67. On the Absolute Configuration of Penlanfuran and Related Sesquiterpenoids of the Sponge *Dysidea fragilis* from the North-Brittany Sea

by **Ines Mancini**[a]), **Graziano Guella**[a]), **Marino Cavazza**[b]), and **Francesco Pietra**[a]) *

[a]) Istituto di Chimica, Università di Trento, I-38050 Povo-Trento

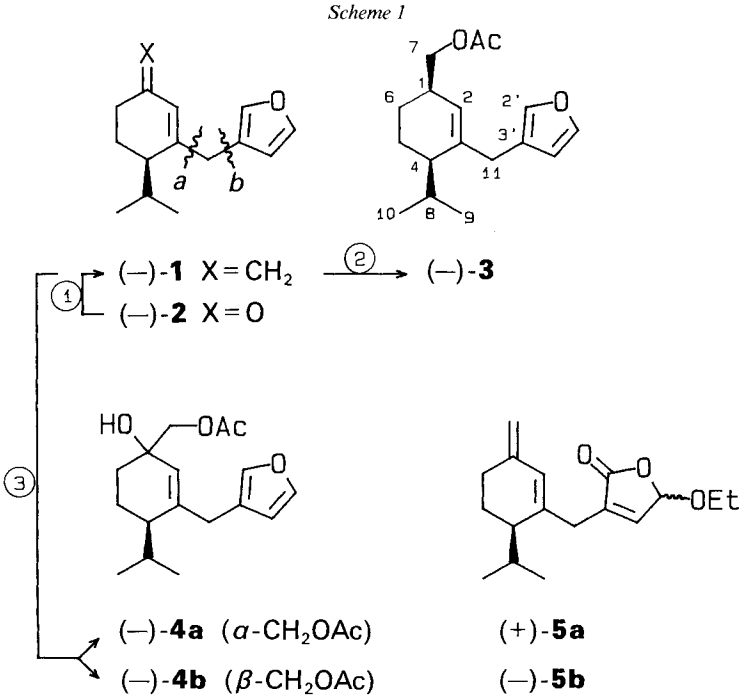
[b]) Dipartimento di Chimica e Chimica Industriale, Università di Pisa, I-56100 Pisa

(29.XII.89)

The 1,4-addition of vinylmagnesium bromide/CuBr·SMe_2 to (+)-(4*S*)-cryptone ((+)-**6**) in THF in the presence of Me_3SiCl gives the silyl enol ether **7** which partly undergoes hydrolysis to ketone **8** on aqueous workup; residual **7** is hydrolyzed with pyridinium *p*-toluenesulfonate (Py·TsOH) to give **8** which is protected *in situ* with ethylene glycol and then ozonolized to give aldehyde (−)-**10**. The latter, on addition of 3-lithiofuran followed by dehydration and deprotection with Py·TsOH, gives the unnatural (4*S*)-enantiomer (+)-**2** of noroxopenlanfuran. All processes, except **11** → (+)-**2**, are of good yield. On the basis of previous chemical transformations, this also establishes the (4*R*)-configuration for penlanfuran ((−)-**1**) and other sesquiterpenoids of the sponge *Dysidea fragilis* from the North-Brittany sea. Non viable routes to (±)-noroxopenlanfuran ((±)-**2**) are also discussed.

1. Introduction. – We have recently reported on penlanfuran ((−)-**1**) [1a], noroxopenlanfuran ((−)-**2**), acetoxydihydropenlanfuran ((−)-**3**), penlanbutenolide ((−)-**5a**), epipen-

Scheme 1



① $Ph_3P{=}CH_2$ ② a) $NaBH_4$, BF_3; b) H_2O_2/OH^-; c) Ac_2O/Py. ③ a) OsO_4/Py, $NaHSO_3$; b) Ac_2O/Py; c) HPLC separation.

lanbutenolide ((−)-**5b**), the two epimeric alcohols (−)-**4a** and (−)-**4b**, and other sesquiterpenoids isolated from the sponge *Dysidea fragilis* of Brittany waters [1b]. Some of these terpenoids have been configurationally correlated with each other by chemical transformations as indicated in *Scheme 1* [1b]; however, their absolute configuration remained undefined. Intrigued by the variability of the organic chemistry of sponges of the genus *Dysidea* [2], with such fine differences as opposite enantiomers in different collections of the same species [3], we deemed worth defining the absolute configuration of penlanfuran and related sesquiterpenoids. This has now been done *via* the synthesis of the unnatural (4*S*)-enantiomer (+)-**2** of noroxopenlanfuran which is reported here.

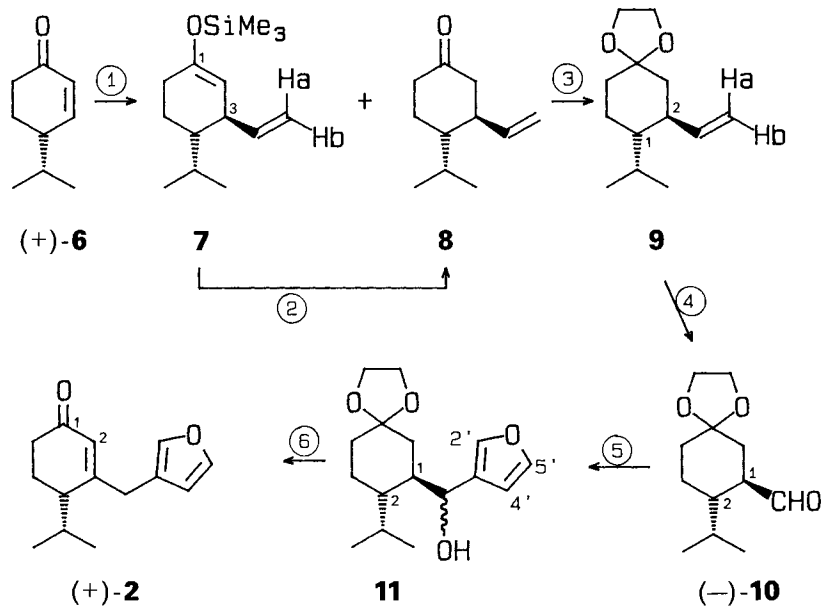
2. Results and Discussion. – Our plans of synthesis of (+)-noroxopenlanfuran ((+)-**2**) have considered bond disconnections *a* or *b* *(Scheme 1)* and starting from (+)-(4*S*)-cryptone ((+)-**6**) which was available from previous studies [4]. Preliminary studies were carried out with racemic cryptone.

Attempts directed to prepare (+)-**2** according to bond disconnection *a* *(Scheme 1)* were met with failure, however[1]). Next, instead of changing to a masked furan reagent with which to establish bond connection *a*, we examined a synthesis according to bond disconnection *b* *(Scheme 1)*. We envisaged to make connection *b* by adding 3-lithiofuran to aldehyde **10** *(Scheme 2)* followed by deprotection, dehydration, and double-bond shift to the conjugated position. Attempts directed at synthesizing aldehyde (±)-**10** from 5,5-(ethylenedioxy)-2-isopropylcyclohexane-1-carbonitrile, obtained by treatment of cryptone ((±)-**6**) with *t*-BuNC [15], gave negative results, however. This carbonitrile was recovered unchanged after treatment with diisobutylaluminium hydride [16], whereas treatment with 0.25 mol-equiv. of $LiAlH_4$ in Et_2O gave only the corresponding amine in *ca.* 20% yield[2]).

[1]) Thus, 1,4-addition of the *Grignard* reagent prepared from 3-(chloromethly)furan [5a] or the more reactive 3-(bromomethyl)furan [5b] to cryptone ((±)-**6**) in the presence of CuI or CuCN [6a] failed; only unaltered (±)-**6** was recovered besides *Wurtz* coupling products. Also 3-(lithiomethyl)furan in the presence of either CuCN, or CuI·$(CH_3)_2S$ [6b], or (CuI·$Bu_3P)_4$ [6c], or, finally, CuI in the presence of Me_3SiCl [7] failed to react with (±)-**6**. These failures recall the resistance of 4-methylcyclohex-2-en-1-one to add either lithium allyl- or benzylcuprates [8]. Our attempts to circumvent the above problems by reacting 3-(lithiomethyl)furan with 5,5-(ethylenedioxy)-2-isopropylcyclohexan-1-one (prepared by conjugate addition of Bu_3Sn^- to (±)-**6** [9] followed by acetalization and oxidation with pyridinium chlorochromate/NaOAc over molecular sieves) were also unsuccessful; acetal-ring opening was observed. This acetal-ring cleavage under basic conditions finds a precedent in the behavior of 2-methylcyclopentane-1,3-dione monoethylene acetal toward amines [10] and must be attributed to the ease of enolization of the starting ketone. In an effort to utilize this rearrangement for the synthesis of (±)-**2**, the above acetal-ring-opened product, protected as tetrahydropyranyl ether, was treated with 3-(lithiomethyl)furan (obtained from crystalline 3-[(triphenylstannyl)methyl]furan [11]); however, only Ph_4Sn and unreacted substrate were recovered. We further reasoned that (3-furyl)cuprate [12] could be added to the spiroepoxide obtained from 5,5-(ethylenedioxy)-2-isopropylcyclohexan-1-one to open a route to (±)-**2**. However, the reaction of 5,5-(ethylenedioxy)-2-isopropylcyclohexan-1-one with dimethylsulfoxonium methylide [13a] gave the desired spiroepoxide in only miserable yield, while with Me_2S/BuLi [13b], only an acetal-ring-opening product was obtained. We also failed in attempts to employ *Barton*'s free radical procedure [14] in our case. Thus, the thiohydroxamate ester prepared *in situ* from furan-3-acetic acid and *N*-hydroxypyridine-2-thione failed to afford the desired adduct in the presence of cryptone ((±)-**6**) under either thermal or photochemical conditions [14]. That, however, the free 3-methylenefuran radical was formed is shown by the isolation of the corresponding thioether besides unreacted (±)-**6** and the free-radical dimerization product.

[2]) We also envisaged, but did not try, 1,4-addition of CN^- to (±)-**6** with trapping of the intermediate enolate as a 2-phenylseleno derivative from which the 2,3-unsaturated analog of aldehyde (±)-**10** could possibly be obtained.

Scheme 2



① CH_2=CHMgBr, CuBr·SMe_2, Me_3SiCl, THF. ② Py·TsOH, C_6H_6, reflux. ③ $HOCH_2CH_2OH$ added to the mixture of step. ②, 73% from (+)-**6**. ④ O_3, CH_2Cl_2, Ph_3P, MeOH, 87%. ⑤ 3-Bromofuran, BuLi, Et_2O, 85%. ⑥ a) $POCl_3$/Py, reflux; b) Py·TsOH, wet acetone, reflux.

Finally, aldehyde (–)-**10** was obtained *via* 1,4-addition of a vinyl group to (+)-4*S*-cryptone ((+)-**6**) followed by ozonolysis. Actually, vinylcuprates were already known to undergo 1,4-addition with cryptone [17]; in our hands, this reaction was found to compete with 1,2-addition to give 1-ethenyl-4-isopropylcyclohex-2-en-1-ol. However, we were able to suppress the 1,2 addition in favor of 1,4 addition by reacting (+)-**6** with vinylmagnesium bromide and stoichiometric amounts of CuBr·SMe_2 in THF in the presence of Me_3SiCl [7] [18]. A mixture **7**/**8** was thus obtained, the latter arising from hydrolysis of the former on aqueous workup *(Scheme 2)*. Hydrolysis of residual **7** was ensured by treatment of **7**/**8** with either KF in MeOH at room temperature (standard method for silyl enol ether hydrolysis) or catalytic amounts of pyridinium *p*-toluenesulfonate (Py·TsOH) in benzene at reflux. The latter methodology was found to be preferable in our case, as it allowed the addition of ethylene glycol directly to the crude reaction mixture to give acetal **9** (73% yield from (+)-**6**) [19]. The stereochemistry of the 1,4 addition to (+)-**6** proved, as expected [17], to be *trans*; this is indicated by $J(3,4) = 11.4$ Hz for both **9** and (–)-**10**.

Ozonolysis of crude **9** followed by reduction with Ph_3P in the presence of MeOH [20] led to (–)-**10** in 87% yield. Addition of 3-lithiofuran [21] to (–)-**10** gave the mixture of epimeric alcohols **11** in 85% yield, while the subsequent steps of dehydration with $POCl_3$/pyridine and deprotection with Py·TsOH led to (+)-**2** in poor yield and was not

optimized[3])[4])[5]). Synthetic (+)-noroxopenlanfuran ((+)-**2**) was shown by ^{1}H-NMR in the presence of the chiral shift reagent [Eu(tfc)$_3$] [22] to have 45% ee *(Exper. Part)*.

3. Conclusions. – The total synthesis of the unnatural enantiomer (+)-**2** of noroxopenlanfuran from (+)-(4*S*)-cryptone ((+)-**6**) reported above allows us to establish (4*R*)-configuration for natural (–)-noroxopenlanfuran ((–)-**2**) [1b]. Moreover, on the basis of the configurational correlations indicated in *Scheme 1* [1b], this establishes the configuration (4*R*) for natural (–)-penlanfuran ((–)-**1**) [1a], (1*R*,4*R*) for (–)-acetoxydihydropenlanfuran ((–)-**3**), (1*S*,4*R*) for natural (–)-**4a**, and (1*R*,4*R*) for (–)-**4b** [1b]. By analogy, both (+)-**5a** and (–)-**5b**, which must be artifacts of ethanolysis of natural γ-hydroxybutenolides formed during extraction from the sponge with EtOH [1b], can also be assigned with confidence to have (4*R*)-configuration.

We thank Mr. *A. Sterni* for recording mass spectra and the M.P.I. and the C.N.R., Roma, for financial support.

Experimental Part

General. Solvents and reagents were distilled as follows: THF and Et_2O from $LiAlH_4$, benzene from Na (and then stored over 4-Å molecular sieves), CH_2Cl_2, Me_3SiCl, hexamethylphosphoramide (HMPA), $(i\text{-}Pr)_2NH$, and DMF from CaH_2, and pyridine from BaO. Commercial BuLi and vinylmagnesium bromide *(Aldrich)* were standardized by acid-base titration [23]. $POCl_3$ and 4-isopropyl-2-cyclohexen-1-one were distilled prior to use, whereas the other commercial reagents were used as received. (±)-Cryptone ((±)-**6**) was either commercially available (*Aldrich*, 1986–87 catalogue) or was synthesized [24]. Mg turnings were activated by successive washing with 1M aq. HCl, H_2O, and acetone and were dried over P_2O_5. CuI was recrystallized according to [6c]. All reactions were carried out in flame-dried glassware under N_2 and all evaporations under reduced pressure at r.t. Yields are given with respect to reacted substrates. Bulb-to-bulb distillation: *Büchi GKR* 'Kugelrohr'. TLC: *Merck* Si_{F254} plates; visualization by either UV light, cerium sulfate, 2,4-dinitrophenylhydrazine, or *Ehrlich* reagent. Flash chromatography (FC): *Merck* silica gel *Si60*, 20–50 μm); HPLC: *Merck-LiChrosorb Si60* (7 μm), for reverse-phase *Merck-LiChroprep RP-8* (7 μm); columns 25 × 1 cm; UV monitoring; flux 5 ml/min. M.p.: *Kofler* hot-stage apparatus. Polarimetric data: *JASCO-DIP-181* digital polarimeter. UV spectra: *Perkin-Elmer-Lambda-3* spectrophotometer; λ_{max} in nm, ε in $dm^3 \cdot mol^{-1} \cdot cm^{-1}$. IR spectra: *Perkin-Elmer-337* spectrometer; $\tilde{\nu}_{max}$ in cm^{-1}. NMR: *Varian XL300* (300 MHz for ^{1}H and 75.4 MHz for ^{13}C); solvent $CDCl_3$, freshly eluted from a Al_2O_3 column; δ (ppm) relative to internal Me_4Si (= 0 ppm) and J in Hz; C-multiplicities by APT [25] or DEPT [26]. EI-MS (*m*/*z* (%)): home-built quadrupole mass spectrometer based on the *ELFS-4-162-8 Extranuclear* quadrupole [27].

1. *2-Ethenyl-4,4-(ethylenedioxy)-1-isopropylcyclohexane* (**9**). To a mixture of $CuBr \cdot SMe_2$ (1.13 g, 5.5 mmol) in dry THF (15 ml) at – 78° under N_2 were added slowly vinylmagnesium bromide (1M, 11.02 ml) and Me_3SiCl (0.7 ml, 5.5 mmol) through a hypodermic syringe. The mixture was stirred for 30 min at – 78°. Then (+)-**6** (0.38 g, 2.75 mmol; $[\alpha]_D^{20} = +81.3$ (*c* = 0.60, EtOH), 68% ee) was added and stirred for further 2 h at – 78° (TLC monitoring:

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[3]) The inverse sequence of first deprotecting and then dehydrating **11** proved not practicable. Thus, the ketone analog obtained from **11** by deprotection with Py·TsOH in wet acetone [19] reacted only in part with $POCl_3$/pyridine to give a complex mixture of products, and it was unreactive toward TsCl in excess in pyridine at room temperature for 3 days.

[4]) It should not be forgotten that 3-substituted furans are highly reactive compounds, which makes workup difficult.

[5]) Epimers **11** were separated from one another, and it was proven that only the less abundant, more polar epimer **11b** (see *Exper. Part*) led to (+)-**2**; the more abundant isomer **11a** gave a mixture which did not contain (+)-**2**. *Dreiding* molecular models suggest that in **11a**, the i-Pr group sterically hinders the esterification of the OH group whereby β-elimination is prohibited.

no (+)-**6** left), followed by 10 ml of H_2O and further stirring at r.t. After extraction with Et_2O, the org. layer was washed with H_2O, dried (Na_2SO_4), and evaporated: 0.43 g of **7**/**8** 3:7 (by ^{1}H-NMR). A small sample of anal. pure **8** was obtained by FC (SiO_2, hexane/Et_2O 4:1). To a soln. of crude **7**/**8** (0.41 g) in benzene (20 ml) was added Py·TsOH (0.12 g). After heating to reflux for 2 h and cooling to r.t., ethylene glycol (0.4 ml) was added and heated under reflux in a *Dean-Stark* apparatus in order to remove H_2O until complete disappearance of **8**. The resulting mixture was evaporated, the residue dissolved in Et_2O (80 ml) and the Et_2O soln. washed with $NaHCO_3$ soln. and H_2O, dried (Na_2SO_4), and evaporated: **9** (0.40 g, 73% from (+)-**6**).

3-Ethenyl-4-isopropyl-1-[(trimethylsilyl)oxy]cyclohexene (**7**): Oil. ^{1}H-NMR: 4.63 (*td*, J = 3.0, 1.5, H–C(2)); 2.68 (*ddd*, J = 8.4, 5.7, 3.0, H–C(3)); 0.90, 0.77 (2 *d*, J = 6.9, $(CH_3)_2CH$); 5.59 (*ddd*, J = 16.8, 10.5, 8.4, CH_2=C*H*); 5.01 (*m*, CH_2=CH); 1.1–2.1 (*m*, 6H). ^{13}C-NMR: 150.8 (*s*, C(1)); 107.1 (*d*, C(2)); 44.3 (*d*, C(3) or C(4)); 42.5 (*d*, C(4) or C(3)); 21.1 (*t*, C(5)); 29.5 (*t*, C(6)); 27.0 (*d*, $CH_3)_2CH$); 21.6, 16.9 (2 *q*, $(CH_3)_2CH$); 143.4 (*d*, CH_2=*C*H); 114.1 (*t*, *C*H_2=CH); 0.3 (*q*, Me_3SiO).

3-Ethenyl-4-isopropylcyclohexanone (**8**): Oil. IR (neat): 3080*w*, 2960*s*, 2940*s*, 2880*s*, 1710*s*, 1640*m*, 1475*m*, 1430*m*, 1393*m*, 1375*m*, 1210*w*, 995*m*, 915*s*. ^{1}H-NMR: 0.95, 0.74 (2 *d*, J = 6.9, $(CH_3)_2CH$); 5.62 (*dd*, J = 17.1, 10.8, 8.1, CH_2=C*H*); 5.02 (*ddd*, J = 17.1, 2.0, 0.9, H_a of CH_2=CH); 4.98 (*dd*, J = 10.8, 2.0, H_b of CH_2=CH); 2.15–2.40 (*m*, 5 H); 1.3–2.0 (*m*, 4H). ^{13}C-NMR: 211.0 (*s*, C(1)); 47.2 (*t*, C(2)); 46.0 (*d*, C(3) or C(4)); 46.1 (*d*, C(4) or C(3)); 24.2 (*t*, C(5)); 40.9 (*t*, C(6)); 27.5 (*d*, $(CH_3)_2CH$); 15.4, 21.5 (2 *q*, $(CH_3)_2CH$); 140.7 (*d*, CH_2=*C*H); 115.0 (*t*, CH_2=CH). MS: 166 (19, $M^{+\cdot}$), 151 (21, $M^{+\cdot}-15$), 139 (23, $M^{+\cdot}-27$), 138 (34), 123 (38, $M^{+\cdot}-43$), 111 (79), 96 (79), 95 (94), 83 (62), 81 (83), 79 (57), 69 (100), 55 (87), 43 (43).

Data of **9**: Oil. IR (neat): 3080*w*, 2960*s*, 2890*s*, 1640*w*, 1466*m*, 1360*m*, 1135*s*, 1090*s*, 1040*m*, 905*s*. ^{1}H-NMR: 1.05 (*m*, H–C(1)); 2.18 (*dddd*, J = 12.0, 11.4, 9.4, 3.5, H–C(2)); 1.70 (*m*, 2H–C(3), 2H–C(5)); 1.45 (*m*, 2H–C(6)); 1.86 (*m*, $(CH_3)_2CH$); 0.88, 0.72 (2*d*, J = 7.0 $(CH_3)_2CH$); 5.56 (*ddd*, J = 17.1, 10.1, 9.4, CH_2=C*H*); 5.00 (*ddd*, J = 17.1, 2.1, 0.9, H_a of CH_2 = CH); 4.93 (*dd*, J = 10.2, 2.1, H_b of CH_2=CH); 3.93 (br. *s*, OCH_2CH_2O). ^{13}C-NMR: 43.5 (*d*, C(1) or C(2)); 46.3 (*d*, C(2) or C(1)); 41.8 (*t*, C(3)); 108.8 (*s*, C(4)); 34.8 (*t*, C(5)); 21.4 (*t*, C(6)); 27.6 (*d*, $(CH_3)_2CH$); 15.2, 21.5 (2*q*, $(CH_3)_2CH$); 142.3 (*d*, CH_2=*C*H); 114.1 (*t*, *C*H_2=CH); 64.2, 64.3 (2*t*, OCH_2CH_2O). MS: 183 (38, $M^{+\cdot}-27$), 125 (100), 99 (86), 86 (16), 55 (21), 43 (22).

2. *1-Ethenyl-4-isopropylcyclohex-2-en-1-ol.* Treatment of (±)-**6** with $CuCN/BF_3\cdot OEt_2$ [33] or $CuBr\cdot SMe_2$ [34], followed by addition of sat. NH_4Cl soln./conc. NH_4OH 9:1 and standard workup led to the products of 1,4- (**8**) and 1,2-addition of the ethenylcuprate in a 4:1 and 3:1 ratio, respectively, as determined by ^{1}H-NMR analysis.

Data of 1,2-Adduct: ^{1}H-NMR (only signals distinct from those of **8** are reported): 5.74 (br. *d*, J = 10.2, H–C(2)); 5.49 (*dd*, J = 10.2, 2.7, H–C(3)); 0.86, 0.84 (2 *d*, J = 6.9, $(CH_3)_2CH$); 5.91 (*dd*, J = 17.4, 10.5, CH_2=C*H*); 5.12 (*dd*, J = 17.4, 1.5, H_b of CH_2=CH); 5.06 (*dd*, J = 10.5, 1.5, H_a of CH_2=CH). ^{13}C-NMR: 65.8 (*s*, C(1)); 133,1 (*d*, C(2) or CH_2=*C*H); 143,5 (*d*, C(3)); 41,7 (*d*, C(4)); 22,3 (*t*, C(5)); 36.4 (*t*, C(6)); 31.8 (*d*, $(CH_3)_2CH$); 19,5, 19,2 (2 *q*, $(CH_3)_2CH$); 131,4 (*d*, CH_2=*C*H or C(2)); 113,9 (*t*, *C*H_2=CH).

3. *5,5-(Ethenylenedioxy)-2-isopropylcyclohexane-1-carbaldehyde* ((–)-**10**). A soln. of crude **9** (0.39 g, 1.87 mmol) in CH_2Cl_2 (16 ml) was cooled to –78°. Ozone was bubbled through it until persistence of the blue color and then O_2 until complete discoloration. After addition of Ph_3P (0.55 g, 2.2 mmol) and MeOH (0.3 ml), the mixture was allowed to reach r.t., stirred for further 3 h, and extracted with CH_2Cl_2 (3 × 20 ml). The org. layer was washed with H_2O, dried (Na_2SO_4), and evaporated. The residue was subjected to FC (hexane/Et_2O 4:1): (–)-**10** (0.34 g, 87%). Colorless oil. $[\alpha]_D^{20} = -12.3$ (c = 1.7, EtOH). IR (neat): 2960*s*, 2860*m*, 2720*m*, 1720*s*, 1470*w*, 1380*w*, 1178*m*, 1155*m*, 1128*m*, 1020*m*. ^{1}H-NMR: 2.52 (*dddd*, J = 11.4, 10.2, 3.9, 3.9, H–C(1)); 1.76, 1.35 (*m*, H–C(2), 2H–C(3), 2H–C(4), 2H–C(6), $(CH_3)_2CH$)); 9.55 (*d*, J = 3.9, CHO); 0.91, 0.82 (2*d*, J = 6.9, $(CH_3)_2CH$); 3.92 (*s*, OCH_2CH_2O). ^{13}C-NMR: 50.9 (*d*, C(1)); 41.9 (*d*, C(2)); 21.8 (*t*, C(3)); 34.2 (*t*, C(4)) or C(6)); 108.0 (*s*, C(5)); 34.1 (*t*, C(6) or C(4)); 204.2 (*d*, CHO); 28.7 (*d*, $(CH_3)_2CH$); 21.2, 16.7 (2*q*, $(CH_3)_2CH$); 64.5, 64.4 (2*t*, OCH_2CH_2O). MS: 183 (17, $M^{+\cdot}-29$), 169 (5, $M^{+\cdot}-43$), 127 (4), 113 (8), 99 (100), 86 (14), 55 (14).

4. *[5,5-(Ethenylenedioxy)-2-isopropylcyclohexyl](furan-3-yl)methanol* (**11**). To a soln. of 3-bromofuran (3.2 mmol in 8 ml of Et_2O) cooled to –78° was added BuLi (3.0 mmol) in 2 ml of hexane *via* a hypodermic syringe under N_2. The mixture was stirred for 1 h at –78°. After dropwise addition of (–)-**10** (0.32 g, 1.5 mmol) in 2 ml of Et_2O, the mixture was stirred for 1 h at –78°, then allowed to reach 0° and quenched with sat. aq. NH_4Cl soln. and H_2O, and finally repeatedly extracted with Et_2O. The org. layer was washed with H_2O, dried (Na_2SO_4), and evaporated: **11** (0.3 g, 85%). Pure less polar **11a** (0.081 g; R_f 0.35) and more polar **11b** (0.038 g; R_f 0.2) were obtained from 0.13 g of crude **11** by column chromatography (silica gel, hexane/Et_2O 1:1).

Data of **11b**: Colorless oil. ^{1}H-NMR: 2.0–1.2 (series of *m*, 9H); 5.07 (*dd*, J = 3.9, 1.5, *C*HOH); 2.62 (br. *s*, OH); 7.34 (*m*, H–C(2′)); 6.32 (*dd*, J = 1.8, 1.5, H–C(4′)); 7.37 (*t*, H–C(5′)); 0.91, 0.86 (2*d*, J = 6.9, $(CH_3)_2CH$); 3.93 (*m*, OCH_2CH_2O).

Data of **11a**: Colorless oil. ^{1}H-NMR: 2.10–1.20 (series of *m*, 10 H); 5.04 (br. *d*, *J* = 2.7, *CH*OH); 7.33 (br. *d*, *J* = 1.8, H–C(2′)); 6.28 (*dd*, *J* = 1.8, 1.5, H–C(4′)); 7.37 (*t*, *J* = 1.8, H–C(5′)); 0.96, 0.83 (2*d*, *J* = 6.9, $(CH_3)_2CH$); 3.87 (*m*, OCH_2CH_2O). ^{13}C-NMR (data for **11b** within brackets): 42.4 [42.7] (*d*, C(1) or C(2)); 41.9 [42.1] (*d*, C(2) or C(1)); 21.5 [21.3] (*t*, C(3)); 32.6 [33.6] (*t*, C(4)); 109.5 [109.3] (*s*, C(5)); 34.2 [34.0] (*t*, C(6)); 66.3 [66.7] (*d*, CHOH); 139.0 [139.5] (*d*, C(2′)); 128.4 [125.7] (*s*, C(3′)); 108.5 [109.4] (*d*, C(4′)); 143.1 [142.7] (*d*, C(5′)); 26.2 [26.4] (*d*, $(CH_3)_2CH$); 21.4, 16.0 [21.3, 15.8] (2*q*, $(CH_3)_2CH$); 64.2, 64.1 [64.2, 64.0] (2*t*, OCH_2CH_2O). MS (identical for both isomers): 280 (3, $M^{+\cdot}$), 184, (33), 183 (60), 141 (36), 123 (21), 99 (100), 97 (27), 95 (26), 86 (21), 79 (11), 55 (25), 43 (15).

5. *3-[(Furan-3-yl)hydroxymethyl]-4-isopropylcyclohexanone.* Treatment of **11** (0.015 g) with Py·TsOH in wet acetone led to the title compound (2:1 mixture).

Data of Major Isomer: ^{1}H-NMR (numbering corresponds to that of (–)-**3**; signals of minor isomer within brackets when not superimposed): 7.34 (*m*, H–C(2′), H–C(5′)); 6.24 [6.32] (*dd*, *J* = 1.8, 1.5, H–C(4′)); 4.93 [4.84] (br. *d*, *J* = 3.3 [*J* = 5.1], *CH*OH); 2.50–1.30 (series of *m*, 10 H); 1.01, 0.86 [0.96, 0.90] (2 *d*, *J* = 6.9, $(CH_3)_2CH$). ^{13}C-NMR: 213.4 [213.0] (*s*, C(1)); 143.5 [143.3] (*d*, C(5′)); 139.1 [139.8] (*d*, C(2′)); 127.7 [126.1] (*s*, C(3′)); 108.3 [108.8] (*d*, C(4′)); 67.0 [67.9] (*d*, CHOH); 44.8 [44.5] (*d*, C(3) or C(4)); 41.7 [40.5] (*d*, C(4) or C(3)); 40.0 [40.3] (*t*, C(2)); 39.0 [39.2] (*t*, C(6)); 27.4 [27.9] (*d*, $(CH_3)_2CH$); 21.5 [21.3] (*t*, C(5)); 21.3, 16.7 [21.1, 17.3] (2 *q*, $(CH_3)_2CH$). MS: 236 (4, $M^{+\cdot}$), 218 (1, $M^{+\cdot} - 18$), 193 (3), 175 (7), 151 (12), 140 (28), 125 (31), 99 (28), 97 (100), 81 (12), 70 (46), 69 (30), 55 (31), 43 (27).

6. *(+)-Noroxopenlanfuran (= (4S)-3-[(Furan-3-yl)methyl]-4-isopropylcyclohex-2-enone;* (+)-**2**). Epimer **11b** (0.035 g) and epimer **11a** (0.078 g) were separately heated under reflux in pyridine for 2 h in the presence of excess $POCl_3$. TLC (silica gel, hexane/Et_2O 1:1) showed that a less polar, UV-detectable, and *Ehrlich*-reactive spot (R_f 0.8) was formed from only **11b**; this mixture was then treated with aq. $CuSO_4$ soln. and extracted with Et_2O. The org. layer was washed with H_2O, dried (Na_2SO_4), and evaporated. The residue was heated at reflux for 2 h in 2 ml of acetone/H_2O 10:1 in the presence of Py·TsOH (0.012 g). The mixture was evaporated and the residue subjected to prep. TLC (hexane/Et_2O 1:1): (+)-**2** (0.0018 g). R_f 0.06. $[\alpha]_D^{20} = +42.1$ (*c* = 0.8, $CHCl_3$). This compound was further purified by HPLC (hexane/AcOEt 9:1; t_R 14.2 min, 0.0011 g). To a soln. of (+)-**2** in 0.5 ml of $CDCl_3$, 0.093M [Eu(tfc)$_3$] in $CDCl_3$ was added in 5-µl portions. After addition of 0.2 mol-equiv. of [Eu(tfc)$_3$], doubling of the ^{1}H-NMR signals for $(CH_3)_2CH$ (1:0.42) was noticed.

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