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Synthesis, Sensory Properties and Structures of Substituted Dodecanolides

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Dedicated to Professor Rolf Huisgen on the occasion of his 80th birthday

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Abstract—The liquid odorants (*R*)-**6** and (*R*)-**7** and their corresponding crystalline model substances (*R*)-**8** and (*R*)-**13** were synthesized. Based on the X-ray analyses of (*R*)-**8** and (*R*)-**13**, geometries for (*R*)-**6** and (*R*)-**7** were determined using semiempirical calculations.

Introduction

In previous studies[1–4] we have shown that the sensory properties of new macrolides and especially their musk notes strongly depend on various structural features such as ring size, the chain length of alkyl substituents, the absolute configuration of stereogenic centres and the position of carbon–carbon double bonds. Predictions concerning the relationship between odour and structure of these compounds are difficult or even impossible for the following reasons. On the one hand the structure of the corresponding protein receptors[5] is not known, on the other hand highly flexible macrocyclic compounds can adopt an enormous diversity of conformers differing only slightly in energy.[6]

Whereas the structure of crystalline odorants can be studied by X-ray analysis,[5,7] it is still a major task to supply information about the geometric and electronic properties of liquid compounds. In this paper, a link between X-ray analysis and computational chemistry for the musk odorants (*R*)-**6** and (*R*)-**7** is described, providing information about geometries including volumes and surfaces as well as dipole moments and the topology of the electrostatic potential surfaces.

As enantiomers generally differ in their sensory characteristics,[1,4,8] we first determined which of the enantiomers of **6** is the more interesting one. Both enantiomers of **6** were synthesized according to our ring enlargement sequence[1] shown in Scheme 1 for (*R*)-**6**. The synthesis started with the alkylation of cyclononanone (**1**)[9] with the chiral building block (*S*)-**2**[10] yielding about 40% of (*R,RS*)-**3a/b**. The following steps were the acid catalysed cyclization to the enol ether (*R*)-**4** and the oxidative cleavage of the enol ether double bond by ruthenium tetroxide oxidation.[11] The keto-lactone was obtained in a yield of about 80% over these two steps. The keto functionality of (*R*)-**5** was then reduced via the corresponding tosylhydrazone in a modified Caglioti reaction.[4,12] The target compound (*R*)-**6** was received in an yield of about 60%. (*S*)-**6** was prepared by the same procedure from the corresponding building block (*R*)-**2**[10] (see Experimental).

The sensory analysis revealed interesting properties of (*R*)-**6**: a faint musk note with very fresh nuances of clary sage and bergamot is accompanied by cedar-wood accents. Only a slightly earthy-musty undertone has to be accounted. The smell of (*S*)-**6** does not differ much in its sensory qualities, however it is of weaker intensity. As the (*R*)-compound turned out to possess a more intensive odour than its enantiomer all further evaluations were carried out with (*R*)-**6**. In the course of our studies we have shown that the introduction of a semicyclic methylene group can improve the odour characteristics significantly.[2,4] Therefore, we prepared (*R*)-**7** from (*R*)-**5** by a Wittig reaction.[13] (*R*)-**7**, which has a relatively strong smell, was obtained in 69% yield. An unconventional fresh and pointed musk note is accompanied by woody, cedar-like and camphoraceous nuances. The smell of (*R*)-**7** appears to be slightly aqueous-aldehydic but interesting as a musk top note.

Having shown that (*R*)-**6** and (*R*)-**7** possess clearly different sensory characteristics we wanted to get information about

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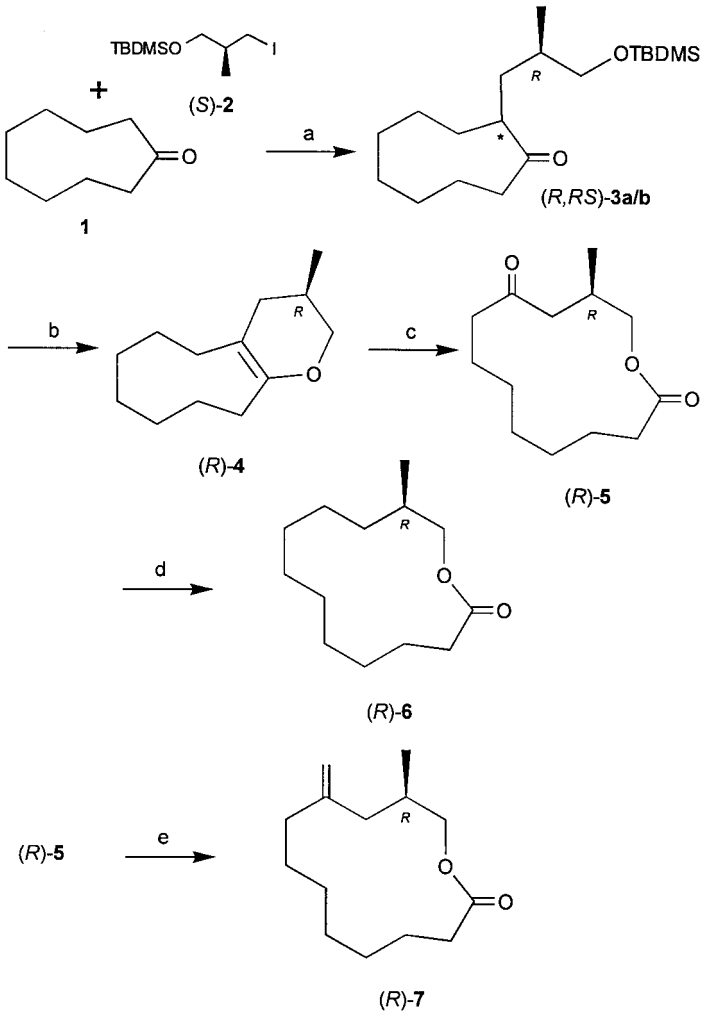


Scheme 1. Synthesis of (*R*)-**6** from cyclononanone (**1**)[9] and the chiral building block (*S*)-**2**.[10] (a) LDA/DMPU, THF. (b) Amberlyst 15, CH_2Cl_2. (c) $RuCl_3$/$NaIO_4$, $MeCN/CCl_4/H_2O$. (d) H_2NNHTs, MeOH; catecholborane, THF. (e) $CH_3PPh_3Br/KO\text{-}^tBu$, Et_2O.

structural differences of these two liquid odorants. For this purpose we synthesized crystalline derivatives suitable for X-ray analysis.

(*R*)-**8** obtained from (*R*)-**6** by standard conditions[14] fulfilled these prerequisites. Its X-ray analysis at ambient temperature showed the coexistence of two different conformers (Fig. 1).

In analogy we chose (*R*)-**11** and (*R*)-**12** as model compounds for (*R*)-**7**. The introduction of the phenylthio substituents was accomplished by the sequence outlined in Scheme 2 (for details see Experimental). (*R*)-**11** provided suitable crystals whereas (*R*)-**12** did not crystallize even at low temperature.

The X-ray analysis of (*R*)-**11** (Fig. 2) shows that the keto oxygen atom is directed towards the middle of the macrocyclic ring. This conformational feature had been already observed for medium sized ring ketones by Prelog.[15] This may be the reason for the relatively rare cases of oxolactones which show a musk note. One example is a homologue of (*R*)-**5** with two additional methylene groups.[16]

Obviously, the *exo*-methylene functionality is sterically more demanding than the keto group. So (*R*)-**11** was transformed via Wittig reaction into (*R*)-**12** which unfortunately did not crystallize even at low temperatures. Therefore, we decided to use (*R*)-**13** as crystalline model substance for (*R*)-**7**. The hydrazone (*R*)-**13** should be sufficiently spatially demanding to mimic the exomethylene functionality. (*R*)-**13** was obtained in a yield of 56% from (*R*)-**5** as orange crystals (Fig. 3).

The X-ray analyses of the model substances (*R*)-**8** and (*R*)-**13** now provided the basis for the theoretical part of our work. The procedure used here implied the conversion of X-ray data of the model substances (*R*)-**8** and (*R*)-**13** in order to perform semiempirical calculations[17] of the sensory molecules (*R*)-**6** and (*R*)-**7**.

This is described in detail for the conformer (*R*)-**6A**: starting with X-ray data from (*R*)-**8A**, primary geometry refinements were carried out using the AM1 method.[18] The resulting conformer, which was topologically identical, was subsequently modified, replacing the phenylthio groups by hydrogen atoms. This was done by application of the MM2 molecular mechanics method[19,20] on the bonds of

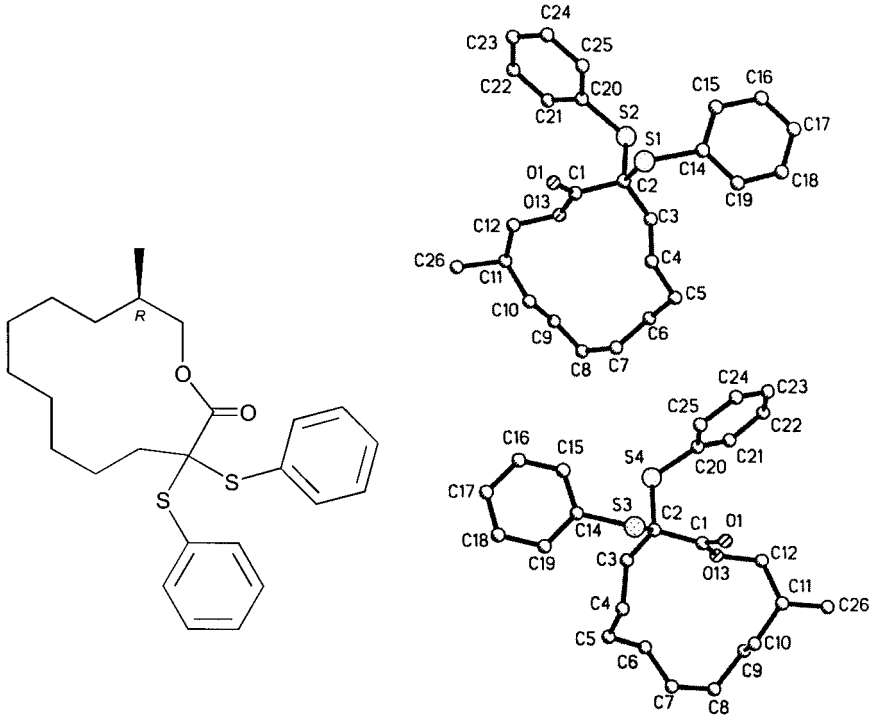
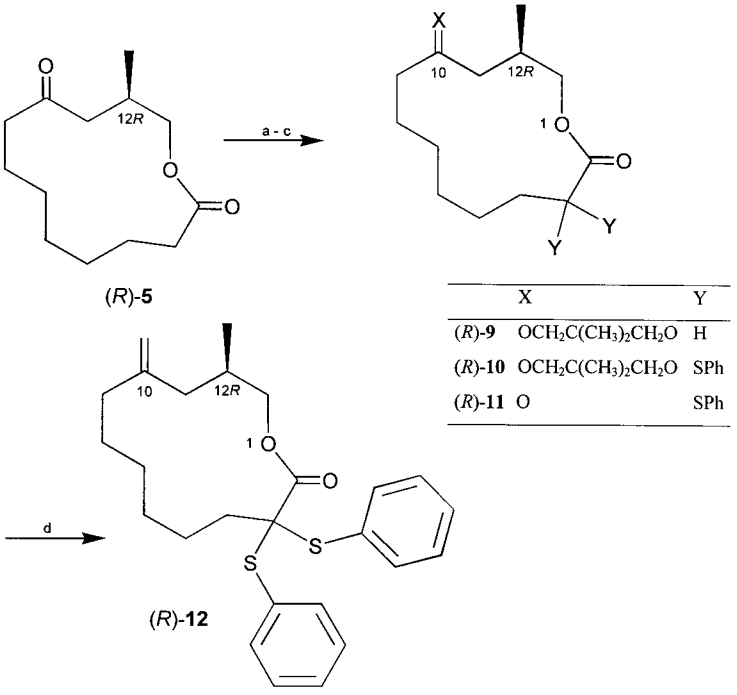


Figure 1. (*R*)-**8** and its two conformers **A** and **B** in the crystal; arbitrary numbering.

only the particular carbon atom. Then the geometry of the obtained conformer of (*R*)-**6A** was fully optimized using the AM1 method[18] in three refinement steps, including the *Eigenvector–Following* method[20] which is known to give results of best precision. No constraints were applied. The integrity of the final results has been validated by calculation of the force constants and the resulting vibrational frequencies. Superposition of (*R*)-**8A** and (*R*)-**6A** revealed an excellent concordance between the two geometries. Supplementary PM3[21] calculations support the results. No interference between the lactone ring and the substituents or between the substituents themselves is observed, which can be explained by the sufficient length of the C–S bonds in (*R*)-**8A**.



	X	Y
(*R*)-**9**	$OCH_2C(CH_3)_2CH_2O$	H
(*R*)-**10**	$OCH_2C(CH_3)_2CH_2O$	SPh
(*R*)-**11**	O	SPh

Scheme 2. Synthesis of (*R*)-**12** from (*R*)-**5**. (a) Amberlyst 15/2,2-dimethyl-propane-1,3-diol, toluene. (b) LDA/PhSSPh, THF. (c) Amberlyst 15, CH_2Cl_2. (d) $CH_3PPh_3Br/KO\text{-}^tBu$, Et_2O.

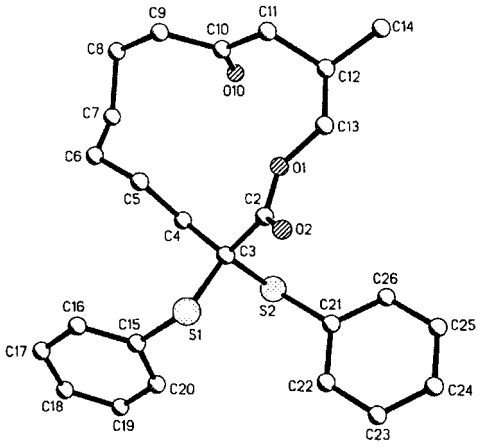


Figure 2. One molecule of (*R*)-**11** in the crystal; arbitrary numbering.

The same procedure was carried out for conformer (*R*)-**8B** to give (*R*)-**6B**. The calculated gas phase conformers (*R*)-**6A** and (*R*)-**6B** show rather similar structures with the macrocycles in an 'inverted' conformation (Fig. 4). In both conformers, all *trans* edges are linked by *gauche* corners with the *Z* ester moiety localized in a zigzag chain, its α-carbon atom being a corner atom. Also the methyl group is situated on a corner atom in both conformers. In conformer (*R*)-**6A**, the lactone carbonyl oxygen is directed transversally into the plain whereas in conformer (*R*)-**6B** the lactone carbonyl oxygen lies vertically above the plain of the macrocycle.

For the *exo*-methylene compound (*R*)-**7**, the geometry optimization was carried out in the same way as above. The replacement of the hydrazone group of (*R*)-**13** by the exomethylene functionality was the key step in the generation of (*R*)-**7**. The hydrazone group is an appropriate substituent that mimics the exomethylene functionality in this case. The resulting geometry for (*R*)-**7** is the nearly quadrangular conformer shown in Fig. 5. The macrocycle and the lactone group are arranged very similar to that of (*R*)-**6B**. The methyl and the *exo*-methylene groups are residing in the same edge of the macrocycle, but on different sides of the macrocyclic ring. This might be explained by their sterical demands. The result that only one conformer exists in the crystals at ambient temperature could be due to a lower flexibility of the macrocycle with an sp^2 configurated carbon atom.

To gain further insight into the geometry of the compounds, the molecular volumes[22] and surfaces[23] as well as the dipole moments were determined (Table 1). The water accessible surfaces and water excluded volumes[24] were calculated as

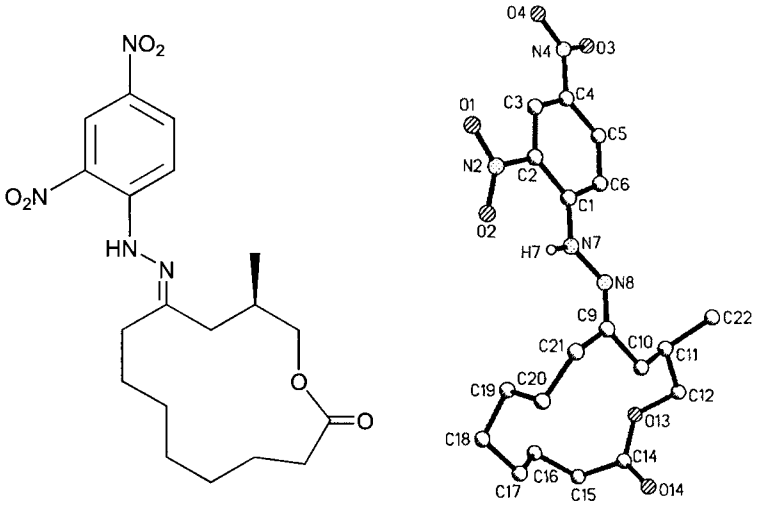


Figure 3. Crystalline model substance (*R*)-**13** and one molecule of (*R*)-**13** in the crystal; arbitrary numbering.

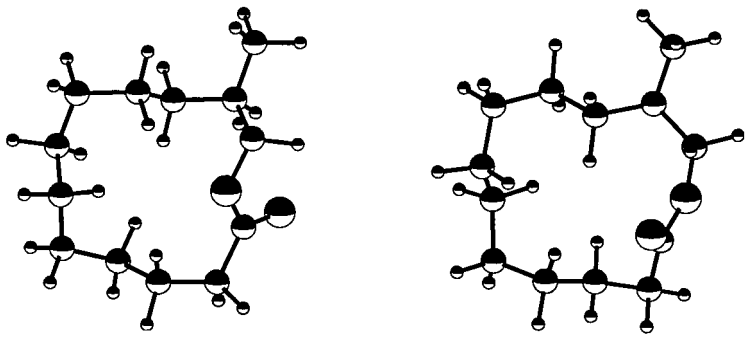


Figure 4. Calculated geometries of (*R*)-**6A** (left) and (*R*)-**6B** (right) (AM1).

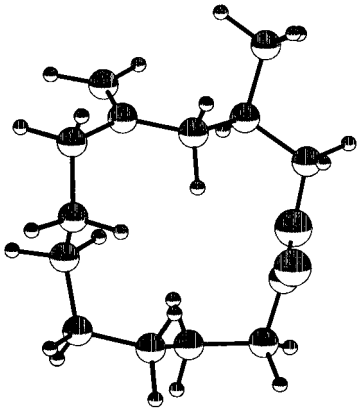


Figure 5. Calculated geometry of (*R*)-**7** (AM1).

Table 1. Calculated values for heat of formation (ΔH); dipole moment (μ); *van der Waals* surface and-volume *(VdW-Vol.)*; water accessible surface (Acc. surface) and water excluded volume (Excl. volume)

	(*R*)-**6A**	(*R*)-**6B**	(*R*)-**7**
$\Delta H^{18,26}$ (kcal/mol) (AM1)	−148.67	−150.68	−125.63
$\Delta H^{21,26}$ (kcal/mol) (PM3)	−133.24	−135.72	−113.18
$\mu^{18,26}$ [D] (AM1)	1.77	1.67	1.41
$\mu^{21,26}$ [D] (PM3)	1.78	1.81	1.48
VdW surface[23,27] (Å^2)	297.6	302.5	313.4
Acc. surface[22,28] (Å^2)	424.0	425.6	438.3
VdW volume[19,24] (Å^3)	309.4	310.4	323.8
Excl. volume[24,29] (Å^3)	700.3	704.1	731.4

biologically interesting parameters.[25] Together with the van der Waals values,[21,23] comparative studies may be performed by means of database search strategies.

Conclusion

The synthesis of two novel musk odorants, (*R*)-**6** and (*R*)-**7**, is described. In addition a combined method of semi-empirical calculations[17] and X-ray analysis of model compounds suitable for highly flexible macrolides is presented. (*R*)-**8** and (*R*)-**13** proved to be suitable solid derivatives for the procedure described here. Along with additional data such as the dipole moment and the electrostatic potential mapping, the geometries including molecular surfaces and volumes give an excellent picture of the investigated molecules. The visualization[20] of the electrostatical potential topology is available as supplementary material.[16]

Experimental

IR: Perkin–Elmer FTIR 1600, 1625; Paragon 1000 FTIR. UV: Zeiss DMR 10. ^{1}H/^{13}C NMR: Bruker AC 200 P, AM 300, DRX 500; TMS int. standard. MS: Finnigan MAT 8200 and MAT 8230; direct inlet (EI: 70 eV; CI isobutane). Column Chromatography (CC): Baker Silica gel 40–60 μm. TLC: Macherey-Nagel SIL G/UV$_{254}$. Melting points (uncorrected): Büchi 510. Optical rotations ($CHCl_3$): Perkin–Elmer 241. Elemental Analyses: Mikroanalytisches Laboratorium Ilse Beetz, D-96301 Kronach. All solvents and reagents were purified and dried according to common procedures. Reactions with organometallic compounds were performed under an argon atmosphere.

(2*R*,2′*R*)- and (2′*R*,2*S*)-2-[3′-(*tert*-Butyl-dimethyl-silyl-oxy)-2-methyl-propyl]-cyclononanone (*R*,*RS*)-3a/b. 57.2 mL (91.5 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane were added to a stirred solution of 12.4 mL (94.0 mmol) diisopropylamine in 200 mL anhydrous THF and 100 mL 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone at −78°C. The mixture was stirred for 10 min and then for 30 min at 0°C. After recooling to −78°C 8.80 g (62.0 mmol) cyclononanone (**1**) were added and stirring was continued for 1 h. Then 19.7 g (62.8 mmol) (2*S*)-(+)-(*tert*-butyl-dimethyl)-(3-iodo-2-methyl-propoxy)-silane ((*S*)-**2**)[10] were injected. After 30 min the reaction mixture was allowed to warm to room temp. and stirred overnight. Then it was poured into a mixture of 400 mL water and 400 mL of Et_2O. The organic layer was separated and the aqueous layer was extracted three times with 200 mL of Et_2O. The combined organic extracts were dried with $MgSO_4$ and concentrated in vacuo. The crude product was purified by CC (Et_2O/pentane 1:20) on silicagel to yield 7.6 g (37%) (*R*,*RS*)-**3a/b** (R_f=0.23) as a colourless oil. IR (film): ν=2928/2856 cm^{-1} (s, ν C–H), 1702 cm^{-1} (s, ν C=O, ketone), 1471 cm^{-1} (m, δ_{as} CH_3), 1095 cm^{-1} (m, ν C–OSi), 838 cm^{-1} (s, ν O–Si), 775 cm^{-1} (m, ν O–Si–CH_3). ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.02 (s, 6H, Si*Me*$_2$), 0.85–0.91 (m, 12H, C*Me*$_3$, 2′-*Me*), 1.25–1.91 (m, 15H), 2.27–2.57 (m, 2H, 9-H$_2$), 2.70 (m$_c$, 1H, 2-H), 3.31 (dd, *J*=9.8 and 5.4 Hz, 1H, 3′-H, part of an AB-system)/3.37 (dd, *J*=9.8 and 5.2 Hz, 1H, 3′-H, part of an AB-system), 3.40 (dd, *J*=9.1 and 5.9 Hz, 1H, 3′-H, part of an AB-system)/3.45 (dd, *J*=9.1 and 5.7 Hz, 1H, 3′-H, part of an AB-system) for the other diastereomer. ^{13}C NMR (50 MHz, $CDCl_3$): δ=−5.40 (q, 4C, Si–*Me*$_2$), 16.65/17.36 (q, 2′-*Me*), 18.30 (s, 2C, *C*-Me$_3$), 24.29/24.38/24.78/24.97/25.05/25.15/25.94 (t, 10C, C-4–C-8), 26.11/26.14 (q, 6C, C-*Me*$_3$), 30.43/31.50 (t, C-3), 33.60/33.72 (d, C-2′), 36.23/37.05 (t, C-1′), 41.57/41.83 (t, C-9), 51.03/51.12 (d, C-2), 68.01/68.41 (t, C-3′), 219.85/219.95(s, C-1). MS (CI): *m*/*z* (%)=327 (100) [$M^{\oplus}$+H], 269 (51) [$M^{\oplus}-C_4H_{10}$], 195 (98) [$M^{\oplus}-C_6H_{16}OSi$]. $C_{19}H_{38}O_2Si$ (326.3): calcd C 69.87%, H 11.73%; found C 69.99%, H 11.76%.

(12*R*)-12-Methyl-oxacyclotridecane-2,10-dione ((*R*)-5). A solution of 7.49 g (22.6 mmol) (*R*,*RS*)-**3a/b** in 350 mL anhydrous CH_2Cl_2 was treated with 3.00 g Amberlyst® 15 and stirred overnight at room temp. The resin was filtered off and extracted thoroughly with CH_2Cl_2. The organic extracts were combined and the solvent was evaporated in vacuo. The crude product was dissolved in 120 mL acetonitrile and 180 mL CCl_4. 180 mL water, 104 mg (0.052 mmol) ruthenium trichloride-trihydrate and 19.3 g (90.2 mmol) sodium periodate were added to the stirred solution. After stirring overnight at room temp. the solution was diluted with CH_2Cl_2. The organic layer was separated and the aqueous one was extracted with CH_2Cl_2. The combined organic extracts were dried with $MgSO_4$, filtered over silica gel and the solvents were removed in vacuo. CC of the crude product (Et_2O/pentane 1:4) provided 4.01 g (77%) (*R*)-**5** (R_f=0.29) as a colourless liquid. IR (film): ν=2936/2855 cm^{-1} (s, ν C–H), 1726 cm^{-1} (s, ν C=O,

lactone), 1702 cm^{-1} (s, ν C=O, ketone), 1458 cm^{-1} (m, δ_{as} CH_3), 1177 cm^{-1} (s, ν C–O–C). ^1H NMR (200 MHz, $CDCl_3$): δ=1.01 (d, J=6.9 Hz, 3H, 2′-*Me*), 1.15–1.45 (m, 6H), 1.53–1.80 (m, 4H), 2.20–2.55 (m, 6H), 2.77 (dd, J=17.5 and 6.8 Hz, 1H, 3-H), 3.91 (dd, J=10.9 and 8.2 Hz, 1H, 13-H), 4.12 (dd, J=10.9 and 3.8 Hz, 1H, 13-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=17.81 (q, 12-*Me*), 23.11/24.26/26.36/27.30/27.52 (t, C-4–C-10), 27.76 (d, C-12), 34.17 (t, C-3), 42.30 (t, C-9), 45.94 (t, C-11), 68.15 (t, C-13), 173.94 (s, C-2), 210.32 (s, C-10). MS (EI): *m/z* (%)=226 (7) [$M^{\oplus}$], 208 (5) [$M^{\oplus}-H_2O$], 169 (22) [$M^{\oplus}-C_4H_9$], 151 (9) [$M^{\oplus}-C_4H_{11}O$], 98 (100) [$C_6H_{10}O^{\oplus}$], 83 (43) [$C_6H_{11}^{\oplus}$], 69 (21) [$C_5H_9^{\oplus}$]. $[\alpha]_D^{21}$=+20.9, $[\alpha]_{578}^{21}$=+22.3, $[\alpha]_{546}^{21}$=+25.8, $[\alpha]_{436}^{21}$=+50.0, $[\alpha]_{365}^{21}$=+98.6 (c=0.7, $CHCl_3$). $C_{13}H_{22}O_3$ (226.2): calcd C 68.99%, H 9.80%; found C 68.99%, H 9.71%.

(12*R*)-12-Methyl-oxacyclotridecan-2-one ((*R*)-6). 4.01 g (17.7 mmol) (*R*)-**5** and 3.63 g (19.5 mmol) 4-toluenesulfonohydrazide were dissolved in 50 mL anhydrous methanol and refluxed for 45 min under argon. The solvent was removed under vacuo. After the crude product had been dried in a high vacuum line for 4 h it was dissolved in 70 mL anhydrous $CHCl_3$. 19.5 mL (19.5 mmol) of a 1 M solution of catecholborane in toluene were added at 0°C. The mixture was stirred for 2 h. Then 4.32 g (52.7 mmol) sodium acetate-trihydrate were added and the mixture was refluxed for 1 h. The cooled reaction mixture was poured into 400 mL Et_2O and 200 mL water, the organic layer was separated and washed twice with water. The organic phase was dried with $MgSO_4$ and the solvent was evaporated in vacuo. CC at silica gel (Et_2O/pentane 1:30) provided 2.11 g (56%) (*R*)-**6** (R_f=0.17) as a colourless oil. IR (film): ν=2930/2860 cm^{-1} (s, ν C–H), 1734 cm^{-1} (s, ν C=O, lactone), 1462 cm^{-1} (m, δ_{as} CH_3), 1250 cm^{-1} (s, ν C–O–C). ^1H NMR (200 MHz, $CDCl_3$): δ=0.92 (d, J=7.0 Hz, 3H, 2′-*Me*), 1.05–1.15 (m, 1H, 11-H), 1.25–1.45 (m, 12H, 5-H_2–10-H_2), 1.50 (m_c, 1H, 11-H), 1.67 (m_c, 2H, 4-H_2), 1.79 (m_c, 1H, 12-H), 2.30 (ddd, J=14.3, 7.1 and 5.6 Hz, 1H, 3-H), 2.42 (ddd, J=14.3, 11.6 and 5.7 Hz, 1H, 3-H), 3.87 (dd, J=10.8 and 9.7 Hz, 1H, 13-H), 4.01 (dd, J=10.8 and 3.4 Hz, 1H, 13-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=17.16 (q, 12-*Me*), 24.46/24.49/24.84/25.27/25.79/26.35/26.42 (t, C-4–C-10), 31.96 (t, C-11), 32.22 (d, C-12), 34.61 (t, C-3), 69.24 (t, C-13), 173.93 (s, C-2). MS (EI): *m/z* (%)=212 (5) [$M^{\oplus}$], 194 (13) [$M^{\oplus}-OH$], 139 (18) [$^{\oplus}-C_{10}H_{19}$], 125 (17) [$C_9H_{17}^{\oplus}$], 111 (27) [$C_8H_{15}^{\oplus}$], 98 (57) [$C_7H_{13}^{\oplus}$], 83 (52) [$C_6H_{11}^{\oplus}$], 69 (100) [$C_5H_9^{\oplus}$]. $[\alpha]_D^{20}$=+25.4, $[\alpha]_{578}^{20}$=+26.4, $[\alpha]_{546}^{20}$=+29.9, $[\alpha]_{436}^{20}$=+50.4, $[\alpha]_{365}^{20}$=+77.7, (c=2.2, $CHCl_3$). $C_{13}H_{24}O_2$ (212.2): calcd C 73.54%, H 11.39%; found C 73.57%, H 11.40%.

(2*R*,2′*S*)- and (2*S*,2′*S*)-2-[3′-(*tert*-Butyl-dimethyl-silyloxy)-2-methyl-propyl]-cyclononanone((*RS*,*S*)-3a/b). Prepared according to (*R*,*RS*)-**3a/b** from cyclononanone (**1**) and (2*R*)-*tert*-butyl-(3-iodo-2-methyl-propoxy)-dimethyl-silane (*R*)-**2** in 44% yield. For spectroscopic data see (*R*,*RS*)-**3a/b**.

(12*S*)-12-Methyl-oxacyclotridecane-2,10-dione ((*S*)-5). Prepared according to (*R*)-**5** from (*RS*,*S*)-**3a/b** in 87% yield. For spectroscopic data see (*R*,*RS*)-**3a/b**. $[\alpha]_D^{20}$=−21.6, $[\alpha]_{578}^{20}$=−22.8, $[\alpha]_{546}^{20}$=−26.5, $[\alpha]_{436}^{20}$=−52.0, $[\alpha]_{365}^{20}$=−104.1, (c=3.0, $CHCl_3$). $^{12}C_{13}H_{22}O_3$ ber. 226.1568, gef. 226.1569.

(12*S*)-12-Methyl-oxacyclotridecan-2-one ((*S*)-6). Prepared according to (*R*)-**6** from (*S*)-**5** in 67% yield. For spectroscopic data see (*R*)-**6**. $[\alpha]_D$=−25.1, $[\alpha]_{578}$=−26.2, $[\alpha]_{546}$=−30.3, $[\alpha]_{436}$=−49.8, $[\alpha]_{365}$=−78.6; (c=2.9, $CHCl_3$, 20°C). $^{12}C_{13}H_{24}O_2$ ber. 212.1776, gef. 212.1775; $^{12}C_{12}{}^{13}CH_{24}O_2$ ber. 213.1809, gef. 213.1807.

(12*R*)-12-Methyl-10-methylene-oxacyclotridecan-2-one ((*R*)-7). A suspension of 598 mg (1.67 mmol) methyltriphenylphosphonium bromide and 175 mg (1.57 mmol) potassium-*tert*-butoxide in 10 mL anhydrous Et_2O was refluxed under argon atmosphere for 30 min. The mixture was allowed to cool to room temp., then 250 mg (1.12 mmol) (*R*)-**5** in 5 mL anhydrous Et_2O were added dropwise and the mixture was heated to reflux for 1.5 h. The reaction mixture was hydrolysed by addition of 8 mL water at room temp. Usual workup and CC at silica gel (Et_2O/pentane 1:20) provided 172 mg (69%) (*R*)-**7** (R_f=0.36) as colourless oil. IR (film): ν=2932/2862 cm^{-1} (s, ν C–H), 1735 cm^{-1} (s, ν C=O, lactone), 1634 cm^{-1} (s, ν C=C), 1461 cm^{-1} (m, δ CH_3), 1239 cm^{-1} (s, ν_{as} C–O–C, lactone). ^1H NMR (300 MHz, $CDCl_3$): δ=0.92 (d, J=6.9 Hz, 3H, 14-*Me*), 1.25–1.67 (m, 9H, 4-H–8-H_2), 1.67 (ddd, J=13.7, 9.7 and 1.2 Hz, 1H, 11-H), 1.74 (ddd, J=14.0, 8.0 and 3.6 Hz, 1H, 4-H), 1.90–1.95 (m, 1H, 12-H), 1.91 (dddd, J=17.1, 7.0, 6.9 and 3.2 Hz, 1H, 9-H), 1.98 (m_c, 1H, 9-H), 2.32 (ddd, J=14.2, 8.8 and 3.8 Hz, 1H, 3-H), 2.34 (ddd, J=14.0, 4.4 and 1.2 Hz, 1H, 11-H), 2.42 (ddd, J=14.2, 8.0 and 3.6 Hz, 1H, 3-H), 3.82 ('t', J=10.6 Hz, 1H, 13-H), 4.09 (dd, J=10.6 and 3.2 Hz, 1H, 13-H), 4.70 (dddd, J=1.2, 1.2, 1.2 and 1.2 Hz, 1H, C=CH_2), 4.77 (dddd, J=1.2, 1.2, 1.2 and 1.2 Hz, 1H, C=CH_2). ^{13}C NMR (75 MHz, $CDCl_3$): δ=16.48 (q, 12-Me), 24.68/25.71/25.95/26.01/26.18 (t, C-4–C-8), 31.69 (d, C-12), 33.59 (t, C-9), 34.57 (t, C-11), 39.10 (t, C-3), 68.83 (t, C-13), 111.46 (t, 10=CH_2), 148.29 (s, C-10), 173.97 (s, C-2). MS (EI): *m/z* (%)=224 (11) [$M^{\oplus}$], 209 (8) [$M^{\oplus}-CH_3$], 195 (5) [$M^{\oplus}-C_2H_5$], 181 (7) [$M^{\oplus}-C_3H_7$], 167 (7) [$M^{\oplus}-C_4H_9$], 96 (100) [$C_7H_{12}^{\oplus}$], 81 (81) [$C_6H_9^{\oplus}$]. $[\alpha]_D^{25}$=+3.2, $[\alpha]_{578}^{25}$=+3.2, $[\alpha]_{546}^{25}$=+3.6, $[\alpha]_{436}^{25}$=+4.4, $[\alpha]_{365}^{25}$=+3.4, (c=2.2, $CHCl_3$). $C_{14}H_{24}O_2$ ber. C 74.95%, H 10.78%; gef. C 75.08%, H 10.76%.

(12*R*)-12-Methyl-3,3-bis-phenylsulfanyl-oxacyclotridecan-2-one ((*R*)-8). 1.60 mL (2.53 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane were added to 0.36 mL (2.53 mmol) diisopropylamine in 10 mL THF at −78°C. After stirring for 15 min, 300 mg (1.41 mmol) (*R*)-**6** were added. The mixture was allowed to warm to −20°C and then 552 mg (2.53 mmol) diphenyldisulphide in 5 mL THF were added dropwise. The mixture was stirred for 1 h at ambient temperature. Subsequently, the reaction mixture was poured into 50 mL Et_2O and 50 mL 2 N hydrochloric acid. The organic phase was separated and washed with 20 mL 2 N hydrochloric acid. Thereafter it was neutralized with saturated $NaHCO_3$, dried with $MgSO_4$ and concentrated in vacuo. CC on silica gel (Et_2O/pentane 1:40) provided 233 mg (38%) (*R*)-**8** (R_f=0.11) as colourless crystals which were recrystallized from (Et_2O/pentane). Mp. 86–88°C. IR (film): ν=2928/2863 cm^{-1} (s, ν C–H), 1717 cm^{-1} (s, ν C=O, lactone), 1472/1438 cm^{-1} (m, ν

phenyl), 1240 cm^{-1} (s, ν_{as} C–O–C, ester), 755/692 cm^{-1} (s, phenyl). UV (MeCN): λ_{max} (lg ϵ)=223 (5.132), 263 (4.657). ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.88 (d, J=7.0, 3H, 12-*Me*), 1.06–1.90 (m, 17H, 4-H_2–11-H_2, 12-H), 3.89 (d, J=6.6, 2H, 13-H_2), 7.33–7.43 (m, 6H, 3′-H–5′-H and 3″-H–5″-H), 7.61 (dd, J=8.1 and 1.2 Hz, 2H, 2′-H and 6′-H), 7.73 (dd, J=8.1 and 1.4 Hz, 2H, 2″-H and 6″-H). ^{13}C NMR (125 MHz, $CDCl_3$): δ=17.16 (q, 12-*Me*), 23.05/24.58/24.74/25.72/26.56 (t, C-5–C-10), 31.82 (d, C-12), 32.25 (t, C-11), 35.36 (t, C-4), 45.50 (t, C-11), 71.45* (t, C-13), 71.50* (s, C-3), 128.55/128.58 (d, C-3′, C-5′ and C-3″, C-5″), 129.31/129.44 (d, C-4′ and C-4″), 130.94/131.31 (s, C-1′ and C-1″), 136.29/136.31 (d, C-2′, C-6′and C-2″, C-6″), 169.67 (s, C-2). MS (EI): m/z (%)=428 (1) [$M^{\oplus}$], 319 (100) [$M^{\oplus}-C_6H_5S$], 209 (5) [$M^{\oplus}-C_{12}H_{11}S_2$], 109 (23) [$C_7H_5S^{\oplus}$]. $[\alpha]_D^{20}$=−42.7, $[\alpha]_{578}^{20}$=−45.2, $[\alpha]_{546}^{20}$=−53.5, $[\alpha]_{436}^{20}$=−118.9, $[\alpha]_{365}^{20}$=−271.7, (c=2.3, $CHCl_3$).

X-ray analysis of (*R*)-**8**:[29] The data of a crystal (Et_2O/pentane) with the approximate dimensions 0.15×0.4×1.3 mm were obtained with a Siemens P4 diffractometer (Mo K_α radiation, graphite monochromator). Cell dimensions: a=1079.9(1), b=1053.3(1), c=2082.7(2) pm; β=93.146(8)°, V=2365.3(4)×10^6 pm^3, monoclinic, space group $P2_1$; Z=4. ρ_{calcd}=1.204 g/cm^3, 10895 unique reflections, of which 8810 [$F_0>3\sigma(F)$] were observed in the θ range 1.75–27.5°, measured with ω-scan technique. The structure was solved by using direct-phase determination and refined on F by using SHELXTL-PLUS. Positional parameters, anisotropic displacement parameters for all atoms except for hydrogen atoms, groupwise isotropic displacement parameters for all hydrogen atoms, treated as rigid groups. R=0.057, R_w=0.057, $w=1/\sigma^2(F)$.

(8*R*)-3,3,8-Trimethyl-1,5,10-trioxa-spiro[5.12]octadecan-11-one ((*R*)-9). 100 mg Amberlyst® 15 were added to a solution of 1.00 g (4.46 mmol) (*R*)-**5** and 2.00 g (19.2 mmol) 2,2-dimethyl-1,3-propanediol in 100 mL anhydrous toluene. The mixture was refluxed in a *Dean* apparatus for 48 h. The resin was filtered off and the filtrate concentrated in vacuo. The crude product was purified by CC at silica gel (Et_2O/pentane 1:10). 905 mg (66%) (*R*)-**9** (R_f=0.20) were obtained as colourless oil besides 174 mg (17%) (*R*)-**5**. IR (film): ν=2950/2866 cm^{-1} (s, ν C–H), 1732 cm^{-1} (s, ν C=O, lactone), 1461 cm^{-1} (m, δ_{as} CH_3), 1193 cm^{-1} (s, ν C–O–C, acetal). ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.89 (s, 3H, 3-*Me*), 1.02 (s, 3H, 3-*Me*), 1.04 (d, J=7.2 Hz, 3H, 8′-*Me*), 1.16–1.96 (m, 15H, 7-H_2, 8-H, 13-H_2–18-H_2), 2.36 (m, 2H, 12-H_2), 3.37–3.56 (m, 4H, 2-H_2, 4-H_2), 3.68 (t, J=10.7 Hz, 1H, 9-H), 4.12 (dd, J=10.7 and 2.9 Hz, 1H, 9-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ=18.61 (q, 8-*Me*), 22.55/22.89 (q, 3-*Me*), 20.75/24.03/25.52, 26.00/26.65/29.03/29.93/ 30.53 (t, C-13–C-18), 34.40 (t, C-12), 38.43 (t, C-7), 69.87/70.00/70.15 (t, C-2, C-4, C-9), 101.15 (s, C-6), 173.71 (s, C-11). MS (CI): m/z (%)=313 (100) [$M^{\oplus}$+H], 227 (53) [$M^{\oplus}-C_4H_6O_2$]. $[\alpha]_D^{28}$=+10.3, $[\alpha]_{578}^{28}$=+10.8, $[\alpha]_{546}^{28}$=+12.0, $[\alpha]_{436}^{28}$= +18.4, $[\alpha]_{365}^{28}$=+28.7, (c=1.8, $CHCl_3$).—$^{12}C_{18}H_{32}O_4$ ber. 312.2300, gef. 312.2300; $^{12}C_{17}{}^{13}CH_{32}O_4$ ber. 313.2334, gef. 313.2334.

(8*R*)-3,3,8-Trimethyl-12,12-bis-phenylsulfanyl-1,5,10-trioxa-spiro[5.12]octadecan-11-one ((*R*)-10). 4.45 mL (7.12 mmol) of a 1.6 M solution of *n*-butyllithium in *n*-hexane were added to 0.980 mL (7.12 mmol) diisopropylamine in 40 mL THF at −78°C and then stirred for 20 min at 0°C. The mixture was recooled to −78°C and 740 mg (2.37 mmol) (*R*)-**9** were added via syringe and then stirred for 30 min. Subsequently, 1.55 g (7.12 mmol) diphenyldisulphide in 10 mL THF were added while cooling with an ice bath. The mixture was allowed to warm to room temperature and stirred for further 30 min. Then the reaction mixture was poured into 300 mL Et_2O and washed successively with 50 mL 2 N hydrochloric acid and 50 mL water. The organic layer was neutralized with sat. aqueous $NaHCO_3$, dried with $MgSO_4$ and concentrated in vacuo. CC at silica gel (Et_2O/pentane 1:10) provided 985 mg (78%) (*R*)-**10** (R_f=0.20) as a colourless, highly viscous oil. IR (film): ν=2954/2849 cm^{-1} (s, ν C–H), 1724 cm^{-1} (s, ν C=O, lactone), 1467 cm^{-1} (m, δ_{as} CH_3), 1465/1436 cm^{-1} (m, ν phenyl), 1234 cm^{-1} (s, ν_{as} C–O–C, lactone), 1129 cm^{-1} (s, ν C–O–C, acetal), 746/690 cm^{-1} (s, phenyl). UV (MeCN): λ_{max} (lg ϵ)=219 (4.352), 264 (sh, 3.673). ^{1}H NMR (200 MHz, $CDCl_3$): δ=0.87 (s, 3H, 3-*Me*), 1.00 (s, 3H, 3-*Me*), 1.01 (d, J=6.8 Hz, 3H, 8′-*Me*), 1.15–2.00 (m, 15H, 7-H_2, 8-H, 13-H_2–18-H_2), 3.34–3.49 (m, 4H, 2-H_2, 4-H_2), 3.698 (t, J=10.47 Hz, 1H, 9-H), 4.102 (dd, J=10.47 and 2.9 Hz, 1H, 9-H), 7.27–7.46 (m, 8H, 2′-H, 3′-H, 5′-H, 6′-H, 2″-H, 3″-H, 5″-H and 6″-H), 7.65–7.70 (m, 2H, 4′-H and 4″-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=18.55 (q, 8-*Me*), 20.21* (t, C-14), 22.52 (q, 3-*Me*), 22.88* (t, C-16), 25.35* (t, C-15), 26.23* (t, C-17), 28.85 (q, 3-*Me*), 29.83 (t, C-18), 30.73 (s, C-3), 30.73 (d, C-8), 34.40 (t, C-13), 38.16 (t, C-7), 69.91/70.04/70.13 (t, C-2, C-4, C-9), 70.17 (s, C-12), 101.05 (s, C-6), 128.35/128.49/128.53/128.59 (d, C-3′, C-5′ and C-3″, C-5″), 129.32/129.44 (d, C-4′ and C-4″), 131.01/131.20 (s, C-1′ and C-1″), 133.45/133.84/136.09/136.49 (d, C-2′, C-6′and C-2″, C-6″), 169.46 (s, C-11). $[\alpha]_D^{20}$=+0.5, $[\alpha]_{578}^{20}$=+9.1, $[\alpha]_{546}^{20}$=+10.4, $[\alpha]_{436}^{20}$=+18.9, $[\alpha]_{365}^{20}$=+32.5; (c=1.2, $CHCl_3$). MS (EI): m/z (%)=528 (3) [$M^{\oplus}$], 419 (100) [$M^{\oplus}-C_6H_5S$], 419 (94) [$M^{\oplus}-C_{11}H_{15}OS$]. $C_{30}H_{40}O_4S_2$ ber. 528.2368, gef. 528.2364.

(12*R*)-12-Methyl-3,3-bis-phenylsulfanyl-oxacyclotridecane-2,10-dione ((*R*)-11). 150 mg Amberlyst® 15 were added to a solution of 732 mg (1.38 mmol) (*R*)-**10** in 25 mL CH_2Cl_2 and stirred overnight at ambient temperature. The resin was filtered off and extracted with CH_2Cl_2. The solvent was removed in vacuo and the product purified by CC at silica gel (Et_2O/pentane 1:10) to yield 277 mg (45%) (*R*)-**11** (R_f=0.23) as colourless crystals. mp. 128–129°C. IR (film): ν=2957/2920 cm^{-1} (s, ν C–H), 1719 cm^{-1} (s, ν C=O, lactone, ketone), 1470 cm^{-1} (m, δ_{as} CH_3), 1233 cm^{-1} (s, ν C–O–C), 753/688 cm^{-1} (s, phenyl). UV (MeCN): λ_{max} (lg ϵ)=220 (4.595), 278 (3.942). ^{1}H NMR (300 MHz, $CDCl_3$): δ=0.98 (d, 3H, J=7.1 Hz, 12-*Me*), 1.10–1.65 (m, 8H, 5-H_2–8-H_2), 1.69 (ddd, J=14.1, 10.5 and 4.6 Hz, 1H, 4-H),), 1.90 (ddd, J=14.1, 10.6 and 5.2 Hz, 1H, 4-H), 2.17 (dd, J=18.1 and 5.0 Hz, 1H, 11-H), 2.25 (dd, J=7.9 and 5.1 Hz, 1H, 9-H), 2.35 (m_c, 1H, 12-H), 2.36 (ddd, J=14.1, 6.8 and 4.5 Hz, 1H, 9-H), 2.73 (dd, J=18.1 and 6.6 Hz, 1H, 11-H), 3.88 (dd, J=10.8 and 8.1 Hz, 1H, 13-H), 3.97 (dd, J=10.8 and 3.6 Hz, 1H, 13-H), 7.30–7.50 (m, 6H, 3′-H–5′-H and 3″-H–5″-H), 7.63 (dd, J=7.9 and 1.5 Hz, 2H, 2′-H, 6′-H), 7.72 (dd, J=7.6 and

1.5 Hz, 2H, 2″-H, 6″-H). ^{13}C NMR (75 MHz, $CDCl_3$): δ=17.76 (q, 12-*Me*), 23.30/24.12/26.50/26.70 (t, C-5–C-8), 27.30 (d, C-12), 35.34 (t, C-4), 42.29 (t, C-9), 45.50 (t, C-11), 69.89 (t, C-13), 71.42 (s, C-3), 128.61/128.66 (d, C-3′, C-5′ and C-3″, C-5″), 129.31/129.50 (d, C-4′ and C-4″), 131.00/131.70 (s, C-1′ and C-1″), 135.95/136.23 (d, C-2′, C-6′ and C-2″, C-6″), 169.57 (s, C-2), 210.07 (s, C-10). $[\alpha]_D^{33}$=−20.1, $[\alpha]_{578}^{33}$=−21.2, $[\alpha]_{546}^{33}$=−25.0, $[\alpha]_{436}^{33}$=−53.9, $[\alpha]_{365}^{33}$=−118.8; (*c*=2.0, $CHCl_3$). $C_{23}H_{30}O_3S_2$ (442.2) ber. C 67.84%, H 6.83%; gef. C 67.79%, H 6.68%.

X-ray analysis of (*R*)-**11**:[29] The data of a crystal (Et_2O/pentane) with the approximate dimensions 0.45×0.4×0.2 mm were obtained with a Siemens P4 diffractometer (MoK_α radiation, graphite monochromator). Cell dimensions: *a*=730.60(4), *b*=964.95(6), *c*=3332.5(2) pm; *V*=2349.4(2)×10^6 pm^3, orthorhombic, space group $P2_12_12_1$; *Z*=4. ρ_{calcd}=1.251 g/cm^3, 5350 unique reflections, of which 4052 [$F_0>3\sigma(F)$] were observed in the θ range 1.75–27.5°, measured with ω-scan technique. The structure was solved by using direct-phase determination and refined on *F* by using SHELXTL-PLUS. Positional parameters, anisotropic displacement parameters for all atoms except for hydrogen atoms, groupwise isotropic displacement parameters for all hydrogen atoms, treated as rigid groups. *R*=0.054, R_w=0.047, $w=1/\sigma^2(F)$.

(12*R*)-12-Methyl-10-methylene-3,3-bis-phenylsulfanyl-oxacyclotridecan-2-one ((*R*)-12). Prepared according to (*R*)-**7**. From 180 mg (0.41 mmol) (*R*)-**11** and 242 mg (0.68 mmol) methyltriphenylphosphonium bromide 84 mg (47%) of (*R*)-**12** were obtained as a slightly yellow oil; R_f=0.48 (Et_2O/pentane 1:10). IR (film): ν=2931 cm^{-1} (s, ν C–H), 1726 cm^{-1} (s, ν C=O, lactone), 1642 cm^{-1} (s, ν C=C), 1434 cm^{-1} (m, δ_{as} CH_3), 1234 cm^{-1} (s, ν C–O–C), 749/691 cm^{-1} (s, phenyl). UV (MeCN): λ_{max} (lg ϵ)=221 (5.322), 262 (4.696). ^{1}H NMR (500 MHz, $CDCl_3$): δ=0.90 (d, 3H, *J*=6.9 Hz, 12-*Me*), 1.20–1.56 (m, 8H, 5-H_2–8-H_2), 1.61 (ddt, *J*=14.4, 9.0 and 1.1 Hz, 1H,11-H), 1.74 (ddd, *J*=14.2, 11.1 and 5.8 Hz, 1H, 4-H), 1.82–1.94 (m, 4H, 9-H-2, 12-H2, therein 1.86 (ddd, *J*=14.2, 11,1 and 4.2 Hz, 4-H), 2.21 (ddd, *J*=14.4, 3.0 and 1.2 Hz, 1H, 11-H), 3.90 (dd, *J*=10.5 and 3.1 Hz, 1H, 13-H), 3.98 (dd, *J*=10.5 and 10.5 Hz, 1H, 13-H), 4.63 (dt, *J*=2.7 and 1.2 Hz, 1H, 10=CH_2), 4.72 (ddd, *J*=2.7, 1.2 and 1.0 Hz, 1H, 10=CH_2), 7.32–7.42 (m, 6H, 3′-H–5′-H and 3″-H–5″-H), 7.61 (dd, *J*=8.1 and 1.3 Hz, 2H, 2″-H, 6″-H), 7.71 (dd, *J*=8.0 and 1.4 Hz, 2H, 2′-H, 6′-H). ^{13}C NMR (125 MHz, $CDCl_3$): δ=16.61 (q, 12-*Me*), 23.41/25.31/25.79/26.04 (t, C-5–C-8), 31.34 (d, C-12), 34.03 (t, C-9), 35.70 (t, C-4), 38.99 (t, C-11), 70.41 (t, C-13), 71.60 (s, C-3), 111.43 (t, 10=CH_2),128.61/128.64 (d, C-3′, C-5′ and C-3″, C-5″), 129.30/129.48 (d, C-4′ and C-4″), 131.12/131.35 (s, C-1′ and C-1″), 136.17/136.34 (d, C-2′, C-6′ and C-2″, C-6″), 147.73 (s, C-10), 169.63 (s, C-2). $[\alpha]_D^{18}$=−38.4, $[\alpha]_{578}^{18}$=−40.5, $[\alpha]_{546}^{18}$=−48.1, $[\alpha]_{436}^{18}$= −105.3, $[\alpha]_{365}^{18}$=−238.3; (*c*=2.6, $CHCl_3$). MS (EI): *m/z* (%)=440 (4) [$M^\oplus$], 331 (100) [$M^\oplus-C_6H_5S$], 303 (64) [$M^\oplus-C_7H_5OS$], 221 (16) [$M^\oplus-S_2C_{12}H_{11}$]. $C_{26}H_{32}O_2S_2$ ber. 440.1844, gef. 440.1844; $C_{25}{}^{13}CH_{32}O_2S_2$, ber. 441.1877, gef. 441.1877.

(12*R*)-10-[(2,4-Dinitro-phenyl)-hydrazono]-12-methyl-oxacyclotridecan-2-one ((*R*)-13). From 100 mg (0.88 mmol) (*R*)-**5** and 0.40 g (2.03 mmol) 2,4-dinitrophenylhydrazine 142 mg (56%) of (*R*)-**13** were obtained as orange crystals under standard conditions; R_f=0.31 (Et_2O/pentane 1:4). Mp. 102–104°C. IR (film): ν=3333 cm^{-1} (s, N–H), 2949/2864 cm^{-1} (s, ν C–H), 1731 cm^{-1} (s, ν C=CO, lactone), 1614 cm^{-1} (s, ν C=N), 1591/1329 cm^{-1} (s, ν NO_2), 1169 cm^{-1} (s, ν_{as} C–O–C), 840 cm−1 (s, ν 1,2,4-trisubstitution). UV (MeCN): λ_{max} (log ϵ)=233 (5.080), 365 (5.226). ^{1}H NMR (500 MHz, $CDCl_3$): δ=1.07 (d, 3H, *J*=6.9 Hz, 12-*Me*), 1.30–1.54/1.65–1.80 (m, 10H, 4-H_2–8-H_2), 2.19 (dd, *J*=15.1 and 8.1 Hz, 1H,11-H), 2.25–2.40 (m, 4H, 3-H, 9-H_2, 12-H), 2.50 (dd, *J*=14.7 and 7.2 Hz, 1H, 3-H), 2.69 (dd, *J*=15.1 and 4.0 Hz, 1H, 11-H), 3.93 (dd, *J*=10.8 and 9.1 Hz, 1H, 13-H), 4.24 (dd, *J*=10.8 and 3.4 Hz, 1H, 13-H), 7.94 (d, *J*=9.6 Hz, 1H, 6′-H), 8.31 (dd, *J*=9.6 and 2.5 Hz, 1H, 5′-H), 9.14 (d, *J*=2.5 Hz, 1H, 3′-H), 11.26 (s, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ=16.96 (q, 12-*Me*), 22.78/24.38/25.81/26.44/26.98/27.84 (t, C-4–C-9), 30.51 (d, C-12), 34.38 (t, C-3), 40.54 (t, C-11), 67.93 (t, C-13), 116.32 (d, C-6′), 123.55 (d, C-3′), 128.93 (s, C-2′), 130.03 (d, C-5′), 137.60 (s, C-4′), 145.21 (s, C-1′), 160.60 (s, C-10), 173.83 (s, C-2).—MS (CI): *m/z* (%)=407 (100) [$M^\oplus$+H], 377 (6) [$M^\oplus$+H−NO], 347 (4) [$M^\oplus$+H−N_2O_2], 226 (7) [$M^\oplus-C_6H_2N_3O_4$]. $[\alpha]_D^{16}$=−59.9, $[\alpha]_{578}^{16}$=−60.0, $[\alpha]_{546}^{16}$=−56.4, (*c*=1.5, $CHCl_3$). $C_{19}H_{26}N_4O_6$ (406.2): ber. C 56.16%, H 6.45%; gef. C 56.25%, H 6.30%.

X-ray analysis of (*R*)-**13**:[29] The data of a crystal (Et_2O/pentane) with the approximate dimensions 0.4×0.4×0.4 mm^3 were obtained with a Siemens P4 diffractometer (MoK_α radiation, graphite monochromator). Cell dimensions: *a*=979.78(5), *b*=1359.30(7), *c*=1520.58(5) pm; *V*=2025.1(7)×10^6 pm^3, orthorhombic, space group $P2_12_12_1$; *Z*=4. ρ_{calcd}=1.333 g/cm^3, 4651 unique reflections, of which 3763 [$F_0>3\sigma(F)$] were observed in the θ range 1.75–27.5°, measured with ω-scan technique. The structure was solved by using direct-phase determination and refined on *F* by using SHELXTL-PLUS. Positional parameters, anisotropic displacement parameters for all atoms except for hydrogen atoms, groupwise isotropic displacement parameters for all hydrogen atoms, treated as rigid groups. *R*=0.045, R_w=0.043, $w=1/\sigma^2(F)$.

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