents) of MeLi is added to a THF solution at -78 °C of **6**. (1*S*,2*R*,1*S*)-(+)-1-(1,2-dihydroxyethyl)-2-(1-hydroxy-1-methylethyl)-1-methylcyclobutane, **8** was obtained as a crystalline solid in 95% yield. Lower ratios of MeLi, trying to obtain the methylketone (*vide infra*), proved to be unfruitful.

Following the short route a), the thionocarbonate **9** was obtained as a white solid in 88% yield from **8** by transesterification with thiocarbonyldiimidazole (TCDI) in THF at 55 °C. Reaction of this thionocarbonate with 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine at 40°C led after column chromatography to the isolation of (1*R*,2*R*)-(-)-2-(1-hydroxy-1-methylethyl)-1-methyl-1-vinylcyclobutane **10**. Since this olefin is very volatile, precaution has to be taken when solvents are evaporated: yields of 80% can be obtained working properly. At this point the enantiomeric excess was determined by *glc* using a Lipodex A chiral column. An e.e. of >99.5% was determined for **10**. Since (+)-grandisol had been already obtained from **10** in 67.3% yield,[10] this route represents a new formal synthesis with an overall yield of 19 % starting from **5**.

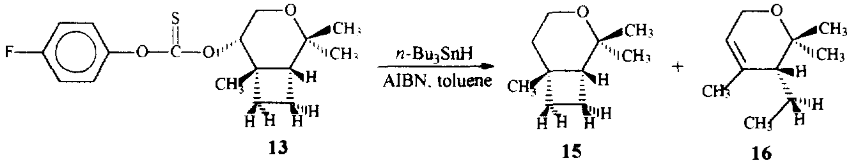
A different approach was followed as is outlined in route b), where the bicyclo ether **15** is the immediate precursor of (+)-grandisol. Triol **8** was cyclized in 86% yield to the oxabicyclo **11** using tosyl chloride in pyridine with a catalytic amount of DMAP. The stereochemistry and the bicyclic structure of this alcohol was established by means of differential n.O.e. and SDEPT-1D[17] experiments. Irradiation of Me-6 gives n.O.e.'s on H-1 (4.0%), H-4a (3.3%) and H-5 (5.9%) indicating that all of them are on the same face. Similarly, Me-2a gives a 5.9% of n.O.e. on H-1a. The SDEPT-1D spectrum after selectively pulsing the H-4a proton affords a decoupled ^{13}C spectrum in which only signals of C-2, C-5 and C-6 are present, confirming that C-2 and C-6 are at three bonds distance of H-4a: this is only compatible with the bicyclic structure.



Reagents: a) excess MeLi, THF; **route a:** b) TCDI, THF, 55-60 °C; c) 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine, 40 °C; d) Lit[10]; **route b:** b) TsCl, py, DMAP, reflux; c) TsCl, py; *p*-F-C_6H_4OCSCl, NHS, py, C_6H_6, 60 °C; TCDI, THF, 55-60 °C; d) *n*-Bu_3SnH, AIBN, toluene, 100 °C; e) LDA, *n*-hexane, 75 °C, Lit.[22].

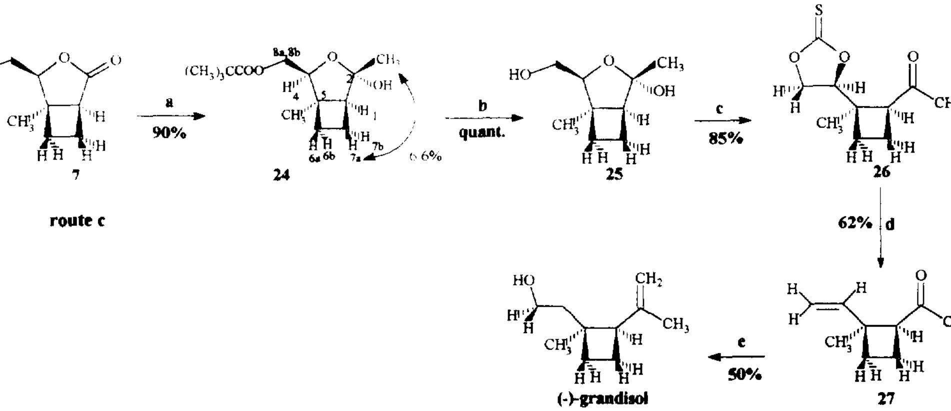
Scheme 2

Reduction of the secondary alcohol of **11** was tried unsuccessfully through the tosylate **12** (prepared directly from **8** with an excess of TsCl). Depending on the conditions, the tosylate **12** decomposed (with NaI and Zn powder),[18] remained unreacted (lithium triethylborohydride, Super Hydride)[19] or lost the tosyl group yielding **11** as the major product of a complex mixture (Super Hydride and heating up to 65°C).[19] It is known that these reactions are efficient only in alcohols with low steric hindrance, which is not the case for tosylate **12**. We decided, therefore, to accomplish the Barton and McCombie reduction of secondary hydroxyl groups[20] that proceeds via free radical intermediates circumventing the steric hindrance.[21] Thus the thiocarbonyl derivatives **13** and **14** were obtained from **11** by treatment with 4-fluorophenylchlorothionoformate and with *N,N'*-thiocarbonyldiimidazole, respectively. Following the standard procedure, **13** was treated with tributyltin hydride in refluxing toluene and a mixture of two compounds was obtained, identified as (1*R*,6*R*)-(-)-2,2,6-trimethyl-3-oxabicyclo[4.2.0]octane **15** and the dihydropyrane compound **16** in a 43:57 ratio:



The thiocarbonyl derivative **14** behaved as **13** under the Barton and McCombie conditions, affording **15** and **16** in a 65:35 ratio. However, we found that by lowering the temperature of the reaction to 100 °C and adding slowly the thiocarbonyl derivatives to the hydride (reverse addition), the yield of **15** (which is the desired product) improved considerably up to 80% (from **14**). Racemic **15**, as well as the levo isomer, have been already described and converted to grandisol by base-catalyzed opening of the cyclic ether using LDA.[22] Therefore, our synthesis of **15** represents a new formal synthesis of (+)-grandisol in an overall yield of 24%. However, we have prepared (+)-grandisol from **15** following the procedure of Dreiding *et al.*[22] The highest yield obtained by us was 62% confirming the 64% yield described by Mattay *et al.*[23] for racemic grandisol, but contrasting other yields reported: 38% by Mori *et al.*[24] and 90% by Hoffman *et al.*[10] for (+)-grandisol. The obtained (+)-grandisol, $[\alpha]_D^{26}$ = +18.3° (c:2.61, *n*-hexane), was enantiomerically pure by chiral *glc* (Lipodex A) analysis. Its structure has been unambiguously assigned from COSY and differential n.O.e. experiments. The *cis* configuration of CH_3-1 and H-2 is confirmed by a large n.O.e. created on H-2 when CH_3-1 is irradiated. From the ^{1}H-^{13}C correlation spectrum, we have assigned unambiguously all the ^{13}C signals. Our assignation of the methyl groups is in accordance with that described by Scharf *et al.*[10]

SYNTHESIS OF (-)-GRANDISOL



Reagents: **route c:** a) MeLi, THF; b) NaMeO, MeOH; c) TCDI, THF, 60-65 °C; d) 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine, 40 °C; e) Lit.[1b,26]

Scheme 3

(-)-Grandisol can be obtained starting with the *syn* cycloadduct **7** and following routes a), b) and c) shown in schemes 2 and 3. Route a) (through compounds **17**, **18** and **19**, see experimental data) and route b) (through compounds **17**, **20**, **21** or **22** and **23**) are parallel to the homologous routes described above to obtain (+)-grandisol from the *anti* cycloadduct **6** and do not show relevant differences. Both are new formal synthesis of (-)-grandisol in 12% and 13% overall yields respectively from butenolide **5**. Following the sequence depicted in route c) (Scheme 3) the hemiketal **24** is obtained as a solid when 1.25 equivalents of MeLi is added to a THF solution of **7** at -78 °C. ^{1}H and ^{13}C spectra do not show the presence of the second diastereomer. The configuration in C-2 is unequivocally established by means of the differential n.O.e. experiments: the 6.6% of n.O.e. created on H-7a when CH_3-2 is irradiated is only possible if the relative configuration of CH_3-2 and the cyclobutane is *cis*. It is worth mentioning the different behaviour of both *syn* and *anti* cycloadducts in their reaction with MeLi: the first reacts with an equivalent of MeLi to give the hemiketal **24** in 90% yield while the second affords a mixture of **28** and **29** in a total yield lower than 22% (Scheme 2). However, the *anti* cycloadduct reacts cleanly with an excess of MeLi to afford the triol **8** which in turn is the door to the operative routes to (+)-grandisol. The *syn* adduct also reacts in these conditions yielding triol **17**. This different behaviour of both cycloadducts is not unexpected since it has been already reported that diastereomeric bicyclic compounds react differently against MeLi.[25] In fact, cycloadducts **6** and **7** have a very different geometry according to MM2 calculations (Figure 2). It can be seen that the carbonyl group in **7** has a lower steric hindrance that in **6**, thus allowing an easier approach of the MeLi molecule. The diol **25** is obtained quantitatively from **24** by transesterification with MeONa in MeOH and it is converted in the thionocarbonate **26** by reaction with TCDI in THF. Treatment of **26** at 40°C with 3.1 equivalents of 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine affords a mixture of the epimers **27a** and **27b** in a 83:17 ratio (by *g/c* and NMR) and in a 62% yield. Both diastereomers were not separated. Since **27a** had been previously described [1b,26] as an immediate precursor of (-)-grandisol and in the synthesis of racemic grandisol, route c) is a new formal synthesis of (-)-grandisol in an overall yield of 7% from butenolide 5.

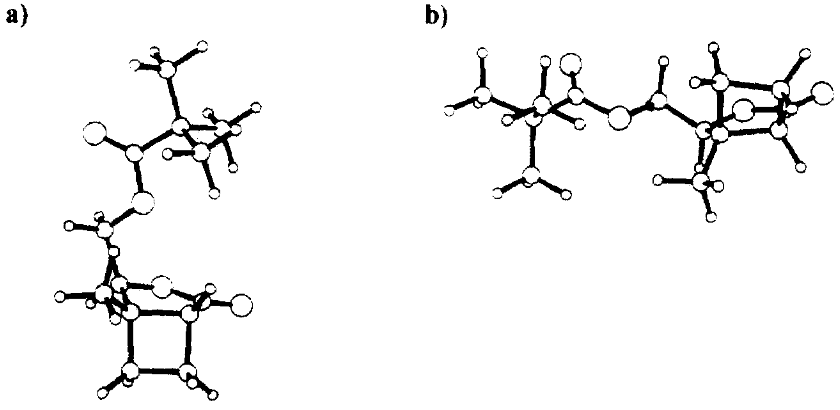


Figure 2. Geometry according to MM2 calculations of a) cycoladduct **6** and b) **7**

To conclude, two new routes to (+)-grandisol and three new routes to (-)-grandisol have been described starting from an homochiral butenolide, all of them being highly efficient and diastereoselective.

ACKNOWLEDGEMENTS

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EXPERIMENTAL SECTION

Melting points were determined on a Kofler hot stage and are uncorrected. Optical rotations were obtained on a Propol polarimeter, Model Dr. Kerchen. Distillations were effected on a rotational distillator, Büchi Model KRV 65/30 (only external or oven temperature are given).

The 250 MHz ^{1}H-NMR and the 62.5 MHz ^{13}C-NMR spectra were recorded on a Bruker spectrometer Model AC250 and the 400 MHz ^{1}H-NMR and the 100 MHz ^{13}C-NMR spectra were recorded on a Bruker spectrometer Model AM400WB. UV and IR spectra were recorded on a Hewlett-Packard 8452A and a Nicolet 20X spectrophotometers respectively.

Gas chromatographic analyses were performed on a Hewlett-Packard model 5930 instrument with a capillary column Hewlett-Packard Ultra 1 (crosslinked methyl silicone gum, 12m x 0.2mm x 0.3 μm) or with a chiral column Lipodex A hexakis-(2,3,6-tri-*O*-pentyl)-α-cyclodextrin 25m x 0.25mm). Mass spectra were recorded with a Hewlett-Packard apparatus Model 5989. Microanalyses were performed either at the Instituto de Química Bio-Orgánica C.S.I.C., Barcelona or at the Servei d'Anàlisi Elemental of the Universitat Autònoma de Barcelona.

(-)-(1*S*,2*R*,1'*S*)-1-1',2'-Dihydroxyethyl-2-1"-hydroxy-1"-methylethyl-1-methylcyclobutane, 8

MeLi (1.6M in ether, 9.2 mL, 14.72 mmol) was added to a stirred solution of **6** (600 mg, 2.50 mmol) in 55 mL of dry THF at -78 °C under Ar atmosphere, and the whole mixture was stirred at -78 °C for 1 h. The reaction was quenched with saturated NH_4Cl (40 mL) and the resulting mixture was extracted with CH_2Cl_2 (3x30 mL) and EtOAc (3x30 mL). The organic layers were combined, washed with brine and dried over $MgSO_4$. Evaporation of the solvent at reduced pressure and crystallization from pentane-ethyl acetate afforded colorless crystals (446 mg, 95% yield) of **8**; mp: 107-108 °C (ethyl acetate-pentane); $[\alpha]_D^{20}$: 2.51° (*c* 1.51, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.06 (s, 3H, Me), 1.08 (s, 3H, Me), 1.28 (s, 3H, Me), 1.53 (m, 2H), 1.72 (m, 1H), 1.94 (m, 2H), 2.70 (s, broad, 1H, OH), 3.30 (s, broad, 1H, OH), 3.52 (dd, J_{gem}: 10.9 Hz, $J_{2'a,1'}$: 8.7 Hz, 1H, H-2'a), 3.58 (dd, J_{gem}: 10.9 Hz, $J_{2'b,1'}$: 2.5 Hz, 1H, H-2'b), 4.10 (dd, $J_{1',2'a}$: 8.7 Hz, $J_{1',2'b}$: 2.5 Hz, 1H, H-1'), 4.54 (s, broad, 1H, OH); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 18.5 (CH_2), 23.3 (CH_3), 27.4 (CH_3), 28.4 (CH_2), 29.0 (CH_3), 46.3 (C, C-1), 56.9 (CH, C-2), 63.1 (CH_2, C-2'), 71.8 (C, C-1"), 74.1 (CH, C-1'); IR (KBr) ν 3379, 3289, 3216 (OH), 2966, 2933, 2879, 1378, 1101, 1059, 1052, 1016 cm^{-1}; Ms m/z (%) 189 (M^++1, 1), 171 (M^+-OH, 2), 155 (3), 153 (3), 139 (14), 110 (15), 97 (10), 95 (44), 81 (44), 69 (71), 55 (26), 43 (100). Anal. Calc. for ($C_{10}H_{20}O_3$): C, 63.80; H, 10.71. Found: C, 64.02; H,10.69.

(-)-(4*S*,1'*S*,2'*R*)-4-2'-1"-Hydroxy-1"-methylethyl-1'-methylcyclobutyl-1,3-dioxolan-2-thione, 9

To a stirred solution of **8** (238 mg, 1.27 mmol) in dry THF (12 mL) *N,N'*-thiocarbonyldiimidazole (323 mg, 1.62 mmol) was added under Ar and the mixture was heated at 55-60 °C for 5 h. Evaporation of the solvent gave a crude that was chromatographed on silica gel using a mixture 1:2 of ethyl acetate/hexane as eluent to afford **9** (258 mg, 88% yield) as a white solid; mp: 84-86 °C (ethyl acetate-pentane); $[\alpha]_D^{18}$: -62.54° (*c* 1.45, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 3H, Me), 1.19 (s, 3H, Me), 1.31 (s, 3H, Me), 1.47 (ddd, J_{gem}: 11.6 Hz, $J_{4'a,3'a}$: 9.1 Hz, $J_{4'a,3'b}$: 2.4 Hz, 1H, H-4'a), 1.68 (ddd, J_{gem}: 11.6 Hz, $J_{4'b,3'a}$: 10.2 Hz, $J_{4'b,3'b}$: 8.5 Hz, 1H, H-4'b), 1.81 (dddd, J_{gem}: 10.9 Hz, $J_{3'b,2'}$: 8.5 Hz, $J_{3'b,4'b}$: 8.5 Hz, $J_{3'b,4'a}$: 2.4 Hz, 1H, H-3'b), 1.93 (dddd, J_{gem}: 10.9 Hz, $J_{3'a,2'}$: 10.9 Hz, $J_{3'a,4'b}$: 10.2 Hz, $J_{3'a,4'a}$: 9.1 Hz, 1H, H-3'a), 2.08 (dd, $J_{2',3'a}$: 10.9 Hz, $J_{2',3'b}$: 8.5 Hz, 1H, H-2'), 4.38 (dd, J_{gem}: 9.1 Hz, $J_{5a,4}$: 6.7 Hz, 1H, H-5a), 4.68 (dd, J_{gem}: 9.1 Hz, $J_{5b,4}$: 9.1 Hz, 1H, H-5b), 5.72 (dd, $J_{4,5b}$: 9.15 Hz, $J_{4,5a}$: 6.7 Hz, 1H, H-4); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 17.5 (CH_2), 22.6 (CH_3), 26.6(CH_2), 28.5 (CH_3, 2xC), 45.2 (C, C-1'), 54.5 (CH, C-2'), 71.1 (CH_2, C-5), 71.2 (C, C-1"), 84.1 (CH, C-4), 191.9 (C=S); IR (KBr) ν 3490 and 3465 (OH), 2987, 1368, 1317, 1285, 1239, 1173, 1153, 941 cm^{-1}; Ms m/z (%) 231 (M^++1, 49), 155 (6), 139 (31), 111 (10), 95 (37), 81 (35), 69 (49), 59 (100). Anal. Calc. for ($C_{11}H_{18}O_3S$): C, 57.38; H, 7.88; S, 13.92. Found: C, 57.30; H, 7.88; S, 13.97.

(1*R*,2*R*)-2-1'-Hydroxy-1'-methylethyl-1-methyl-1-vinylcyclobutane 10

A suspension of **9** (172 mg, 0.75 mmol) in 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine (413 μL, 2.24 mmol) was stirred at 40 °C for 24 h under Ar atmosphere. After cooling, the contents were directly chromatographed on silica gel using a mixture 5:95 ether/pentane as eluent. The solvent was removed by distillation at atmospheric pressure to afford **10** (92 mg, 80% yield) as an oil; $[\alpha]_D^{15}$: -34.92° (*c* 1.26, $CDCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 0.98 (s, 3H, Me), 1.15 (s, 3H, Me), 1.22 (s, 3H, Me), 1.60-1.90 (m, 4H), 1.95-2.15 (m, 2H), 5.09 (dd, J_{trans}: 17.5 Hz, J_{gem}: 1.5 Hz, 1H, H-2"a), 5.11 (dd, J_{cis}: 11.3 Hz, J_{gem}: 1.5 Hz, 1H, H-2"b), 6.37 (dd, J_{trans}: 17.5 Hz, J_{cis}: 11.3 Hz, 1H, H-1"); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 17.3 (CH_2), 27.7 (CH_3), 28.0 (CH_3), 28.2 (CH_3), 30.4 (CH_2), 44.9 (C, C-1), 56.4 (CH, C-2), 72.1 (C-1"), 112.6 (CH_2, $H_2\underline{C}$=), 143.7 (CH, $H\underline{C}$=); IR ($CDCl_3$) ν 3570 (OH), 3080, 2973, 2935, 2859, 1630, 1550, 1462, 1371, 1321, 1234 cm^{-1}; Ms m/z ($C_{10}H_{18}0$) (%) 139 (M^+-15, 3), 121 (19), 111 (16), 93 8379, 85 (16), 81 (26), 71 (44), 68 (100), 67 (73), 59 (59).

(-)-(1*R*,5*S*,6*S*)-5-Hydroxy-2,2,6-trimethyl-3-oxabicyclo[4.2.0]octane, 11

To an ice-cooled solution of **8** (543 mg, 2.88 mmol) in dry pyridine (15 mL), *p*-toluenesulfonyl chloride (660 mg, 3.46 mmol) and a catalytic amount of DMAP were added. The mixture was refluxed for 4 h under Ar atmosphere. After addition of CH_2Cl_2 (40 mL), the organic layer was washed with 10% HCl (2x15 mL) and brine (10 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude chromatographed on silica gel using a mixture 1:3 of ethyl acetate/hexane as eluent to afford **11** (422 mg, 86% yield) as an oil; $[\alpha]_D^{20}$: -76.51° (*c* 1.32, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.03 (s, 3H, Me-2b), 1.12 (s, 3H, Me-cyclobutane), 1.18 (s, 3H, Me-2a), 1.53 (ddd, J_{gem}: 11.0 Hz, $J_{7a,8a}$: 8.6 Hz, $J_{7a,8b}$: 8.6 Hz, 1H, H-7a), 1.72 (m, 2H, H-8a, H-8b), 1.90 (dd, $J_{1,8a}$: 9.9 Hz, $J_{1,8b}$: 9.9 Hz, 1H, H-1), 2.13 (ddd, J_{gem}: 11.0 Hz, $J_{7b,8b}$: 8.6 Hz, $J_{7b,8a}$: 2.4 Hz, 1H, H-7b), 2.24 (s, broad, 1H, OH), 3.35 (broad, 1H, H-5), 3.6 (dd, J_{gem}: 12.2 Hz, $J_{4b,5}$: 3.6 Hz, 1H, H-4b), 3.73 (dd, J_{gem}: 12.2 Hz, $J_{4a,5}$: 1.8 Hz, 1H, H-4a); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.6 (CH_2), 25.9 (CH_3), 26.0 (CH_3), 27.1 (CH_2), 27.8 (CH_3), 40.0 (C, C-6), 47.6 (CH, C-1), 63.0 (CH_2, C-4), 70.5 (CH, C-5), 71.6 (C, C-2); IR (film) ν 3442, 3412 (OH), 2954, 2924, 2853, 1483, 1082 cm^{-1}; Ms m/z (%) 156 (M^+-15, 6), 155 (52), 140 (2), 127 (5), 119 (2), 111 (3), 97 (9), 95 (15), 85 (6), 84 (19), 79 (6), 71 (54), 70 (44), 69 (37), 67 (27), 59 (24), 43 (100). Anal. Calc. for ($C_{10}H_{18}O_2$): C, 70.53; H, 10.66. Found C, 70.69; H, 10.70.

(-)-(1*R*,5*S*,6*S*)-5-Tosyloxy-2,2,6-trimethyl-3-oxabicyclo[4.2.0]octane, 12

a) To an ice-cooled solution of **11** (15 mg, 0.09 mmol) and dry pyridine (20 μL, 0.25 mmol) in CH_2Cl_2 (2 mL) *p*-toluenesulfonyl chloride (48 mg, 0.25 mmol) was added. The mixture was stirred at room temperature for 60 h. After adding 4 mL of CH_2Cl_2, the organic layer was washed successively with 10% HCl (2x5 mL) and brine (5 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude chromatographed on silica gel using an ethyl acetate/hexane 1:4 mixture as eluent to afford **12** (26 mg, 91% yield) as an oil; $[\alpha]_D^{20}$:-30.85° (*c* 1.75, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.00 (s, 3H, Me), 1.10 (s, 3H, Me), 1.12 (s, 3H, Me), 1.56 (m, 1H), 1.65 (m, 1H), 1.87 (m, 2H), 2.02 (m, 1H), 2.40 (s, 3H, $C\underline{H}_3$-C_6H_4), 3.59 (dd, J_{gem}: 12.8 Hz, $J_{4a,5}$: 3.0 Hz, 1H, H-4a), 3.61 (dd, J_{gem}: 12.8 Hz, $J_{4b,5}$: 3.0 Hz, 1H, H-4b), 4.32 (dd, $J_{5,4a}$: 3.0 Hz, $J_{5,4b}$: 3.0 Hz, 1H, H-5), 7.34 (d, J: 8.0 Hz, 2H), 7.71 (d, J: 8.0 Hz, 2H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.2 (CH_2), 21.4 (CH_3), 25.6 (CH_3), 25.8 (CH_3), 27.4 (CH_2), 27.6 (CH_3), 38.8 (C, C-6), 47.7 (CH, C-1), 60.7 (CH_2, C-4), 71.3 (C, C-2), 80.5 (CH, C-5), 127.5 (=C-H, 2C), 129.6 (=C-H, 2C), 134.1 (=C, 1C), 144.4 (=C, 1C); IR (film) ν 2974, 2951, 1357, 1175, 1096, 912, 668 cm^{-1}; Ms m/z (%) ($C_{17}H_{24}O_4S$) 309 (M^+-15, 13), 281 (M^+-43, 1), 224 (7), 173 (2), 156 (9), 155 (100), 137 (25), 109 (36), 95 (70), 81 (20), 69 (42), 55 (24).

b) To an ice-cooled solution of **8** (112 mg, 0.59 mmol) in dry pyridine (2.5 mL), *p*-toluenesulfonyl chloride (152 mg, 0.80 mmol) and a catalytic amount of DMAP were added. The mixture was refluxed for 4 h under Ar atmosphere. The mixture was cooled to 0 °C and dry pyridine (1 mL) and *p*-toluenesulfonyl chloride (300 mg, 1.57 mmol) were added. The mixture was stirred at room temperature for 48 h. After addition of CH_2Cl_2 (10 mL), the organic layer was washed with 10% HCl (2x5 mL) and brine (5 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude chromatographed on silica gel using an ethyl acetate/hexane 1:4 mixture as eluent to afford **12** (171 mg, 89% yield).

(-)-(1*R*,5*S*,6*S*)-5-*O*-[(4-fluorophenoxy)thiocarbonyl]-2,2,6-trimethyl-3-oxabicyclo[4.2.0]octane, 13

To a solution of **11** (200 mg, 1.18 mmol), *N*-hydroxysuccinimide (13 mg, 0.11 mmol) and dry pyridine (238 μL, 3.52 mmol) in dry benzene (5.2 mL), 4-fluorophenyl chlorothionoformate (213 μL, 1.52 mmol) was added dropwise under Ar atmosphere. The resulting solution was heated at 60 °C for 4h. After cooling, the contents were directly chromatographed on silica gel (0→10% ether in hexane as eluent) to afford **13** (327 mg, 86% yield); bp:125 °C (oven)/ 0.07 Torr; $[\alpha]_D^{15}$: -58.49° (*c* 1.26, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.05 (s, 3H, Me), 1.18 (s, 3H, Me), 1.26 (s, 3H, Me), 1.50-1.70 (m, 2H), 1.80-1.95 (m, 3H), 3.80 (dd, J_{gem}: 13.9 Hz, $J_{4a,5}$: 2.2 Hz, 1H, H-4a), 3.95 (dd, J_{gem}: 13.9 Hz, $J_{4b,5}$: 2.2 Hz, 1H, H-4b), 5.16 (dd, $J_{5,4a}$: 2.2 Hz, $J_{5,4b}$: 2.2 Hz, 1H, H-5) 7.02-7-09 (m, 4H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 19.7 (CH_2), 24.9 (CH_3), 25.8 (CH_3), 28.0 (CH_3), 28.4 (CH_2), 39.3 (C, C-6), 47.4 (CH, C-1), 59.7 (CH_2, C-4), 71.3 (C, C-2), 83.05 (CH, C-5), 116.1 (d, $J_{C\text{-}Forto}$: 24.1 Hz, 2C, C-3'), 123.4 (d, $J_{C\text{-}Fmeta}$: 8.3 Hz, 2C, C-2'), 149.1 (d, $J_{C\text{-}Fpara}$: 2.7 Hz, 1C, C-1'), 160.5 (d, $J_{C\text{-}Fipso}$: 245.1 Hz, 1C, C-4'), 194.9 (C=S); IR (film) ν 3118, 3080, 2973, 2946, 1503, 1366, 1298, 1280, 1244, 1209,1189, 1094, 1057 cm^{-1}; Ms (CI/NH_3) m/z (%) 342 (M^++18,44), 325 (M^++1, 4), 170 (84), 154 (9), 153 (81), 123 (35), 95 (100); Ms m/z (%) 155(1), 154 (1),137 (2), 123 (47), 112 (19), 95 (100), 69 853), 43 (32). Anal. Calc. for ($C_{17}H_{21}O_3SF$): C, 62.94; H, 6.53; S, 9.86. Found: C, 62.77; H, 6.56; S, 9.72.

(-)-(1*R*,5*S*,6*S*)-5-*O*-thiocarbonylimidazolyl-2,2,6-trimethyl-3-oxabicyclo[4.2.0]octane, 14

A mixture of **11** (422 mg, 2.48 mmol) and *N,N'*-thiocarbonyldiimidazole (982 mg, 4.96 mmol) in dry THF (25 mL) was heated at 65-70 °C for 6 h under Ar atmosphere. After cooling, the solvent was evaporated and the residue was chromatographed on silica gel eluting with an ethyl acetate/hexane 1:1 mixture to afford **14** (611 mg, 88% yield) as a pale yellow solid; mp: 85-86 °C (ethyl acetate-pentane); $[\alpha]_D^{19}$: -113.11° (*c* 1.22, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.07 (s, 3H, Me), 1.20 (s, 3H, Me), 1.30 (s, 3H, Me), 1.68 (m, 2H), 1.89 (m, 3H), 3.83 (dd, J_{gem}: 13.9 Hz, $J_{4a,5}$: 2.2 Hz, 1H, H-4a), 3.93 (dd, J_{gem}: 13.9 Hz, $J_{4b,5}$: 2.2 Hz, 1H, H-4b), 5.37 (dd, $J_{5,4a}$: 2.2 Hz, $J_{5,4b}$: 2.2 Hz, 1H, H-5), 7.0 (s, 1H, H-4'), 7.65 (s, 1H, H-5'), 8.40 (s, 1H, H-2'); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 20.0 (CH_2), 24.7 (CH_3), 25.8 (CH_3), 27.9 (CH_3), 28.4 (CH_2), 39.5 (C, C-6), 47.1 (CH, C-1), 59.6 (CH_2, C-4), 71.2 (C, C-2), 81.9 (CH, C-5), 117.9 (C-4'), 130.8 (C-5'), 136.9 (C-2'), 184.0 (C=S); IR (KBr) ν 2970, 1466, 1382, 1335, 1291, 1235, 1101, 1038, 977 cm^{-1}; Ms (CI/NH_3) m/z (%) 298 (M^++18, 1), 281 (M^++1, 100); Ms m/z (%) 153 (M^+-127, 1), 152 (8), 123 (19), 109 (41), 95 (52), 94 (83), 79 (100), 43 (33). Anal. Calc. for ($C_{14}H_{20}N_2O_2S$): C, 59.97; H, 7.20; N, 10.00; S, 11.41. Found: C, 59.95; H, 7.27; N, 10.01; S, 11.38.

(-)-(1*R*,6*R*)-2,2,6-Trimethyl-3-oxabicyclo[4.2.0]octane, 15

To a heated (100 °C) solution of tributyltin hydride (570 μL, 2.12 mmol) in dry toluene (2 mL), a solution of **14** (151 mg, 0.53 mmol) and azobisisobutyronitrile AIBN (10 mg, 0.06 mmol) in dry toluene (4 mL) was added dropwise under Ar atmosphere. The reaction mixture was heated for 1 h. After cooling, the contents were directly chromatographed on silica gel (0→5% ether in pentane as eluent) to afford **15** (66 mg, 80% yield). The solvent was removed by distillation at atmospheric pressure and the residue was purified by bulb to bulb distillation; bp: 95 °C (oven)/45 Torr; $[\alpha]_D^{18}$: -20.10° (*c* 1.31, $CDCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 0.97 (s, 3H, Me), 1.09 (s, 3H, Me), 1.12 (s, 3H, Me), 1.20-1.40 (m, 1H), 1.40-1.75 (m, 4H), 1.79-1.96 (m, 2H), 3.53 (ddd, J_{gem}: 12.2 Hz, $J_{5,4}$: 12.2 Hz, $J_{5,4}$: 2.4 Hz, 1H, H-5), 3.59 (ddd, J_{gem}: 12.2 Hz, $J_{5,4}$: 6.1 Hz, $J_{5,4}$: 1.8 Hz, 1H, H-5); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 18.2 (CH_2), 24.7 (CH_3), 26.2 (CH_3), 27.9 (CH_3), 32.7 (CH_2), 33.9 (CH_2), 35.4 (C, C-6), 47.7 (CH, C-1), 57.7 (CH_2, C-4), 70.7 (C, C-2); IR ($CDCl_3$) ν 2974, 2951, 2867, 1483, 1377, 1366, 1215, 1179, 1088, 1069 cm^{-1}; Ms m/z (%) 154 (M^+, 1), 139 (M^+-15, 93), 111 (48), 95 (10), 81 (82), 71 (24), 69 (100), 55 (22), 43 (48), 41 (50).

(-)-(*R*)-5-Ethyl-4,6,6-trimethyl-5,6-dihydro-2*H*-pyrane 16

To a refluxed (135 °C) solution of **14** (80 mg, 0.29 mmol) and AIBN (10 mg, 0.06 mmol) in dry toluene (6.6 mL), a solution of tributyltin hydride (156 μL, 0.58 mmol) in dry toluene (1.1 mL) was added dropwise under Ar atmosphere. The reaction mixture was heated for 2 h. After cooling, the contents were directly chromatographed on silica gel (0→5% ether in pentane as eluent). The solvent was removed by distillation at atmospheric pressure to afford **16** (30 mg, 68% yield); $[\alpha]_D^{18}$: -128.4° (*c* 1.76, $CDCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 0.85 (t, $J_{2',1'}$: 7.6 Hz, 3H, Me-2'), 1.15 (s, 3H, Me), 1.19 (s, 3H, Me), 1.48-1.60 (m, 3H, H-5, 2H-1'), 1.68 (s, 3H, Me-4), 4.05 (m, 2H, H-2), 5.38 (s, broad, 1H, H-3); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 11.5 (CH_3), 21.7 (CH_2, C-2'), 22.5 (CH_3), 25,1 (CH_3), 25.9 (CH_3), 47.3 (CH, C-5), 61.5 (CH_2, C-2), 72.3 (C, C-6), 119.5

(CH, C-3), 133.6 (C, C-4); IR ($CDCl_3$) ν 2956, 2933, 2875, 1453, 1382, 1355, 1144, 1105 cm^{-1}; Ms m/z (%) 154 (M^+, 2), 139 (M^+-15, 4), 125 (M^+-CH_3-CH_2, 1), 121 (2), 111 (4), 97 (6), 96 (47), 81 (100), 79 (11), 69 (13), 55 (12), 43 (32).

(1*R*,2*S*)-1-2'-Hydroxyethyl-2-isopropenyl-1-methylcyclobutane, (+)-grandisol

n-BuLi (1.6M in hexane, 7.3 mL, 11.68 mmol) was added to a stirred solution of **15** (150 mg, 0.97 mmol) in freshly distilled diisopropylamine (1.73 mL, 12.66 mmol) at -78 °C under Ar atmosphere. The mixture was kept at -78 °C for 20 min., allowed to warm to room temperature, and then heated to 75-80 °C for 56 h. The reaction mixture was slowly poured into a two-phase system of saturated NH_4Cl solution (8 mL) and ether (8 mL) and the aqueous phase was extracted with ether (4x8 mL). The combined organic phases were washed successively with 1% HCl (2x5 mL) and brine (5 mL), dried over $MgSO_4$ and concentrated under atmospheric pressure. The residue was chromatographed on silica gel eluting with 10:90 ether/pentane. The first fraction gave 39 mg (26%) of the starting compound **15**. The second fraction gave (+)-grandisol (95 mg, 62% yield). The solvent was removed by distillation at atmospheric pressure and the compound was purified by bulb to bulb distillation; bp: 100-120 °C (oven)/10 Torr; $[\alpha]_D^{26}$: +18.3° (*c* 2.61, *n*-hexane); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.15 (s, 3H, CH_3-C-1), 1.42 (dddd, J_{gem}: 13.4 Hz, $J_{1',2'}$: 9.2 Hz, $J_{1',2'}$: 6.2 Hz, $J_{1',4a}$: 1.4 Hz, 1H, H-1'), 1.58 (dddd, J_{gem}: 11.2 Hz, $J_{4a,3b}$: 10.1 Hz, $J_{4a,3a}$: 8.5 Hz, $J_{4a,1'}$: 1.4 Hz, 1H, H-4a), 1.64 (s, broad, $C\underline{H}_3C{=}CH_2$), 1.65 (dddd, J_{gem}: 13.4 Hz, $J_{4b,3b}$: 9.0 Hz, $J_{4b,3a}$: 2.6 Hz, $J_{4b,2}$: 0.8 Hz, 1H, H-4b), 1.73 (ddd, J_{gem}: 13.4 Hz, $J_{1',2'}$: 9.1 Hz, $J_{1',2'}$: 5.8 Hz, 1H, H-1'), 1.78 (dddd, J_{gem}: 11.3 Hz, $J_{3a,4a}$: 8.5 Hz, $J_{3a,2}$: 8.3 Hz, $J_{3a,4b}$: 2.6 Hz, 1H, H-3a), 1.95 (dddd, J_{gem}: 11.3 Hz, $J_{3b,2}$: 10.4 Hz, $J_{3b,4a}$: 10.1 Hz, $J_{3b,4b}$: 9.0 Hz, 1H, H-3b), 2.51 (dd, $J_{2,3b}$: 10.4 Hz, $J_{2,3a}$: 8.3 Hz, 1H, H-2), 3.62 (ddd, J_{gem}: 10.4 Hz, $J_{2',1'}$: 9.2 Hz, $J_{2',1'}$: 5.8 Hz, 1H, H-2'), 3.67 (ddd, J_{gem}: 10.4 Hz, $J_{2',1'}$: 9.2 Hz, $J_{2',1'}$: 6.2 Hz, 1H, H-2'), 4.63 (dq, J_{gem}: 1.9 Hz, $J_{2''a,Me}$: 0.9 Hz, 1H, H-2"a), 4.82 (m, 1H, H-2"b); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 19.1 (CH_2, C-3), 23.1 (CH_3, $\underline{C}H_3$-$C{=}CH_2$), 28.3 (CH_3, $\underline{C}H_3$-C), 29.2 (CH_2, C-4), 36.8 (CH_2, C-1'), 41.2 (C, C-1), 52.4 (CH, C-2), 59.8 (CH_2, C-2'), 109.6 (CH_2, $\underline{C}H_2{=}C$), 145.1 (C, $CH_2{=}\underline{C}$-); ^{13}C signals assigned unambiguously through ^{1}H-^{13}C correlation; IR (film) ν 3340 (OH), 3080, 2951, 2859, 1646 ($\nu_{C=C}$), 1454, 1376, 1239, 1052, 1013 cm^{-1}; Ms m/z (%) 139 (M^+-15, 1), 121 (5), 109 (26), 93 (12), 81 (10), 68 (100), 67 (77), 53 (31), 41 (46).

(-)-(1*R*,2*S*,1'*S*)-1-1',2'-Dihydroxyethyl-2-1"-hydroxy-1"-methylethyl-1-methylcyclobutane, 17

MeLi (1.6M in ether, 8.5 mL, 13.60 mmol) was added to a stirred solution of **7** (550 mg, 2.30 mmol) in 51 mL of dry THF at -78 °C under Ar atmosphere, and the whole mixture was stirred at -78 °C for 1h. The reaction was quenched with saturated NH_4Cl (35 mL) and the resultant mixture was extracted with CH_2Cl_2 (3x25 mL) and EtOAc (3x25 mL). The organic layers were combined, washed with brine and dried over $MgSO_4$. Evaporation of the solvent at reduced pressure and crystallization from pentane-ethyl acetate afforded colorless crystals (413 mg, 96% yield) of **17**; mp: 104-106 °C (ethyl acetate-pentane); $[\alpha]_D^{18}$: -21.8° (*c* 1.28, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.02 (s, 3H, Me), 1.07 (s, 3H, Me), 1.28 (s, 3H, Me), 1.48 (m, 1H), 1.64-1.78 (m, 1H), 1.90-2.15 (m, 3H), 2.90 (s, broad, 1H, OH), 3.42 (dd, J_{gem}: 10.9 Hz, $J_{2'b,1'}$: 9.5 Hz, 1H, H-2'b), 3.58 (m, broad, 2H, H-2'a, H-OH), 4.00 (dd, $J_{1',2'a}$: 9.5 Hz, $J_{1',2'b}$: 2.9 Hz, 1H, H-1'), 5.60 (s, broad, 1H, OH); ^{1}H-NMR (250 MHz, benzene-d_6) δ 0.9 (s, 6H, 2xMe), 1.05 (s, 3H, Me), 1.40 (m, 1H), 1.60-1.82 (m, 2H), 2.12-2.38 (m, 2H), 2.85 (s, broad, 1H, OH), 3.55 (dd, J_{gem}: 10.9 Hz, $J_{2'b,1'}$: 10.2 Hz, 1H, H-2'b), 3.65 (dd, J_{gem}: 10.9 Hz, $J_{2'a,1'}$: 3.6 Hz, 1H, H-2'a), 4.07 (dd, $J_{1',2'b}$: 10.2 Hz, $J_{1',2'a}$: 3.6 Hz, 1H, H-1'); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 18.7 (CH_2), 25.5 (CH_2), 27.4 (CH_3), 28.7 (CH_3), 29.0 (CH_3), 45.4 (C, C-1), 57.7 (CH, C-2), 62.1 (CH_2, C-2'), 71.5 (C, C-1"), 73.6 (CH, C-1'); IR (KBr) ν 3369-3289 (OH), 2972, 2948, 2890, 2854, 1478, 1380, 1200, 1085, 1056 cm^{-1}; Ms m/z (%) 173 (M^+-15, 1), 157 (3), 155 (6), 139 (28), 110 (32), 99 (13), 95 (77), 82 (18), 81 (51), 69 (100), 59 (36). Anal. Calc. for ($C_{10}H_{20}O_3$): C, 63.80; H, 10.71. Found: C, 63.72; H, 10.77.

(-)-(4*S*,1'*R*,2'*S*)-4-2'-1"-Hydroxy-1"-methylethyl-1'-methylcyclobutyl-1,3-dioxolan-2-thione, 18

To a stirred solution of **17** (250 mg, 1.33 mmol) in dry THF (13 mL) under Ar, *N,N'*-thiocarbonyldiimidazole (343 mg, 1.73 mmol) was added and the mixture was heated at 55-60 °C for 5 h. Evaporation of the solvent gave a crude, which was chromatographed on silica gel using a mixture 1:2 of ethyl acetate/hexane as eluent to afford **18** (257 mg, 84% yield) as a white solid; mp: 107-109 °C (ethyl acetate-pentane); $[\alpha]_D^{18}$: -56.3° (*c* 1.54,

$CHCl_3$); ^1H-NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 3H, Me), 1.16 (s, 3H, Me), 1.18 (s, 3H, Me), 1.68 (m, 1H), 1.81 (m, 1H), 1.98 (m, 1H), 2.09 (m, 2H), 4.51 (dd, J_{gem}: 9.5 Hz, $J_{5a,4}$: 7.3 Hz, 1H, H-5a), 4.74 (dd, J_{gem}: 9.5 Hz, $J_{5b,4}$: 8.1 Hz, 1H, H-5b), 5.62 (dd, $J_{4,5b}$: 8.1 Hz, $J_{4,5a}$: 7.3 Hz, 1H, H-4); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 18.0 (CH_2), 21.5 (CH_3), 28.82 (CH_2), 28.86 (CH_3), 29.6 (CH_3), 45.2 (C, C-1'), 54.8 (CH, C-2'), 71.1 (C, C-1"), 71.6 (CH_2, C-5), 86.3 (CH, C-4), 192.5 (C=S); IR (KBr) ν 3447 and 3412 (OH), 2970, 1378, 1362, 1275, 1208, 1183 cm^{-1}; Ms m/z (%) 231 (M^++1,1), 230 (M^+, 5), 169 (1), 155 (10), 140 (9), 139 (91), 121 (13), 111(23), 97 (12), 95 (49), 81 (38), 69 (100), 67 (30), 60 (64), 43 (90). Anal. Calc. for ($C_{11}H_{18}O_3S$): C, 57.38; H, 7.88; S, 13.92. Found: C, 57.35; H, 7.89; S, 13.88.

(+)-(1*S*,2*S*)-2-1'-Hydroxy-1'-methylethyl-1-methyl-1-vinylcyclobutane, 19

A suspension of **18** (167 mg, 0.72 mmol) in 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine (416 μL, 2.26 mmol) was stirred at 40 °C for 24 h under Ar. After cooling, the contents were directly chromatographed on silica gel using a mixture 5:95 ether/pentane as eluent. The solvent was removed by distillation at atmospheric pressure to afford **19** (86 mg, 77% yield) as an oil; $[\alpha]_D^{15}$: +35.24° (*c* 1.30, $CDCl_3$). The ^1H-NMR, ^{13}C-NMR, IR and Ms spectra were identical with those of **10**.

(+)-(1*S*,5*S*,6*R*)-5-Hydroxy-2,2,6-trimethyl-3-oxabicyclo [4.2.0]octane 20

To an ice-cooled solution of **17** (220 mg, 1.17 mmol) in dry pyridine (6 mL), *p*-toluenesulfonyl chloride (268 mg, 1.40 mmol) and a catalytic amount of DMAP were added. The mixture was refluxed for 4 h under Ar atmosphere. After addition of CH_2Cl_2 (20 mL), the organic layer was washed with 10% HCl (2x10 mL) and brine (10 mL), and dried over $MgSO_4$. The solvent was removed under reduced pressure and the crude chromatographed on silica gel using a mixture 1:3 ethyl acetate/hexane as eluent to afford **20** (162 mg, 82% yield) as a white solid; mp: 68-70 °C (ethyl acetate-pentane); $[\alpha]_D^{18}$: + 4.56° (*c* 1.09, $CHCl_3$); ^1H-NMR (250 MHz, $CDCl_3$) δ 0.98 (s, 3H, Me), 1.11 (s, 3H, Me), 1.16 (s, 3H, Me), 1.42 (d, J: 5.1 Hz, 1H, OH), 1.52-1.74 (m, 3H), 1.82-2.00 (m, 2H), 3.30 (dd, J_{gem}: 11.0 Hz, $J_{4b,5}$: 11.0 Hz, 1H, H-4b), 3.45 (dd, J_{gem}: 11.0 Hz, $J_{4a,5}$: 4.4 Hz, 1H, H-4a), 4.10 (m, $J_{5,4b}$: 11.0 Hz, $J_{5,OH}$: 5.1 Hz, $J_{5,4a}$: 4.4 Hz, 1H, H-5); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 19.1 (CH_2), 20.8 (CH_3), 25.1 (CH_3), 25.6 (CH_3), 30.7 (CH_2), 41.4 (C, C-7), 50.8 (CH, C-1), 61.4 (CH_2, C-4), 71.6 (CH, C-5), 71.8 (C, C-2); IR (film) ν 3415 (OH), 2974, 2936, 2908, 2873, 1082,1050 cm^{-1}; Ms m/z (%) 170 (M^+, 1), 155 (M^+-15, 100), 127 (13), 97 (25), 95 826), 83 (12), 71 (54), 69 (32), 59 (27). Anal. Calc. for ($C_{10}H_{18}O_2$): C, 70.55; H, 10.66. Found: C, 70.58; H, 10.70.

(+)-(1*S*,5*S*,6*R*)-5-*O*-[4-(fluorophenoxy)thiocarbonyl]-2,2,6-trimethyl-3-oxabicyclo[4.2.0]octane, 21

To a solution of **20** (76 mg, 0.45 mmol), *N*-hydroxysuccinimide (5 mg, 0.11 mmol) and dry pyridine (113 μL, 1.41 mmol) in dry benzene (2.0 mL), 4-fluorophenyl chlorothionoformate (131 μL, 0.94 mmol) was added dropwise under Ar atmosphere. The resulting solution was heated at 55 °C for 2 h. After cooling, the contents were directly chromatographed on silica gel (0→10% ether in hexane as eluent) to afford **21** (130 mg, 90% yield as a solid; mp: 97-99 °C (ether-pentane); $[\alpha]_D^{15}$: +32.0° (c 1.0, $CHCl_3$); ^1H-NMR (250 MHz, $CDCl_3$) δ 1.03 (s, 3H, Me), 1.22 (s, 6H, 2xMe), 1.57-1.82 (m,2H), 1.90 (m, 1H), 1.92-2.15 (m, 2H), 3.50 (dd, J_{gem}: 11.1 Hz, $J_{4b,5}$: 10.8 Hz, 1H, H-4b), 3.78 (dd, J_{gem}: 11.1 Hz, $J_{4a,5}$: 5.1 Hz, 1H, H-4a), 5.70 (dd, $J_{5,4b}$: 10.8 Hz, $J_{5,4a}$: 5.1 Hz, 1H, H-5), 7.03-7.09 (m, 4H); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 19.1 (CH_2), 20.04 (CH_3), 24.8 (CH_3), 25.4 (CH_3), 30.9 (CH_2), 41.1 (C, C-6), 51.5 (CH, C-1), 57.1 (CH_2, C-4), 71.8 (C, C-2), 83.6 (CH, C-5), 116.1 (d, $J_{C\text{-}Forto}$: 23.2 Hz, 2C, C-3'), 123.3 (d, $J_{C\text{-}Fmeta}$: 8.7 Hz, 2C, C-2'), 149.1 (d, $J_{C\text{-}Fpara}$: 2.8 Hz, 1C, C-1'), 160.5 (d, $J_{C\text{-}Fipso}$: 243.9 Hz, 1C, C-4'), 195.1 (C=S); IR (film) ν 3071, 2977, 1504, 1353, 1327, 1287, 1241,1192,1133,1076, 1039 cm^{-1}; Ms (CI/NH_3) m/z (%) 342 (M^++18,16), 325 (M^++1,0.3), 281 (2), 154 (11), 153 (95), 112 (29), 95 (100); Ms m/z (%) 243 (1), 155(1), 153 (4),137 (2), 95 (100), 83 (21), 79 (55), 69 (38), 43 (31). Anal. Calc. for ($C_{17}H_{21}O_3SF$): C, 62.94; H, 6.52; S, 9.88. Found: C, 62.59; H, 6.26; S, 9.40.

(-)-(1*S*,5*S*,6*R*)-5-*O*-thiocarbonylimidazolyl-2,2,6-trimethyl-3-oxabicyclo[4.2.0]octane, 22

A mixture of **20** (80 mg, 0.47 mmol) and *N*,*N*'-thiocarbonyldiimidazole (196 mg, 1.22 mmol) in dry THF (4 mL) was heated at 65-70 °C for 6 h under Ar atmosphere. After cooling, the solvent was evaporated and the residue was chromatographed on silica gel eluting with an ethyl acetate/hexane 1:1 mixture to afford **22** (108 mg, 82% yield) as an oil; $[\alpha]_D^{17}$: -15.68° (*c* 1.28, $CHCl_3$); ^1H-NMR (250 MHz, CDCl3) δ 1.05 (s, 3H, Me), 1.24 (s, 3H, Me), 1.28 (s, 3H, Me), 1.60-1.91 (m, 3H), 2.10 (m, 2H), 3.50 (dd, J_{gem}: 11.0 Hz, $J_{4b,5}$: 10.2 Hz, 1H, H-4b), 3.78 (dd, J_{gem}: 11.0 Hz, $J_{4a,5}$: 5.1 Hz, 1H, H-4a), 5.96 (dd, $J_{5,4b}$: 10.2 Hz, $J_{5,4a}$: 5.1 Hz, 1H, H-5), 7.00 (s, 1H, H-4'), 7.56 (s, 1H, H-5'), 8.30 (s, 1H, H-2'); ^{13}C-NMR (62.5 MHz, CDCl3) δ 19.2 (CH_2), 22.3 (CH_3), 24.8 (CH_3), 25.4 (CH_3), 30.8 (CH_2), 41.2 (C, C-6), 51.6 (CH, C-1), 56.9 (CH_2, C-4), 71.9 (C, C-2), 82.6 (CH, C-5), 117.8 (CH, C-4'), 130.8 (CH, C-5'), 136.7 (CH, C-2'), 183.9 (C=S); IR (KBr) ν 2971, 1465, 1387, 1355, 1334, 1314, 1265, 1231, 1183, 1098, 995 cm^{-1}; Ms (CI/NH3) m/z (%) 298 (M^++18, 2), 281 (M^++1, 100), 154 (5), 153 (43), 112 (29), 95 (84); Ms m/z (%) 199 (2), 154 (1), 153 (M^+-127, 3), 152 (12), 124 (17), 109 (47), 95 (100), 79 (86), 60 (30). Anal. Calc. for: ($C_{14}H_{20}N_2O_2S$): C, 59.97; H, 7.20; N, 10.00; S, 11.41. Found: C, 59.97; H, 7.09; N, 10.00; S, 11.12.

(+)-(1*S*,6*S*)-2,2,6-Trimethyl-3-oxabicyclo[4.2.0]octane 23

To a heated (80 °C) solution of tributyltin hydride (355 μL, 1.32 mmol) in dry toluene (528 μL) a solution of **22** (95 mg, 0.33 mmol) and azobisisobutyronitrile AIBN (10 mg, 0.06 mmol) in dry toluene (3.7 mL) was added dropwise under Ar atmosphere. The reaction mixture was heated for 2 h. After cooling, the contents were directly chromatographed on silica gel (0→5% ether in pentane as eluent) to afford **23** (39 mg, 75% yield). The solvent was removed by distillation at atmospheric pressure. **23**; bp: 95 °C (oven)/ 45 Torr; $[\alpha]_D^{18}$: +19.41° (*c* 0.42, $CDCl_3$). The ^1H-NMR, ^{13}C-NMR, IR and Ms spectra were identical with those of **15**.

(1*S*,2*R*)-1-2'-Hydroxyethyl-2-isopropenyl-1-methylcyclobutane, (-)-grandisol

n-BuLi (1.6M in hexane, 3.6 mL, 5.76 mmol) was added to a stirred solution of **23** (75 mg, 0.49 mmol) in freshly distilled diisopropylamine (850 μL, 6.06 mmol) at -78 °C under Ar atmosphere. The mixture was kept at -78 °C for 20 min. allowed to warm to room temperature and then heated to 75-80 °C for 48 h. The reaction mixture was carefully poured into a two-phase system of saturated NH_4Cl solution (5 mL) and ether (5 mL) and the aqueous phase was extracted with ether (4x8 mL). The combined organic phases were washed successively with 1% HCl (2x3 mL) and brine (5 mL), dried over $MgSO_4$ and concentrated under atmospheric pressure. The residue was chromatographed on silica gel eluting with 10:90 ether/pentane to afford (-)-grandisol (53 mg, 71% yield). The solvent was removed by distillation at atmospheric pressure and the compound purified by bulb to bulb distillation; bp: 100-120 °C (oven)/10 Torr; $[\alpha]_D^{26}$: -17.6° (*c* 1.1, *n*-hexane). The ^1H-NMR, ^{13}C-NMR, IR and Ms spectra were identical with those of (+)-grandisol.

(+)-(1*S*,2*S*,4*S*,5*R*)-2,5-Dimethyl-4-pivaloyloxymethyl-3-oxabicyclo[3.2.0]heptan-2-ol, 24

MeLi (1.6 M in ether, 800 μL, 1.28 mmol) was added dropwise to a stirred solution of **7** (246 mg, 1.02 mmol) in 20 mL of dry THF at -78 °C under Ar atmosphere, and the whole mixture was stirred at -78 °C for 2 h. The solution was allowed to warm up at room temperature and added dropwise to a cold (0 °C), and vigorously stirred saturated NH_4Cl solution (10 mL). The resulting mixture was extracted with CH_2Cl_2 (3x15 mL) and EtOAc (3x15 mL). The organic layers were combined, washed with brine and dried over $MgSO_4$. After evaporation of the solvents, the residue was chromatographed on silica gel using an ethyl acetate/hexane 1:4 mixture as eluent to afford **24** (236 mg, 90% yield) as a colorless needles; mp.: 64-66 °C (ethyl acetate-pentane); $[\alpha]_D^{15}$: + 39.41° (*c* 1.37, $CHCl_3$); ^1H-NMR (400 MHz, $CDCl_3$) δ 1.18 (s, 9H, $(CH_3)_3C$), 1.30 (s, 3H, $C\underline{H}_3$-C-5), 1.42 (s, 3H, $C\underline{H}_3$-C-2), 1.60 (m, 2H, H-7a, H-6b), 1.95 (m, 2H, H-7b, H-6a), 2.22 (s, broad., 1H, OH), 2.37 (ddd, $J_{1,7a}$: 6.5 Hz, $J_{1,7b}$: 4.3 Hz, $J_{1,6b}$: 3.3 Hz, 1H, H-1), 3.94 (dd, $J_{4,8a}$: 6.7 Hz, $J_{4,8b}$: 5.5 Hz, 1H, H-4), 4.12 (dd, J_{gem}: 11.6 Hz, $J_{8b,4}$: 5.5 Hz, 1H, H-8b), 4.15 (dd, J_{gem}:11.6 Hz, $J_{8a,4}$: 6.7 Hz, 1H, H-8a); ^1H-NMR (400 MHz, benzene-d_6) δ 1.38 (s, 12H, 4xMe), 1.46 (s, 3H, Me), 1.57 (ddd, J_{gem}: 11.6 Hz, $J_{6b,7b}$: 10.4 Hz, $J_{6b,7a}$: 7.3 Hz, 1H, H-6b), 1.62 (dddd, J_{gem}: 11.6 Hz, $J_{7a,6a}$: 9.7 Hz, $J_{7a,6b}$: 7.3 Hz, $J_{7a,1}$: 5.5 Hz, 1H, H-7a), 1.89 (dddd, J_{gem}: 11.6 Hz, $J_{7b,6b}$: 10.4 Hz, $J_{7b,1}$: 9.1 Hz, $J_{7b,6a}$: 6.1 Hz, 1H, H-7b), 2.02 (ddd, J_{gem}: 11.6 Hz, $J_{6a,7a}$: 9.77 Hz, $J_{6a,7b}$: 6.1 Hz, 1H, H-6a), 2.14 (s, b.a., 1H, OH), 2.50 (dd, $J_{1,7b}$: 9.1 Hz, $J_{1,7a}$: 5.5 Hz, 1H, H-1), 4.33 (dd, $J_{4,8a}$: 7.3 Hz, $J_{4,8b}$: 4.9 Hz, 1H, H-4), 4.44 (dd, J_{gem}: 11.6 Hz, $J_{8b,4}$: 4.9 Hz, 1H, H-8b), 4.59 (dd, J_{gem}: 11.6 Hz, $J_{8a,4}$: 7.3 Hz, 1H, H-8a); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 17.2 (CH_2), 23.1 (CH_3), 23.9 (CH_2), 24.1 (CH_3), 27.1 ($(CH_3)_3$), 38.6 (C, $((CH_3)_3$), 46.8 (C, C-5), 53.3 (CH, C-1), 63.7 (CH_2, C-8), 81.5 (CH, C-4), 105.9 (C, C-2), 178.0 (C=O); IR (KBr) ν 3476 (OH), 2977, 2955, 2934, 2884, 1714 ($\nu_{C=O}$), 1476, 1397, 1318, 1190, 1144, 1121, 1038 cm $^{-1}$, Ms m/z (%) 239 (M^+-OH, 2), 145 (12), 136 (30), 111(23), 108 (31), 97 (44), 79 (46), 57 (100), 43 (54); Ms (CI/NH_3) m/z (%) 274 (M^+-18, 1), 256 (M^+,2), 241 (M^+-15,2). Anal. Calc. for: C, 65.58; H, 9.44. Found: C, 65.69; H, 9.50.

(4*S*,1'*R*,2'*S*)-4-2'-Acetyl-1'-methylcyclobutyl-1,3-dioxolan-2-thione, 26

Sodium methoxide (62 mg, 1.15 mmol) was added to a solution of **24** (177 mg, 0.69 mmol) in 20 mL of dry methanol, and the mixture was heated to reflux for 3 h. After addition of water (15 mL) and concetration, the residue was extracted with CH_2Cl_2 (4x15 mL) and EtOAc (4x15 mL). The organic layers were combined and dried over $MgSO_4$. Concentration gave the crude diol **25** (119 mg, quant.) as an oil. A mixture of this diol and *N,N'*-thiocarbonyldiimidazole (272 mg, 1.78 mmol) in dry THF (5 mL) was heated at 60-65 °C for 5 h under Ar atmosphere. Evaporation of the solvent gave a crude, which was chromatographed on silica gel using a mixture 1:2 ethyl acetate/hexane as eluent to afford **26** (123mg, 83% yield) as an oil; ^1H-NMR (400 MHz, $CDCl_3$) δ 1.1 (s,3H, Me-1'), 1.82 (m, 1H), 2.02 (s, 3H, $C\underline{H}_3CO$), 2.03-2.30 (m, 3H), 3.07 (dd, $J_{2',3'a}$: 9.7 Hz, $J_{2',3'b}$: 9.1 Hz, 1H, H-2'), 4.38 (dd, J_{gem}: 9.7 Hz, $J_{5a,4}$: 6.7 Hz, 1H, H-5a), 4.75 (dd, J_{gem}: 9.7 Hz, $J_{5b,4}$: 8.5 Hz, 1H, H-5b), 5.39 (dd, $J_{4,5b}$: 8.5 Hz, $J_{4,5a}$: 6.7 Hz, 1H, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 20.4, 21.8, 27.6, 27.9, 44.2 (C-1'), 53.9 (C-2'), 70.9 (C-5), 85.0 (C-4), 191.8 (C=S), 209 (C=O); IR (film) ν 2959, 1703 ($\nu_{C=O}$), 1479, 1385, 1360, 1329, 1287, 1159 cm^{-1}; Ms m/z ($C_{10}H_{14}O_3S$) (%) 214 (M^+, 3), 213 (26), 112)12), 110 (25), 98 (19), 97 (73), 85 (23), 69 (19), 67 (20), 57 (100), 53 (14), 41 (78).

(1*S*,2*S*)-2-Acetyl-1-methyl-1-vinylcyclobutane 27a and (1*S*,2*R*)-2-Acetyl-1-methyl-1-vinylcyclobutane 27b

A suspension of **26** (37 mg, 0.17 mmol) in 1,3-dimethyl-2-phenyl-1,3,2-diazaphospholidine (100 µL, 0.54 mmol) was stirred at 40 °C for 24 h under Ar. After cooling, the contents were directly chromatographed on silica gel using a mixture 1:4 ether/pentane as eluent. The solvent was removed by distillation at atmospheric pressure to afford an epimeric mixture 83:17 (glc and ^1H-NMR) of **27a** and **27b** (15 mg, 62% yield). **27**; ^1H-NMR (250 MHz, $CDCl_3$) : 1.42 (s, 3H, Me), 1.85 (m, 2H), 1.92 (s, 3H), 2.32 (m, 2H), 3.05 (m, 1H, H-2), 5.02 (dd, $J_{2'b,1}$: 11.0 Hz, J_{gem}: 1.5 Hz, 1H, H-2'b), 5.04 (dd, $J_{2'a,1}$: 17.5 Hz, J_{gem}: 1.5 Hz, 1H, H-2'a), 5.95 (dd, $J_{1',2'a}$: 17.5 Hz, $J_{1',2'b}$: 11.0 Hz, 1H, H-1'); Ms m/z (%) ($C_9H_{14}O$): 138 (M^+,2), 123 (M^+-15, 23), 109 (17), 95 (M^+-CH_3CO, 69), 80 (14), 71 (11), 67 (100), 53 (30), 43 (65). **27b**: ^1H-NMR (250 MHz, $CDCl_3$) δ 1.11 (s, 3H, Me), 1.85 (m, 2H), 1.98 (s, 3H), 2.32 (m, 2H), 3.18 (m, 1H, H-2), 5.03 (dd, $J_{2'b,1}$: 11.0 Hz, J_{gem}: 1.5 Hz, 1H, H-2'b), 5.04 (dd, $J_{2'a,1}$: 17.5 Hz, J_{gem}: 1.5 Hz, 1H, H-2'a), 6.06 (dd, $J_{1',2'a}$: 17.5 Hz, $J_{1',2'b}$: 11.0 Hz, 1H, H-1'); Ms m/z (%) ($C_9H_{14}O$) 138 (M^+,1), 123 (M^+-15, 21), 109 (13), 95 (M^+-CH_3CO, 70), 80 (15), 71 (12), 68 (83), 67 (100), 55 (18), 53 (29), 43 (69).

(1*S*,2*R*,1'*S*)-2-acetyl-1-1'-hydroxy-2'-pivaloyloxyethyl-1-methylcyclobutane, 28

MeLi (1.6 M in ether, 437 µL, 0.70 mmol) was added dropwise to a stirred solution of **6** (120 mg, 0.50 mmol) in 11 mL of dry THF at -45 °C under Ar atmosphere. After 3 h at -45 °C the solution was allowed to warm up at room temperature and was stirred for 14 h. The reaction mixture was added dropwise to a cold (0 °C), and vigorously stirred saturated NH_4Cl solution (8 mL) and the resulting mixture was extracted with CH_2Cl_2 (3x20 mL). The organic layers were combined, washed with brine and dried over $MgSO_4$. After evaporation of the solvents, the residue was chromatographed on silica gel (mixtures of ethyl acetate/hexane as eluents) to obtain: 68 mg (56%) of the starting lactone **6**, **28** (16 mg, 13% yield) as an oil and **29** (7mg, 9%). (1*S*,2*R*,1'*S*)-2-acetyl-1-1'-hydroxy-2'-pivaloyloxyethyl-1-methylcyclobutane **28**; ^1H-NMR (400 MHz, $CDCl_3$) δ 1.00 (s, 3H, Me-cyclobutane), 1.20 (s, 9H, $(C\underline{H}_3)_3C$), 1.50 (m, 1H), 1.92 (m, 2H), 2.14 (s, 3H, $C\underline{H}_3$-CO), 2.34 (m, 1H), 3.00 (d, J: 2.5 Hz, 1H, OH), 3.09 (dd, $J_{2,3}$: 8.5 Hz, $J_{2,3}$: 8.4 Hz, 1H, H-2), 3.82 (ddd, $J_{1',2'b}$: 7.6 Hz, $J_{1',2'a}$: 3.7 Hz, J: 2.5 Hz, 1H, H-1'), 3.94 (dd, J_{gem}: 11.2 Hz, $J_{2'b,1'}$: 7.6 Hz, 1H, H-2'b), 4.05 (dd, J_{gem}: 11.2 Hz, $J_{2'a,1'}$: 3.7 Hz, 1H, H-2'a); ^{13}C-NMR (62.5 MHz, $CDCl_3$) δ 14.7 (CH_3), 17.8 (CH_2), 27.1 (CH_3, $(\underline{C}H_3)_3$), 27.7 (CH_2), 28.9 (CH_3), 38.78 (C, $\underline{C}$-$(CH_3)_3$), 45.8 (C, C-1), 53.3 (CH, C-2), 65.3 (CH_2, C-2'), 77.8 (CH, C-1'), 178.9 (C=O), 210.7 (C=O); IR (film) ν 3442 (OH), 2962, 2931, 2874, 1729 ($\nu_{C=O}$), 1703 ($\nu_{C=O}$), 1155 cm^{-1}; Ms m/z (%) ($C_{14}H_{24}O_4$) 239 (M^+-OH, 1), 173 (1), 141 (12), 136. (12), 111 (54), 97 (12), 85 (28), 71 (31), 57 (100), 43 (72).

(1*R*,4*S*,5*S*)-4-hydroxymethyl-5-methyl-3-oxabicyclo[3.2.0]heptan-2-one, 29

MeLi (1.6 M in ether, 880 µL, 1.40 mmol) was added dropwise to a stirred solution of **6** (152 mg, 0.63 mmol) in 11 mL of dry THF at -78 °C under Ar atmosphere, and the whole mixture was stirred at -78 °C for 2 h. The solution was allowed to warm up at room temperature and added dropwise to a cold (0 °C), and vigorously stirred saturated NH_4Cl solution (10 mL). The resultant mixture was extracted with CH_2Cl_2 (3x20 mL) and EtOAc (2x30 mL). The organic layers were combined, washed with brine and dried over $MgSO_4$. After evaporation of the solvents, the residue was chromatographed on silica gel using an ethyl acetate/hexane 1:1 mixture as eluent to obtain: 26 mg (17%) of the starting lactone **6**, **29** (52 mg, 52% yield) as colorless needles and **8** (10 mg, 8% yield). (1*R*,4*S*,5*S*)-4-hydroxymethyl-5-methyl-3-oxabicyclo[3.2.0]heptan-2-one **29**; mp: 44-46 °C (ether-pentane); $[\alpha]_D^{20}$: -28.07° (*c* 0.57, $CHCl_3$); ^{1}H-NMR (250 MHz, $CDCl_3$) δ 1.35 (s, 3H, Me), 1.81 (dddd, J_{gem}: 11.6 Hz, $J_{6',7'}$: 9.8 Hz, $J_{6',1}$: 3.6 Hz, $J_{6',7}$: 3.2 Hz, 1H, H-6'), 2.01 (dddd, J_{gem}: 11.7 Hz, $J_{7,6}$: 8.7 Hz, $J_{7,6'}$: 3.2 Hz, $J_{7,1}$: 2.9 Hz, 1H, H-7), 2.25 (ddd, J_{gem}: 11.6 Hz, $J_{6,7'}$: 9.5 Hz, $J_{6,7}$: 8.7 Hz, 1H, H-6), 2.48 (dddd, J_{gem}: 11.7 Hz, $J_{7',6'}$: 9.8 Hz, $J_{7',6}$: 9.5 Hz, $J_{7',1}$: 9.1 Hz, 1H, H-7'), 2.65 (ddd, $J_{1,7'}$: 9.2 Hz, $J_{1,6'}$: 3.6 Hz, $J_{1,7}$: 2.9 Hz, 1H, H-1), 3.60 (dd, J_{gem}: 12.4 Hz, $J_{8a,4}$: 2.9 Hz, 1H, H-8a), 3.80 (dd, J_{gem}: 12.4 Hz, $J_{8b,4}$: 2.9 Hz, 1H, H-8b), 4.19 (dd, $J_{4,8a}$: 2.9 Hz, $J_{4,8b}$: 2.9 Hz, 1H, H-4); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 17.7 (CH_3), 21.5 (CH_2), 32 (CH_3), 43.3 (C, C-5), 44.4 (CH, C-1), 61.6 (CH_2, C-8), 87.5 (CH, C-4), 181.2 (C-2); IR (film) ν 3451-3428 (OH), 2958, 2927, 1751 ($\nu_{C=O}$), 1166, 1085, 1026 cm^{-1}; Ms m/z (%) 156 (M^+,2), 139 (1), 126 (11), 125 (91), 98 (48), 97 (28), 81 (57), 69 (39), 66 (20), 54 (36), 41 (100). Anal. Calc. for ($C_8H_{12}O_3$): C, 61.52; H, 7.74. Found: C, 61.48; H, 7.67.

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