A Convenient Method for the Preparation of Bicyclic Dihydro-1,4-dioxins, Dihydro-1,4-oxathiins, Dihydro-1,4-dithiins and Related Compounds

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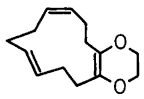
Acid catalysed reactions of cyclic α-hydroxy ketones with ethylene glycol, 2-mercaptoethanol and 1,2-ethanedithiol furnished in most cases the corresponding dihydro-1,4-dioxin, dihydro-1,4-oxathiin and dihydro-1,4-dithiin derivatives, respectively, in high yields. Similar reactions of 2-hydroxycyclooctanone and 2-hydroxycyclododecanone with 1,3-propanediol gave the corresponding bicyclic dihydro-1,4-dioxepins as sole products. From 2-hydroxycyclohexanone and 1,3-propanedithiol the corresponding bicyclic dihydro-1,4-dithiepin was obtained. In some cases the reaction gave rise to mixtures of isomeric products. A general mechanism for the reaction is proposed.

In the course of some synthetic work we adventiously discovered that the α-hydroxy ketone (5*E*,9*Z*)-2-hydroxycyclododecadien-1-one reacted with ethylene glycol forming the bicyclic dihydrodioxin **1** in 90 % yield. This result provoked our interest in the reaction generally, and a literature search revealed that Summerbell and Berger[1] about thirty years ago reported the isolation of 2,3-diphenyldihydro-1,4-dioxin (**2**) in about 30 % yield from the acid catalyzed reaction of benzoin and ethylene glycol. Although subsequent use of this reaction has been reported,[2] the scope has apparently not been investigated.

The present study indicates that the reaction is quite general for cyclic α-hydroxy ketones **3**, giving rise to the bicyclic dihydrodioxins **4** in high yields using ethylene glycol, and the corresponding homologues when 1,3- and 1,4-diols were used. Moreover, 2-mercaptoethanol, 1,2-ethanedithiol and 1,3-propanedithiol undergo similar reactions even more readily.

The starting materials, the α-hydroxy ketones



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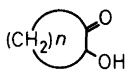

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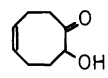

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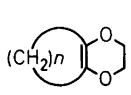

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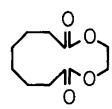
a: *n* = 3
b: " = 4
c: " = 5
d: " = 6
e: " = 10



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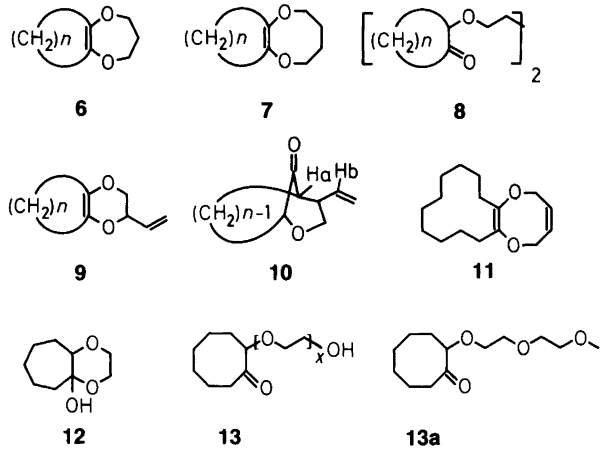
3, were prepared by permanganate oxidation of the corresponding cyclic olefins under almost neutral conditions.[3] The reaction is very simple experimentally, but the yields were moderate at best and particularly poor in the case of cyclopentene and cyclohexene. Hence, the acyloins **3a** and **3b** were prepared in high yields from the corresponding ketones by oxidation with *o*-iodosylbenzoic acid in methanol followed by hydrolysis.[4] However, we found that the cyclic α,α-dimethoxy alcohols, the primary product of this oxidation, can conveniently replace the acyloins as starting material, thus rendering the hydrolysis step superfluous.

Reactions of the acyloins **3** or the corresponding dimethyl acetals with the diols were carried out by heating under reflux a benzene solution of the reagents in the presence of catalytic amounts of *p*-toluenesulfonic acid monohydrate while water was removed azeotropically. The progress of the reactions was followed by GLC analysis of aliquots. Under these conditions and with ethylene glycol as the diol component, the sole products were the corresponding dihydro-1,4-dioxins **4a-e**.

The compounds were characterised spectroscopically. The IR spectra exhibited a strong band at approximately 1700 cm^{-1} due to the double bond stretching vibration. The NMR spectra fully supported the structures. Noteworthy is the signal at $\delta \sim 64$ ppm in the ^{13}C NMR spectra, assigned to the methylene carbon adjacent to oxygen. Chemical evidence for the position of the double bond was obtained by oxidative cleavage; [5,2b] treatment of compound **4d** with *m*-chloroperbenzoic acid in dichloromethane at room temperature afforded the dilactone **5** in 89 % yield.

Other diols underwent the reaction as well. Thus, treatment of the α-hydroxy ketone **3d** with 1,3-propanediol under the above conditions afforded as sole product the dihydro-1,4-dioxepin derivative **6d** in 75 % yield, and from **3e** the corresponding derivative **6e** was obtained in 83 % yield. These reactions were slower than those with ethylene glycol. On the other hand, reactions of the acyloins **3d** and **3c** with 1,4-butanediol did not give rise to the tetrahydro-1,4-dioxacin **7**, but the diketones **8d** and **8e** were obtained in 80 and 84 % yields, respectively. Changing the reaction conditions had no significant effect on these results. The double bond of compounds **6d** and **6e** appears to be sensitive to air oxidation; in chloroform solution most of the latter was oxidized after a few hours in contact with air.

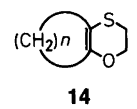
The results from reactions of (2*Z*)-1,4-butenediol and the acyloins turned out to depend on the ring size. The product from the reaction of **3b** consisted of a single volatile compound which was isolated in 74 % yield. This was determined spectroscopically to be the vinyl-substituted dihydrodioxin **9b**. The product of reaction of **3d** and the butenediol consisted of two compounds which were isolated in 62 and 24 % yields. The major component was identified as the vinyldihydrodioxin **9d**, while the minor one was characterized as the isomeric ketone **10**. The presence of a carbonyl group in the latter was established



by IR absorption at 1710 cm^{-1} and a signal at δ 220 ppm in the ^{13}C NMR spectrum. The other spectral data also support the structure **10d**, but the assignment of the *exo* configuration rests on conclusions drawn from NOE experiments only. The bridgehead proton H_a interacts with the vinyl proton H_b (see structure **10**), which is compatible with an *exo* configuration. Similar results were obtained from the reaction of **3e** and the butendiol. The product obtained in 82 % yield consisted of the structural isomers **9e** and **10e** in a 2.9:1 ratio. The assignment of structure **10e** is based on spectral arguments similar to those presented above for the homologue. We were not able to detect any of the initially expected dihydro-1,4-dioxacin derivatives (**11**).

While monitoring the reactions by GLC we noticed in many cases the initial formation of a compound with higher retention time than that of the final product, e.g. the dihydrodioxin. In most cases this compound reacted further at a rate comparable to that of its formation. However, in the case of **3c** the conversion of the intermediate was comparatively slow; this allowed its isolation in 75 % yield. It was characterized spectroscopically as the hydroxydioxane **12**. The IR spectrum exhibited strong absorption at 3350 cm^{-1} due to the hydroxy group, and in the ^{13}C NMR spectrum the signal for the hemiacetal carbon appeared at δ 112.15 ppm. In a separate experiment, compound **12** was transformed quantitatively to the dihydrodioxin **4c** in the presence of *p*-toluenesulfonic acid.

We also carried out reactions of the acyloins with polyethylene glycols, anticipating the formation of crown ethers. Employing the usual conditions, e.g. a small excess of the diol, reactions of the acyloins **3b** and **3d** with diethylene glycol afforded the dihydrodioxins **4b** and **4d** in 73 and 74 % yields, respectively; apparently, elimination of a two-carbon fragment had occurred. However, employing a large excess of diethylene glycol, **3d** was converted into a 1:1 mixture of **4d** and the hydroxy ketone **13** (x = 2). On the other hand, treatment of **3d** with diethylene glycol monomethyl ether in the same way furnished the ketone **13a** as the only product in 92 % yield. In separate experiments under the same conditions, **3d** reacted with triethylene and tetraethylene glycol to give the corresponding hydroxy ketones **13** (x = 3 and 4, respectively) in better than 80 % yields. Cyclization was not accomplished under a variety of conditions, including the use of the template effect of lithium tetrafluoroborate.[6]



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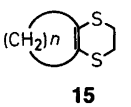

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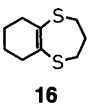

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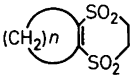

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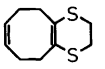


15f

Reactions of the acyloins **3a,b,d,e** with 2-mercaptoethanol under the above conditions gave as sole products the dihydrooxathiins **14a,b,d,e**, respectively. Similarly, treatment of **3a-e** with 1,2-ethanedithiol gave exclusively the corresponding dihydrodithiins **15a-e**, and reaction of the acyloin **3b** with 1,3-propanedithiol afforded the dihydro-1,4-dithiepin **16**. The products were isolated in 82–92 % yields and characterized spectroscopically. Furthermore, compounds **15b,d** were oxidized to the corresponding sulfones **17b,d** with peracid.

In the NMR spectra of the dihydrooxathiins, the signals for the protons α to oxygen appear at δ ~ 4.2 ppm and the corresponding carbon at δ ~ 65 ppm, both slightly downfield from those for the dihydrodioxins **4**. The signals for methylene protons adjacent to sulfur in compound **14** appear at δ ~ 3.0 ppm, slightly upfield from those for the dihydrodithiins **15**; hence, with regard to the chemical shifts of the methylene groups α to the hetero atoms in compounds **4**, **14** and **15**, the presence of the second hetero atom has little effect. However, the olefinic carbon adjacent to sulfur in compounds **14** is strongly shielded (~ 20 ppm) compared with that in the dihydrodithiins, while the olefinic carbon adjacent to oxygen is deshielded (~ 10 ppm) relative to those in the dihydrodioxins. An explanation for this effect has been presented.[7] It should be noted that the olefinic carbons of compound **4a** give rise to a signal about 15 ppm upfield compared with the other dihydrodioxins. Normally, the shielding of the olefinic carbons in five-membered or larger carbocyclic rings are not that strongly affected by the ring size.

Discussion

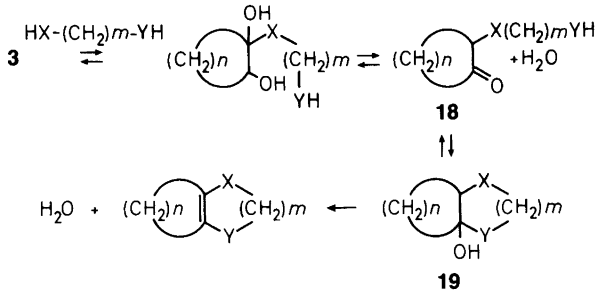
In their original work, Summerbell and Berger[1] explained the formation of dihydrodioxin **1** by rearrangement of the initially formed ethylene ketal of benzoin; however, the present results do not indicate or require the presence of the corresponding ketals. The mechanism outlined in Scheme 1 accommodates our findings starting from acyloins. With α-hydroxy acetals as starting material the mechanism will be very similar, also proceeding through ketone **18**.

Protonation of the carbonyl group of the acyloin facilitates nucleophilic addition of a hydroxy or thiyl group of the reactant. Subsequent elimination of water leads to the ketone **18**, which may be a product of the reaction as evidenced by isolation of the hydroxy ketones **13**. However, the ketone **18** may react further intramolecularly to the hydroxy compound **19** or, in cases where this is unfavoured, react with a second molecule of the acyloin. These reaction modes are born out by the isolation of compounds **12** and **8**, respectively. Elimination of a molecule of water from **19** yields the observed bicyclic products. The equilibria depicted in Scheme 1 require that the products **4**, **14** and **15** may be hydrolyzed back to the acyloins and, furthermore, that two heterobicyclic compounds may be interconverted. The first condition was satisfied when the compounds **4b**, **14b** and **15b**, respectively, were hydrolyzed in acidic aqueous acetone to the acyloin **3b**. According to standard heat of formation data, the reaction of dihydrodioxin **4d** with 1,2-ethanedithiol to give the dihydrodithiin **15d** is exothermic, and the latter was indeed formed quantitatively by heating a benzene solution of these reagents in the presence of *p*-toluenesulfonic acid.

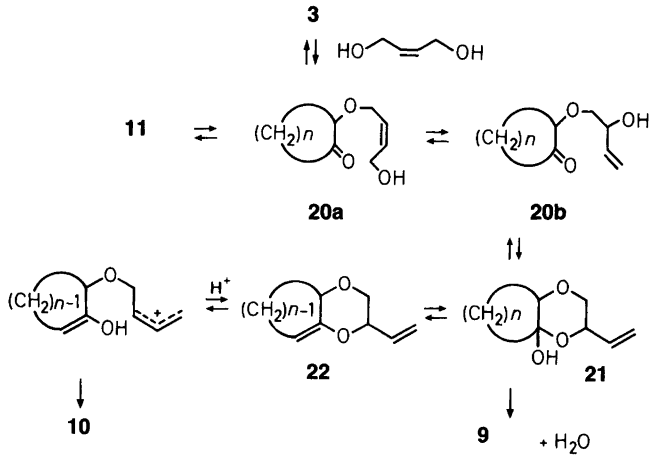
Isolation of the dihydrodioxins **4b** and **4d** from reactions of the respective acyloins and diethylene glycol appeared interesting at first, but we soon discovered that under the reaction conditions the latter was cleaved to ethylene glycol which gives rise to these compounds. Moreover, the hydroxyketone **13** ($x = 2$) was stable under the same conditions and thus could not be the source of the dihydrodioxins.

The formation of the vinyl-substituted compounds **9** and **10** needs further explanation as well. We assume the reactions leading to these compounds proceed with formation of the ketone **20a**, as depicted in Scheme 2. The allylic hydroxy group of **20a** equilibrates under the acidic conditions and the secondary hydroxy group of **20b** evidently reacts faster intramolecularly, furnishing the products **9** and **10** (Scheme 2). It is quite clear that the course of these reactions is governed by conformational effects. On its way to product, **20b** passes through the intermediate **21**, which on loss of water may give rise to the observed compounds **9** or the isomer **22**. The latter was not encountered, but results from similar reactions[8] suggest that its formation is feasible. The acid catalyzed rearrangement of **22**, most probably stepwise, explains the presence of the bicyclic ketone **10** in the product. It is important to note that compounds **9** and **10** are not interconverted under the reaction conditions.

Depending on the availability of cyclic α-hydroxy ketones, the present one-step method seems a competitive supplement to the synthetic procedures already available for these fused het-



Scheme 1.



Scheme 2.

erocyclic compounds.[8,9] Moreover, the reaction may be useful as a way of protecting an α-hydroxy ketone function.

Experimental

General. GLC analyses were performed on a 2.4 m packed column of 3% SP2100, and a 30 m wall-coated capillary column of SP2100. IR spectra were recorded on Perkin-Elmer 225 and 281B instruments. NMR spectra were recorded on Varian EM 360A and XL-300 spectrometers. MS spectra were obtained on a Micromass 7070 F instrument coupled to a Carlo Erba 4200 GLC apparatus.

Materials. Commercially available reagents and solvents were purified and dried when necessary by usual methods. The α-hydroxy ketones were prepared by permanganate oxidation of the respective olefins (Method A[3]) or by *o*-iodosylbenzoic acid oxidation of the respective ketones followed by hydrolysis (Method B[4]), and identified by comparison with physical data reported in the literature. Method A: 2-hydroxycyclohexanone (**3b**)[10], 20%; 2-hydroxycycloheptanone (**3c**),[10] 50%; 2-hydroxycyclooctanone (**3d**),[10] 47%; 2-hydroxycyclododecanone (**3e**),[10] 36%. Method B: 2-hydroxycyclopentanone (**3a**),[10] 82%; **3b**, 74%.

The compound (5*Z*)-2-hydroxycycloocten-1-one (**3c**) was prepared using the following literature procedures: Oxidation of *trans*-(5*Z*)-cyclooctene-1,2-diol[11] with dicyclohexylcarbodiimide-DMSO[12] furnished the dione in 79% yield, and its reduction with zinc in aq. DMF[13] provided the acyloin **3f**[14] in 72% yield. The α-hydroxy acetals were prepared according to Method B, without the hydrolysis step.

General Procedure. A solution of α-hydroxy ketone **3** or the corresponding dimethyl acetal (1 equiv), the diol, mercaptoethanol or dithiol (1.3 equiv.) and *p*-toluenesulfonic acid (15 mg per mmol of **3**) in benzene, unless stated otherwise (~ 15 ml per mmol of **3**) was heated under reflux while water was collected using a Dean-Stark trap. The reaction was monitored by GLC and the time required for completion is indicated below for each compound. The acid was neutralized with 10% $NaHCO_3$ solution, and the organic phase dried ($MgSO_4$) and evaporated under vacuum. The residue was purified by flash chromatography on neutral alumina (100–120 mesh) and recrystallized when appropriate.

$\Delta^{1(12)}$-13,16-Dioxabicyclo[10.4.0]hexadeca-(4Z, 8E)-8-triene (**1**). The compound was obtained from (5*E*,9*Z*)-2-hydroxycyclododecadien-1-one and ethylene glycol as a liquid in 90% yield. The reaction time was 3 h. ^1H NMR (60 MHz, CCl_4): δ 2.09 (m, 12H), 3.92 (s, 4H), 5.38 (m, 4H). ^{13}C NMR (15 MHz, CCl_4): δ 26.18 (CH_2), 26.83 (CH_2), 28.00 (CH_2), 29.11 (CH_2), 29,56 (CH_2), 30.54 (CH_2), 63.87 (CH_2-O), 128,13, 130,21 (=CH), 133.07 (=C-O). IR (film): 1695 (s), 1200 (s), 975 (s), 730 cm^{-1}. MS(EI): *m/z* 220 (66; M^+), 112(100).

$\Delta^{1(6)}$-2,5-Dioxabicyclo[4.3.0]nonene (**4a**). The compound was prepared from the dimethyl acetal of **3a** and ethylene glycol as a liquid in 84 % yield after 10 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.74 (m, 6H), 3.90 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.58 (CH_2), 35.95 (CH_2), 64.24 (CH_2O), 118.55 (=C–O). IR (film): 1722, 1210, 1110 cm^{-1}.

$\Delta^{1(6)}$-2,5-Dioxabicyclo[4.4.0]decene (**4b**). The compound was obtained from **3b** and ethylene glycol as a liquid in 90% yield after 10 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.62(m,4H), 2.08 (m,4H), 4.05 (s,4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.83 (CH_2), 26.21 (CH_2), 64.62 (CH_2–O), 130.18 (=C–O). IR(film): 1700(s), 1200(s), 1115(s) cm^{-1}. GC/MS (EI): *m/z* 140(33,M^+), 112(23), 84(60), 55(100).

$\Delta^{1(7)}$-8,11-Dioxabicyclo[5.4.0]undecene (**4c**). The compound was obtained from **3c** and ethylene glycol as a liquid in 91 % yield after 4 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.59 (m,6H), 2.17 (m,4H), 3.95 (s,4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 25.85 (CH_2), 30.30 (CH_2), 30.64 (CH_2), 64.14 (CH_2–O), 134.09 (=C–O). IR (film): 1695(s), 1175(s) cm^{-1}. GC/MS (EI): *m/z* 154(49; M^+), 98(64), 70(30), 69(41), 55(100).

$\Delta^{1(8)}$-9,12-Dioxabicyclo[6.4.0]dodecene (**4d**). The compound was obtained from **3d** and ethylene glycol as a liquid in 92 % yield after 3 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.58 (m,8H), 2.15 (t, 4H, J = 7,5 Hz), 4.00 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.53 (CH_2), 29.04 (CH_2), 29.12 (CH_2), 64.56 (CH_2–O), 131.27 (=C–O). IR(film): 1700 (s), 1190 (s), 730 (s) cm^{-1}. GC/MS (CI): *m/z* 169 (100; M^++1).

$\Delta^{1(12)}$-13,16-Dioxabicyclo[10.4.0]hexadecene (**4e**). The compound was obtained from **3e** and ethylene glycol as a liquid in 92 % yield after 4 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (m, 12H), 1.55 (m, 4H), 2.11 (t, 4H, J = 7,5 Hz), 3.90 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.36 (CH_2), 24.30 (CH_2), 24.40 (CH_2), 24.80 (CH_2), 26.29 (CH_2), 64.24 (CH_2–O), 132.17 (=C–O). IR(film): 1680 (s), 715 (s) cm^{-1}.

1,4-Dioxacyclododecane-5,12-dione (**5**). A solution of the dihydrodioxin **4d** (2.00 g, 14 mmol) in CH_2Cl_2 (12.5 ml) was added dropwise to a solution of *m*-chloroperbenzoic acid (10.41 g) (70 % pure, 60 mmol) in CH_2Cl_2 (50 ml) at room temp. over a period of 40 min. After 16 h the precipitated *m*-chlorobenzoic acid was removed by filtration and the filtrate washed successively with 5 % NaOH solution (2 × 50 ml) and water (50 ml), and dried ($MgSO_4$). Evaporation of solvent and recrystallization of the residue from CH_2Cl_2-pet.ether gave **5** (1.95 g; 89 %), m.p. 38–40 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.40 (m, 4H), 1.75 (m, 4H), 2.39 (m, 4H), 4.20 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.95 (CH_2), 25.06 (CH_2), 32.97 (CH_2), 60.79 (CH_2–O), 173.77 (C=O). IR (KBr): 1730 (s), 1230 (s), 1115 (s) cm^{-1}. GC/MS (CI): *m/z* 201 (100; M^+ + 1).

$\Delta^{1(8)}$-9,13-Dioxabicyclo[6.5.0]tridecene (**6d**). The compound was obtained from **3d** and 1,3-propanediol as a liquid in 75 % yield after 10 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.52 (m, 8H), 2.00 (m, 2H), 2.11 (t, 4H, J = 5.9 Hz), 4.08 (t, 4H, J = 5.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.73 (CH_2), 29.10 (CH_2), 31.10 (CH_2), 32.32 (CH_2), 69.73 (CH_2–O), 138.84 (=C–O). IR (film): 1670 (s), 1185 (s), 730 (s) cm^{-1}.

$\Delta^{1(12)}$-13,17-Dioxabicyclo[10.5.0]heptadecene (**6e**). The compound was obtained from **3e** and 1,3-propanediol as a liquid in 83 % yield after 10 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.37 (m, 12H), 1.59 (m, 4H), 1.98 (m, 2H), 2.09 (t, 4H, J = 6.0 Hz), 3.98 (t, 4H, J = 6.9 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.34 (CH_2), 24.15 (CH_2), 24.37 (CH_2), 24.57 (CH_2), 27.87 (CH_2), 32.06 (CH_2), 69.90 (CH_2–O), 142.00 (=C–O). IR (film): 1710 (s), 1070 (s), 730 (s) cm^{-1}.

1,4-Bis(2-oxocyclooctyloxy)butane (**8d**). The diketone was obtained from **3d** and 1,4-butanediol as a liquid in 80 % yield after 6 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31 (m, 2H), 1.52 (m, 8H), 1.68 (m, 6H), 1.84 (m, 2H), 1.98 (m, 6H), 2.28 (m, 2H), 2.65 (m, 2H), 3.42 (m, 4H), 3.83 (t, 2H, J = 5,7 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.44 (CH_2), 25.06 (CH_2), 25.48 (CH_2), 26.37 (CH_2), 26.79 (CH_2), 31.65 (CH_2), 39.14 (CH_2), 69.47 (CH_2–O), 84.15 (CH–O), 216.77 (C=O). IR (film): 1690 (s), 1230 (s), 1070 (s) cm^{-1}.

1,4-Bis(2-oxocyclododecyloxy)butane (**8e**). The diketone was obtained from **3e** and 1,4-butane-

diol as a crystalline compound, m.p. 68–70 °C, in 84 % yield after 5 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (m, 28H), 1.78 (m, 12H), 2.28 (m, 2H), 2.85 (m, 2H), 3.41 (m, 4H), 3.80 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.69 (CH_2), 21.16 (CH_2), 22.09 (CH_2), 22.17 (CH_2), 22.69 (CH_2), 23.84 (CH_2), 26.44 (CH_2), 26.68 (CH_2), 29.67 (CH_2), 33.47 (CH_2), 69.88 (CH_2–O), 86.29 (CH–O), 212.86 (C=O). IR (film): 1705, 1240, 1105 cm^{-1}.

$\Delta^{1(6)}$-3-Vinyl-2,5-dioxabicyclo[4.4.0]decene (**9b**). The compound was obtained from **3b** and (2*Z*)-1,4-butenediol as a liquid in 74 % yield after 3 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.62 (m, 4H), 2.09 (m, 4H), 3.69 (q, 1H, *J* = 6.4 Hz), 4.04 (dd, 1H, *J* = 0.6 and 0.9HZ), 4.39 (m, 1H), 5.30 (m, 2H), 5.83 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.83 (CH_2), 26.00 (CH_2), 26.26 (CH_2), 67.97 (CH_2), 73.77 (CH), 118.10 (CH_2), 129.66 (=C–O), 129.78 (=C–O), 133.49 (CH). IR (film): 1705 (s), 1200 (s), 890 (s) cm^{-1}.

$\Delta^{1(8)}$-10-Vinyl-9,12-dioxabicyclo[6.4.0]dodecene (**9d**) *and 10-vinyl-8-oxabicyclo[5.3.1]undecan-11-one* (**10d**). The reaction of **3d** and (2*Z*)-1,4-butenediol furnished a mixture of **9d** and **10d** as liquids in 62 % and 24 % yields, respectively, after 10 h reaction time.

9d: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.50 (m, 8H), 2.18 (m, 4H), 3.62 (q, 1H, *J* = 7,2 Hz), 4.00 (dd, 1H, *J* = 1.8 Hz and 2.4 Hz), 4.36 (m, 1H), 5.35 (m, 2H), 5.85 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.49 (CH_2), 26.55 (CH_2), 28.80 (CH_2), 29.03 (CH_2), 29.08 (CH_2), 29.12 (CH_2), 67.87 (CH_2–O), 73.62 (CH), 117.91 (=CH_2), 130.81 (=C–O), 133.73 (=CH). IR (film): 1680 (s), 1180 (s), 910 (s) cm^{-1}. GC/MS (EI): *m/z* 194 (25; M^+).

10d: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (m, 1H), 1.50–2.20 (m, 9H), 2.39 (m, 1H), 3.00 (m, 1H), 3.28 (t, 1H, *J* = 12Hz), 4.00 (m, 1H), 4.15 (q, 1H, *J* = 6 Hz), 5.08 (m, 2H), 5.58 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.40 (CH_2), 25.48 (CH_2), 26.13 (CH_2), 34.60 (CH_2), 35.26 (CH_2), 44.08 (CH_2), 51.85 (CH_2), 69.07 (CH_2–O), 83.26 (CH), 116.26 (=CH_2), 137.45 (=CH), 220.56 (C=O). IR (film): 1710 (s), 1110 (s), 1070 (s), 990 (s), 910 (s) cm^{-1}. GC/MS (EI): *m/z* 194 (47; M^+).

$\Delta^{1(12)}$-14-Vinyl-13,16-dioxabicyclo[10.4.0] hexadecene (**9e**) *and 14-Vinyl-12-oxabicyclo[9.3.1]pentadecan-15-one* (**10e**). The reaction of **3e** and (2*Z*)-1,4-butenediol furnished a mixture of **9e** and **10e** as liquids in 61 % and 21 % yields, respectively, after 5 h reaction time.

9e: ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.40 (m, 16H) 2.18 (m, 4H), 3.62 (m, 1H), 4.02 (dd, 1H), 4.38 (m, 1H), 5.35 (m, 2H), 5.86 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.27 (CH_2), 24.22 (CH_2), 24.32 (CH_2), 24.73 (CH_2), 24.80 (CH_2), 26.06 (CH_2), 26.19 (CH_2), 67.49 (CH_2–O), 73.08 (CH–O), 117.40 (=CH_2), 131.36 (=C–O), 131.41 (=C–O), 133.54 (=CH). IR (film): 1710, 1205, 990, 930, 910 cm^{-1}.

10e: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (m, 1H), 1.40 (m, 17H), 2.38 (m, 1H), 3.05 (m, 1H), 3.65 (m, 1H), 3.82 (m, 2H), 5.08 (m, 2H), 5.82 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 19.69 (CH_2), 22.38 (CH_2), 22.66 (CH_2), 22.79 (CH_2), 23.22 (CH_2), 23.57 (CH_2), 26.08 (CH_2), 26.84 (CH_2), 28.48 (CH_2), 44.79 (CH), 50.76 (CH), 68.22 (CH_2–O), 84.19 (CH), 116.89 (=CH_2), 138.28 (=CH), 214.80 (C=O). IR (film): 1720, 1090, 1080, 990, 915 cm^{-1}.

1-Hydroxy-8,11-dioxabicyclo[5.4.0]undecene (**12**). The compound was obtained from **3c** and ethylene glycol as a liquid in 75 % yield after 2 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.55 (m, 10H), 2.46 (m, 1H), 3.39 (m, 1H), 3.61 (m, 1H), 3.92 (m, 2H), 4.15 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.91 (CH_2), 27.22 (CH_2), 30.48 (CH_2), 34.01 (CH_2), 64.75 (CH_2), 65.22 (CH_2), 75.25 (–CH–O), 112.15 (C–OH). IR (film): 3350, 1100, 1040 cm^{-1}.

5-(2-Oxocyclooctyloxy)-3-oxapentan-1-ol (**13**), (*x*=2). This compound was prepared according to the general procedure from **3d** and diethylene glycol (two equiv.). The product was obtained as a 1:1 mixture of **13** (*x*=2) and **4d**. The former was obtained by flash chromatography in 47 % yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25–1.62 (m, 6H), 2.03 (m, 3H), 2.55 (m, 2H), 2.65 (m, 1H), 2.85 (s, 1H), 3.68 (m, 7H), 3.94 (m, 1H), 4.23 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.75 (CH_2), 25.20 (CH_2), 26.92 (CH_2), 31.67 (CH_2), 39.50 (CH_2), 61.73 (CH_2), 69.55 (CH_2), 70.55

(CH_2), 84.70 (CH), 216.60 (C=O). IR (film): 3450, 1710, 1140–1070 cm^{-1}.

8-(2-Oxocyclooctyloxy)-3,6-dioxaoctan-1-ol (**13**), (x=3). The compound was obtained from **3d** and triethylene glycol in 85 % yield after 4 h reaction time. ^1H NMR (300 MHz, $CDCl_3$): δ 1.33–2.04 (m, 10H), 2.35 (m, 1H), 2.61 (m, 1H), 3.36 (s, 1H), 3.66 (m, 12H), 3.96 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.68 (CH_2), 25.26 (CH_2), 25.77 (CH_2), 27.03 (CH_2), 31.85 (CH_2), 39.45 (CH_2), 61.62 (CH_2), 69.36 (CH_2), 70.36 (CH_2), 70.70 (CH_2), 72.63 (CH_2), 84.68 (CH), 216.71 (C=O). IR (film): 3450, 1734, 1710, 1110 cm^{-1}.

11-(2-Oxocyclooctyloxy)-3,6,9-trioxaundecan-1-ol (**13**), (x=4). The compound was obtained from **3d** and tetraethylene glycol in 83 % yield after 4 h reaction time. ^1H NMR (300 MHz, $CDCl_3$): 1.33–2.10 (m, 10H), 2.34 (m, 1H), 2.64 (m, 1H), 3.11 (s, 1H), 3.65 (m, 16H), 3.96 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 21.62 (CH_2), 25.17 (CH_2), 25.71 (CH_2), 26.95 (CH_2), 31.73 (CH_2), 39.42 (CH_2), 61.58 (CH_2), 69.27 (CH_2), 70.26 (CH_2), 70.55 (CH_2), 72.55 (CH_2), 84.58 (CH), 216.67 (C=O). IR (film): 3450, 1735, 1710, 1110 cm^{-1}.

1-(2-Oxocyclooctyloxy)-3,6-dioxaheptane (**13a**). This compound was obtained from **3d** and diethylene glycol methyl ether as a liquid in 92 % yield. The reaction time was 5 h. ^1H NMR (300 MHz, $CDCl_3$): δ 1.54 (m, 5H), 1.78 (m, 2H), 2.00 (m, 3H), 2.32 (m, 1H), 2.62 (m, 1H), 3.37 (s, 3H), 3.54 (m, 2H), 3.64 (m, 6H), 3.95 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 21.72 (CH_2), 25.31 (CH_2), 25.70 (CH_2), 27.14 (CH_2), 32.03 (CH_2), 39.52 (CH_2), 58.93 (CH_3), 69.40 (CH_2), 70.60 (CH_2), 70.81 (CH_2), 72.00 (CH_2), 84.68 (CH), 216.52 (C=O). IR (film): 1710 (s), 1420, 1400, 1110 cm^{-1}. GC/MS (CI): m/z 245 (100; M^++1).

$\Delta^{1(6)}$-2,5-Oxathiabicyclo[4.3.0]nonene (**14a**). The compound was obtained from the dimethyl acetal of **3a** and 2-mercaptoethanol as a liquid in 89 % yield after 3 h reaction time. ^1H NMR (300 MHz, $CDCl_3$): δ 1.78 (m, 2H), 2.51 (m, 4H), 2.82 (m, 2H), 4.17 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 18.66 (CH_2), 24.96 (CH_2), 31.94 (CH_2), 32.91 (CH_2–S), 66.26 (CH_2–O), 97.04 (=C–S), 147.08 (=C–O). IR (film): 1649, 1135, 1058 cm^{-1}.

$\Delta^{1(6)}$-2,5-Oxathiabicyclo[4.4.0]decene (**14b**). The compound was obtained from **3b** and 2-mercaptoethanol as a liquid in 92 % yield after 2 h reflux in benzene as solvent. The spectral data were identical with those of the literature.[9i]

$\Delta^{1(8)}$-9,12-Oxathiabicyclo[6.4.0[dodecene (**14d**). The compound was obtained from **3d** and 2-mercaptoethanol as a liquid in 90 % yield after 2 h reaction time. ^1H NMR (300 MHz, $CDCl_3$): δ 1.50 (m, 8H), 2.16 (t, 2H, J = 5.9 Hz), 2.25 (t, 2H, J = 5.9 Hz), 2.92 (m, 2H), 4.19 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.20 (CH_2), 26.56 (CH_2), 29.05 (CH_2), 29.61 (CH_2), 31.16 (CH_2), 31.57 (CH_2–S), 65.28 (CH_2–O), 99.37 (=C–S), 146.25 (=C–O). IR (film): 1630, 1200, 1100 cm^{-1}. GC/MS (CI): m/z 184 (100; M^+).

$\Delta^{1(12)}$-13,16-Oxathiabicyclo[10.4.0]hexadecene (**14e**). The crystalline compound, m.p. 39–40 °C from methanol, was obtained from **3e** and 2-mercaptoethanol in 92 % yield after 3 h reaction time. ^1H NMR (300 MHz, $CDCl_3$): δ 1.40 (m, 12H), 1.58 (m, 4H), 2.21 (q, 4H, J = 6.9 Hz), 2.97 (m, 2H), 4.17 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.38 (CH_2), 22.52 (CH_2), 24.29 (CH_2), 24.34 (CH_2), 24.48 (CH_2), 24.64 (CH_2), 24.89 (CH_2), 26.21 (CH_2), 26.29 (CH_2), 28.24 (CH_2), 29.05 (CH_2–S), 65.04 (CH_2–O), 102.64 (=C–S), 145.82 (=C–O). IR (film): 1620, 1200, 1080 cm^{-1}. GC/MS (CI): m/z 241 (100; M^++1).

$\Delta^{1(6)}$-2,5-Dithiabicyclo[4.3.0]nonene (**15a**). The compound was prepared from the dimethylacetal of **3a** and 1,2-ethanedithiol as a liquid in 90 % yield after 3 h reaction time. ^1H NMR (300 MHz, $CDCl_3$): δ 1.62 (m, 2H), 2.15 (m, 4H), 2.87 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 20.94 (CH_2), 27.15 (CH_2), 37.34 (CH_2–S), 120.72 (=C–S). IR (film): 1588, 1298, 1278, 1138, 1105, 842 cm^{-1}.

$\Delta^{1(6)}$-2,5-Dithiabicyclo[4.4.0]decene (**15b**). The compound was obtained from **3b** and 1,2-ethanedithiol as a liquid in 91 % yield after 1 h reaction time. The ^1H NMR were consistent with those of the literature.[9f] ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.35 (CH_2), 28.50 (CH_2), 31.93 (CH_2–S), 119.52 (=C–S). GC/MS (CI): m/z 173 (100; M^++1).

$\Delta^{1(7)}$-8,11-Dithiabicyclo[5.4.0]undecene (**15c**). The compound was obtained from **3c** and 1,2-

ethanedithiol as a liquid in 90 % yield after 1 h reaction time. Its preparation has been reported [9e] without any spectral data. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.48 (m, 4H), 1.67 (m, 2H), 2.18 (t, 4H, J = 5,4 Hz), 3.07 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.69 (CH_2), 28.94 (CH_2), 32.00 (CH_2), 37.55 (CH_2–S), 123.25 (=C–S). IR (film): 1595, 1150, 730 cm^{-1}. GC/MS (CI): *m/z* 187 (100; M^++1).

$\Delta^{1(8)}$-9,12-Dithiabicyclo[6.4.0]dodecene (**15d**). The compound was obtained from **3d** and 1,2-ethanedithiol as a liquid in 85 % yield after 2 h reaction time. Its preparation has been reported[9e] without spectral data. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.58 (m, 8H), 2.32 (t, 4H; J = 5.9 Hz), 3.17 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 26.26 (CH_2), 29.23 (CH_2), 29.77 (CH_2), 34.02 (CH_2–S), 122.35 (=C–S). IR (film): 1590, 1430, 1125, 815, 725 cm^{-1}. GC/MS (CI): *m/z* 201 (100; M^++1).

$\Delta^{1(12)}$-13,16-Dithiabicyclo[10.4.0]hexadecene (**15e**). The compound was obtained from **3e** and 1,2-ethanedithiol as a solid, m.p. 53–54 °C (lit.[8] 54–54.5 °C), in 91 % yield after 3 h reaction time. The spectral data are consistent with those of the literature.[8] ^{13}C NMR (75 MHz, $CDCl_3$): δ 22.57 (CH_2), 24.66 (CH_2), 25.05 (CH_2), 26.70 (CH_2), 29.34 (CH_2), 31.64 (CH_2–S), 125.13 (=C–S). IR (KBr): 1580, 1460, 795, 675 cm^{-1}. GC/MS (CI): *m/z* 257 (100; M^++1).

$\Delta^{1(8),4}$-9,12-Dithiabicyclo[6.4.0]dodecadiene (**15f**). The compound was obtained from **3f** and 1,2-ethanedithiol as a liquid in 89 % yield after 6 h reaction time. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.45 (m, 8H) 3.12 (s, 4H), 5.55 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.49 (CH_2), 29.23 (CH_2), 35.22 (CH_2–S), 121.58 (=C–S), 128.24 (=CH). IR (film): 1610 (w) 1430, 760, 690 cm^{-1}. GC/MS (CI): *m/z* 199 (100; M^++1).

$\Delta^{1(7)}$-2,6-Dithiabicyclo[5.4.0]undecene (**16**). The compound was obtained from **3b** and 1,3-propanedithiol as a liquid in 82 % yield after 10 h reaction time. ^{1}H NMR (300 MHz, CDCl): δ 1.59 (m, 4H), 2.25 (m, 6H), 3.28 (t, 4H, J = 6,3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 23.09 (CH_2), 30.57 (CH_2), 31.51 (CH_2), 34.27 (CH_2), 127.78 (=C–S). IR (film): 1605, 1415, 800, 740 cm^{-1}.

$\Delta^{1(6)}$-2,5-Dithiabicyclo[4.4.0]decene-2,5-tetroxide (**17b**). To an ice-cooled solution of **15b** (1.00 g, 7 mmol) in CH_2Cl_2 (20 ml) was added dropwise over 40 min a solution of *m*-chloroperbenzoic acid (6.94 g, 70 %; 28.1 mmol) in CH_2Cl_2 (40 ml). The mixture was stirred for 2 h and filtered. The filtrate was washed with aq. $NaHCO_3$ (4 × 30 ml) and dried ($MgSO_4$). Evaporation and recrystallization of the residue from methanol gave **17b** (1.19 g, 72 %), m.p. 172–173 °C (lit.[9b] 172–173 °C).

$\Delta^{1(8)}$-9,12-Dithiabicyclo[6.4.0]dodecene-9,12-tetroxide (**17d**). This compound was prepared from **15d** in the same way as described for **17b**. It was obtained in 74 % yield, m.p. 158–160 °C, after recrystallization from methanol. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.59 (m, 4H), 1.89 (m, 4H), 2.68 (m, 4H), 3.88 (s, 4H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 24.94 (CH_2), 25.90 (CH_2), 30.42 (CH_2), 48.44 (CH_2–SO_2), 143.01 (=C–SO_2). IR (KBr): 1300 (s), 1105 (s), 1125 (s) cm^{-1}. GC/MS (CI): *m/z* 265 (100; M^++1).

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