An Unusual Domino Claisen−Conia Reaction Producing 3,5-Dispirodihydrofuran-2,4-diones

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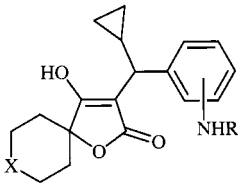
Allyl tetronates **3** can be selectively converted either (in acetonitrile) into Claisen-rearranged 3-allyltetronic acids **5** or (in toluene) into novel Claisen–Conia-rearranged 3-(spirocyclopropyl)dihydrofuran-2,4-diones **6**, featuring up to three new stereogenic centres. The mechanism and the stereochemistry of this process is discussed and an X-ray crystal structure of one of the two diastereoisomers of (±)–**6c** is presented.

Introduction

3,5-Disubstituted tetronic acids exhibit a variety of biological activities including antibiotic, antiviral, and antitumour properties.[1] Driven by the need to develop an effective treatment of patients with AIDS, the focus of pharmaceutical research within this field has recently shifted to derivatives with pronounced HIV-protease inhibitor activity,[2] such as the 5-spiro-3-(α-cyclopropylbenzyl)tetronic acids of type **1**.[3,4] On the basis of X-ray structural analyses of respective HIV-protease−drug complexes, a rationale was developed for the observed structure-activity dependencies of **1** and of analogous 4-hydroxy(benzo)pyran-2-ones. This enabled elaborate drug refinement to be carried out by means of computer modelling.[5]



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We have now applied our established domino Wittig olefination−Claisen rearrangement approach[6] to build up immediate precursor compounds − 5-spiro-3-allyl derivatives **5** − from allyl esters **2** of cyclic α-hydroxycarboxylic acids and ketenylidenetriphenylphosphorane **4**. These should then be amenable to cyclopropanation, yielding tetronic acids of the desired type **1**. Remarkably, the outcome of this domino sequence, and especially of the rearrangement steps, was found to be strongly dependent on, and controllable by, parameters such as substrate structure, temperature and solvent polarity. These findings are reported below, with the usual "one-pot" domino methodology broken down into individual reaction steps for reasons of clarity.

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Results and Discussion

Controllable Domino Synthesis of 3,5-Dispirodihydrofuran-2,4-diones 6

Allyl esters **2** of α-hydroxycycloalkanoic acids can readily be prepared either by direct acid-catalysed esterification between the corresponding allyl alcohol and the carboxylic acid (R = H), or by treatment of the latter with an allylisourea (R = Ph).[7] Gentle refluxing of solutions of **2** and ketenylidenetriphenylphosphorane **4**[8] in THF afforded the corresponding 5-spirotetronates **3** in good to excellent yields. These compounds are products of a domino sequence, consisting of the addition of the hydroxy group in **2** across the C=C bond of **4** and a subsequent, intramolecular Wittig olefination reaction between the resulting acyl ylide and its ester carbonyl group. Under these relatively mild conditions, no follow-up rearrangement processes were observed (Scheme 1). From earlier work we knew that such extended cascades tend to require more rigorous conditions, such as working in toluene at reflux or even in sealed glass tubes. Previously, all such thermally induced sequential reactions undergone by allyl tetronates, congener 4-allyloxycoumarins and 4-allyloxyquinolones had been of the [3.3]-sigmatropic Claisen type, producing the respective 3-allyl-4-hydroxy derivatives.[9] In a deviation from this rule, tetronates **3**, when kept in toluene solution at 200 °C in a sealed glass tube for 48 h, were not converted into the expected Claisen-rearranged 3-allyltetronic acids **5**, but exclusively into dispirolactones **6** (Scheme 2). A reasonable mechanistic explanation would be that the first reaction step should still be a Claisen rearrangement to give **5**, but that 5-spiroannulation would then enable compounds **5** to

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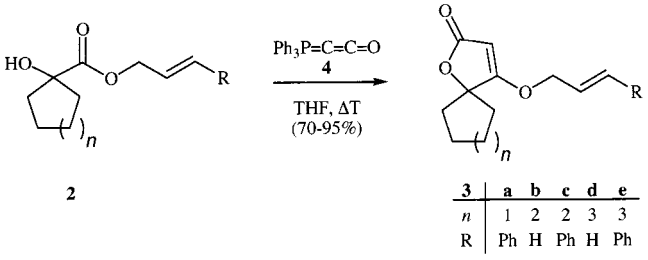
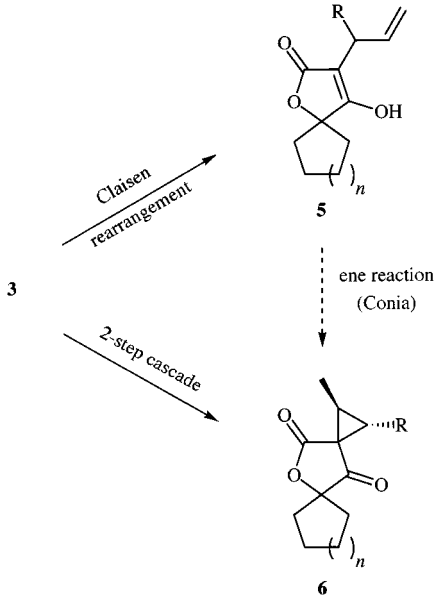
undergo a subsequent, quick oxa-ene reaction of the Conia[10] type to close the 3-spirocyclopropyl ring. As well as the 5-substituents on the tetronic acid **5**, other factors influencing the progress of this domino Claisen−Conia sequence include the nature of R in the allyl side chain, the reaction temperature and the polarity of the solvent. It proved possible to find conditions suitable for producing either the pure dispirolactone or the tetronic acid **5** (exclusively in some cases, in others as mixtures with **6**) (Table 1).



Scheme 1



Scheme 2. (Domino) sigmatropic rearrangement reactions of allyl spirotetronates **3**

Some results are evident from Table 1. Most important is the fact that dispirolactones **6** could be obtained exclusively and in pure form in each case, using toluene as solvent. Derivatives in which R = Ph reacted more readily, and the yields of the respective products were considerably higher than those for the analogous reactions with R = H (**6a**: 74%, **6c**: 66%, **6e**: 77% vs. **6b**: 30% and **6d**: 35%). Spirotetronates **3**, with seven-membered rings at C-5, reacted more rapidly and more readily than their congeners bearing five-membered and six-membered rings. For instance, formation of **6e** in 77% yield required only 48 h in refluxing toluene. 5-Spiro annulation is not a prerequisite for this domino process to occur, but produces considerable increases in the yields of the corresponding 3-(spirocyclopropyl)dihydrofuran-2,4-diones **6** (which otherwise are < 30%). The rate of Claisen rearrangement reactions is known to be significantly accelerated by an increase in solvent polarity.[11] When we kept solutions of **3** in acetonitrile at a gentle reflux for at least 24 h, the starting compounds were converted either into pure Claisen-rearranged 3-allyltetronic acids **5** (**5c**: 32% after 24 h) or − upon prolonged heating − to mixtures still consisting predominantly of these, but with minor amounts of the respective Conia-rearranged dispirolactones **6**. Such mixtures could easily be separated by column chromatography.

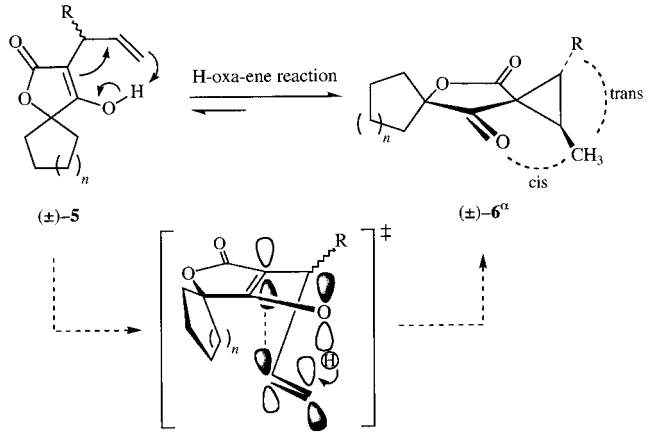
Stereochemistry and Structure of the Dispirolactones 6

Although many Conia reactions, including those resulting in spiro systems,[12] can be found in the literature, the formation of three-membered rings is so far unprecedented. In fact, the reverse reaction is well documented and acylcyclopropanes are known to undergo ring opening under thermal conditions (150 °C and above) to give the corresponding γ-unsaturated ketones.[13] Theoretically, the equilibrium between these two lies far to the side of the cyclopropane whenever the ketone can form a stable enol. Tetronic acids such as **5** exist almost exclusively as the enol tautomer depicted, a fact that would account for the ease with which they form the spirocyclopropanes **6**. Equally striking are the stereochemical implications of this process. The Conia rearrangement of **5** to **6** can be regarded mechanistically as an oxa-ene reaction. A formal frontier orbital

Table 1. 3-Allylspirotetronic acids **5** and 3,5-dispirodihydrofuran-2,4-diones **6** from **3**: conditions and yields

Starting compound	*n*	R	Reaction conditions	Yield of **5** (%)	Yield of **6** (%)
3a	1	Ph	toluene, 200 °C, 48 h, sealed tube	−	74
3a	1	Ph	acetonitrile, reflux, 48 h	56	19
3b	2	H	toluene, 200 °C, 48 h, sealed tube	−	30
3b	2	H	toluene, 160 °C, 48 h, sealed tube	60	−
3c	2	Ph	toluene, 200 °C, 48 h, sealed tube	−	66
3c	2	Ph	acetonitrile, reflux, 24 h	32	−
3c	2	Ph	acetonitrile, reflux, 48 h	54	22
3d	3	H	toluene, 200 °C, 48 h, sealed tube	−	35
3d	3	H	toluene, 160 °C, 24 h, sealed tube	−	23
3e	3	Ph	acetonitrile, reflux, 48 h	49	−
3e	3	Ph	toluene, reflux, 48 h	−	77
3e	3	Ph	toluene, 200 °C, 48 h, sealed tube	−	75

description of the transition state, using the HOMO of the enol radical and the LUMO of the alkene, provides a rationale for the observed stereoselectivity of this particular Conia reaction (Scheme 3). The product isomer with a *cis* constellation of the newly created methyl group and the oxo group that participated (as the enol tautomer) in the reaction should be formed exclusively. A further steric constraint in derivatives **6a**, **6c**, and **6e**, containing three stereogenic centres, is the *trans* orientation of the phenyl and the methyl group.



Scheme 3

Since we had started from achiral compounds **3** and had not resolved the racemates of the intermediate tetronic acids **5a**, **5c**, and **5e**, we had anticipated that we would obtain the respective Conia products as a single racemate (±)–$\mathbf{6^{\alpha}}$. NMR spectroscopy revealed the presence of a 1:1 mixture of two diastereoisomers $\mathbf{6^{\alpha}}$ and $\mathbf{6^{\beta}}$, though. Both were tentatively assigned *trans* configurations between the methyl and phenyl groups (J_{HH} = 9.25 Hz). The diastereoisomers of dispirolactone **6c** could easily be separated by complete crystallization of one of them ($\mathbf{6c^{\beta}}$) and an X-ray single-crystal structure analysis was carried out with this diastereopure racemate (Figure 1). It revealed *trans* relationships not only between the phenyl residue and the methyl group but also between the phenyl residue and the carbonyl moiety at C-2. Given the *cis* selectivity of the Conia reaction, the formation of $\mathbf{6c^{\beta}}$ must have taken place by means of a reaction between the terminal olefin and the enol of the ester carbonyl group. When toluene solutions of the pure individual diastereoisomers of **6c** were kept at 160 °C in a sealed glass tube for 12 h, they re-equilibrated to give back the initial 1:1 mixture of α and β diastereomers. One rationalisation of these findings is the assumption that both enol forms of **5** are present as an equilibrium mixture under the applied high temperature conditions and independently undergo reversible Conia rearrangements to produce the respective diastereoisomers (ester enol → $\mathbf{6^{\beta}}$; oxo enol → $\mathbf{6^{\alpha}}$). The Conia rearrangement equilibria apparently lie far to the product side, as no residual starting materials could be detected either by TLC or by NMR (Scheme 4). The diastereopure racemate $\mathbf{6c^{\beta}}$ could also be resolved on an analytical scale on a Kromasil CHI-DMB column, with 0.1% *tert*-butyl methyl ether (TBME) in hexane as the mobile phase. The CD spectra showed absorption maxima at 238 nm, with the first eluted enantiomer being levorotatory at this wavelength. An asymmetrically perturbed carbonyl transition (n→π*) was also found at ca. 302 nm (Figure 2). Thus, all four stereoisomeric dispirolactones **6** can in principle be obtained in pure form by means of a four-step domino reaction between ylide **4** and allyl α-hydroxycycloalkanoates **2**, followed by a recrystallization and two chromatographic resolutions.

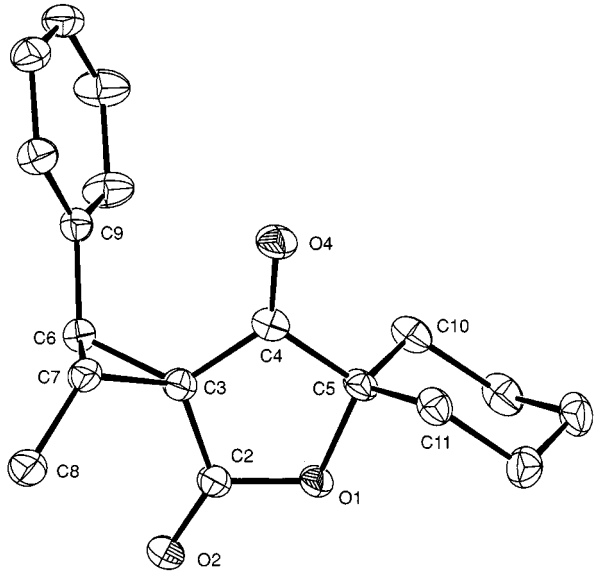
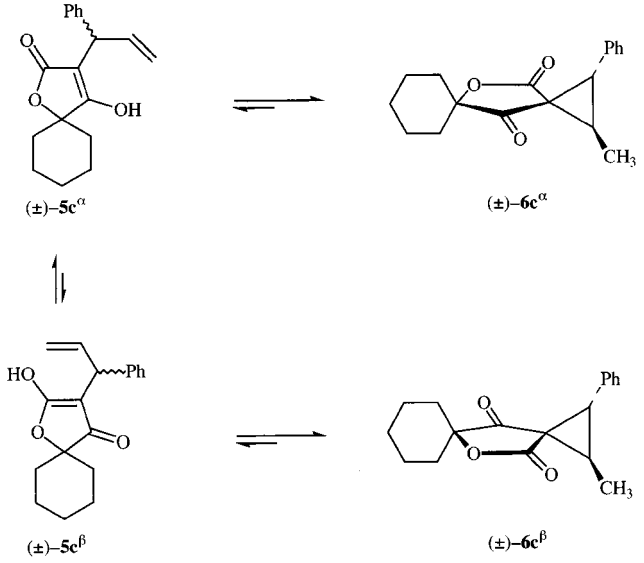


Figure 1. Molecular structure of (±)-$\mathbf{6c^{\beta}}$; hydrogen atoms are omitted; selected bond lengths [A], angles [°], and dihedral angles [°]: C5–O1 1.471(2), O1–C2 1.358(2), C2–O2 1.203(2), C2–C3 1.477(3), C3–C4 1.468(3), C4–O4 1.210(2), C4–C5 1.523(3), C3–C6 1.560(2), C3–C7 1.544(3), C6–C7 1.472(3); C5–O1–C2 112.22(13), C2–C3–C4 106.78(15), C3–C4–C5 107.35(15) C3–C6–C7 61.14(12), C6–C3–C7 56.61(12); C4–C3–C6–C9 5.4(2), C2–C3–C6–C7 112.14(18)



Scheme 4

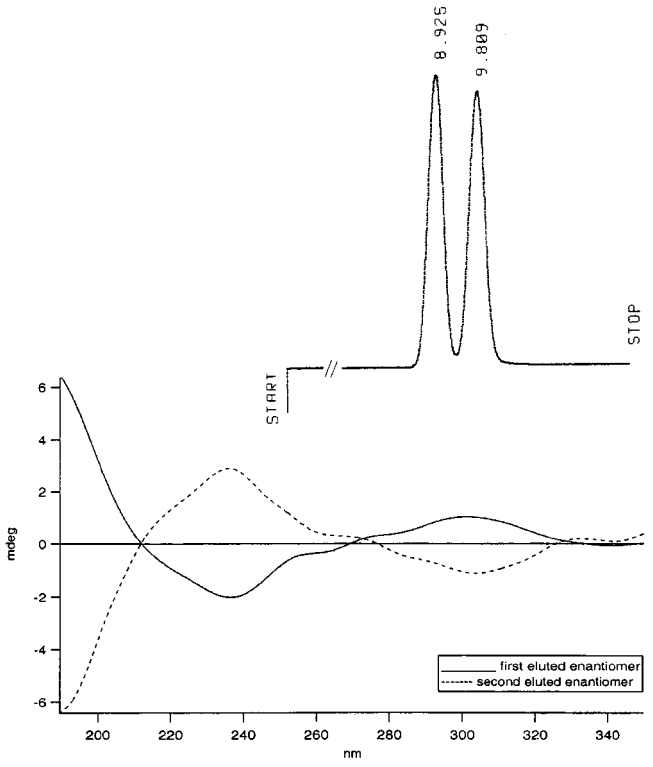


Figure 2. Top: analytical resolution of (±)-**6c**$^{\beta}$ on a Kromasil CHI-DBM column, flow 1.0 mL/min, UV 235 nm; bottom: CD spectra of the main fractions with t_r = 8.9 and 9.8 min, CH_3CN, unknown concentration

Further work to resolve racemic tetronic acids **5** and to carry out the Conia reaction with the enantiopure compounds is now in progress. Dispirolactones **6** should also be amenable to ring-opening reactions and so could open access to 3,5-difunctionalized tetronic acids. Biological testing both of structurally modified 3-(α-cyclopropylbenzyl)tetronic acids and their corresponding Conia-rearranged dispirolactones **6** is underway.

Experimental Section

General Information: Ylide **4**[8] and the 1-hydroxycycloalkanoic acids[14] required for the preparation of their esters **2** were prepared by the literature methods quoted, all other starting compounds were purchased from Aldrich and used as such without further purification. All reactions involving ylide **4** were carried out under nitrogen. Solvents were dried and distilled under nitrogen prior to use, according to standard procedures. − Melting points were recorded using a Gallenkamp apparatus and are not corrected. − NMR: Bruker DPX 300 and DRX 500; δ given in ppm; TMS as internal standard. − IR: Perkin−Elmer 983G; recorded as potassium bromide disks (KBr) or films (film). − MS: Double Focusing Triple Sector VG Auto Spec, and Varian MAT 311A (EI). − MA: Perkin−Elmer 2400 CHN. − X-ray single-crystal structure analysis: Siemens P4. − HPLC: Varian 9021Q solvent delivery pump and 9050 UV detector; column: 4.6 × 250 mm Kromasil CHI-DBM (EKA Chemicals Co., Bohus, Sweden), injection volume 20 μL.

1. Synthesis of Allyl Esters 2b and 2d. − General Procedure for the Azeotropic Esterification of 1-Hydroxycycloalkanoic Acids: A mixture of the respective 1-hydroxycycloalkanoic acid (10.00 mmol), allyl alcohol (2.90 g; 50.00 mmol), conc. H_2SO_4 (2−4 mmol), and chloroform (50 mL) was heated under reflux using a Dean−Stark apparatus for solvents heavier than water. When the separation of water in the trap had ceased (ca. 6−10 h), the apparatus was dismantled and the reaction mixture cooled to room temperature. It was washed first with water, then twice with saturated $NaHCO_3$ solution and finally once more with water. The solution was dried with $MgSO_4$, the solvent was evaporated and the residue thus obtained purified by column chromatography (silica gel 60, solvent as indicated).

Allyl 1-Hydroxycyclohexanoate (2b): This compound (1.46 g, 7.93 mmol, 79%) was obtained from 1-hydroxycyclohexanecarboxylic acid (1.44 g); colourless oil; R_f = 0.57 (diethyl ether/*n*-pentane, 1:4, v/v). − IR (film): $\tilde{\nu}$ = 3503 cm^{-1}, 2936, 1731, 1449, 1234, 1156, 995. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.58−1.82 (m, 10 H, 2-H, 3-H, 4-H, 5-H, 6-H), 2.87 (s, br., 1 H, OH), 4.66 (dt, ^3J = 5.65 Hz, ^4J = 1.35 Hz, 2 H, OCH_2), 5.26 (ddt, ^3J = 10.24 Hz, ^2J = 2.24 Hz, ^4J = 1.35 Hz, 1 H, CH=C*H*H-*cis*), 5.33 (ddt, ^3J = 17.23 Hz, ^2J = 2.24 Hz, ^4J = 1.35 Hz, 1 H, CH=CH*H*-*trans*), 5.92 (ddd, ^3J = 17.23, 10.24, 5.65 Hz, 1 H, C*H*=CH_2). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.6 (C-3, C-5), 25.6 (C-4), 35.2 (C-2, C-6), 66.4 (OCH_2), 74.0 (C-1), 118.9 (CH=*C*H_2), 132.1 (C*H*=CH_2), 177.4 (*C*O_2). − MS (EI, 70 eV): *m*/*z* (%) = 185 (69) [MH^+], 167 (63) [$MH^+ - H_2O$], 155 (39), 139 (14), 127 (25) [$M^+ - C_3H_5O$], 121 (43), 109 (52) [*167* − $C_3H_5O^+$], 99 (89) [$M^+ - C_4H_5O_2$], 81 (86) [*99* − H_2O^+], 69 (33), 55 (100), 43 (75). − $C_{10}H_{16}O_3$ (184.24): calcd. C 65.19, H 8.75; found C 65.29, H 8.70.

Allyl 1-Hydroxycycloheptanoate (2d): This compound (1.44 g, 7.29 mmol, 73%) was obtained from 1-hydroxycycloheptanecarboxylic acid (1.44 g); colourless oil; R_f = 0.58 (diethyl ether/*n*-pentane, 1:4, v/v). − IR (film): $\tilde{\nu}$ = 3511 cm^{-1}, 2927, 1731, 1239, 1124, 1060. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.56−1.99 (m, 12 H, 2-H, 3-H, 4-H, 5-H, 6-H, 7-H), 2.95 (s, 1 H, OH), 4.66 (dt, ^3J = 5.65 Hz, ^4J = 1.37 Hz, 2 H, OCH_2), 5.27 (ddt, ^3J = 10.44 Hz, ^2J = 2.50 Hz, ^4J = 1.37 Hz, 1 H, CH=C*H*H-*cis*), 5.34 (ddt, ^3J = 17.01 Hz, ^2J = 2.50 Hz, ^4J = 1.37 Hz, 1 H, CH=CH*H*-*trans*), 5.93 (ddt, ^3J = 17.01, 10.44, 5.65 Hz, 1 H, C*H*=CH_2). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 23.0 (C-3, C-6), 30.0 (C-4, C-5), 39.4 (C-2, C-7), 66.5 (OCH_2), 77.3 (C-1), 119.0 (CH=*C*H_2), 132.1 (*C*H=CH_2), 178.3 (*C*O_2). − MS (EI, 70 eV): *m*/*z* (%) = 199 (51) [MH^+], 181 (63) [$MH^+ - H_2O$], 169 (15), 135 (20), 123 (38) [*181* − $C_3H_5O_2^+$; *141* − H_2O^+], 113 (96), 95 (86) [*181* − $C_4H_5O_2^+$; *123* − CO^+], 83 (27), 69 (66), 55 (100). − $C_{11}H_{18}O_3$ (198.26): calcd. C 66.64, H 9.15; found C 66.56, H 9.04.

2. Synthesis of Esters 2a, 2c, 2e. − General Procedure for the Esterification of 1-Hydroxycycloalkanoic Acids with *N*,*N*′-Dicyclohexyl-*O*-phenylallylisourea:[7] A solution of the respective 1-hydroxycarboxylic acid (10.0 mmol) and *N*,*N*′-dicyclohexyl-*O*-(*trans*-3′-phenylallyl)isourea (4.08 g; 12.00 mmol) in dry THF (50 mL) was stirred under reflux for 16 h. After cooling to room temperature, the solution was filtered to remove the precipitated urea. The solvent was then evaporated under reduced pressure to leave a crude product which was purified by column chromatography (silica gel 60; solvent as indicated).

***trans*-3′-Phenylallyl 1-Hydroxycyclopentanecarboxylate (2a):** This compound (1.32 g, 5.36 mmol; 54%) was obtained from 1-hydroxycyclopentanecarboxylic acid (1.30 g); colourless oil; R_f = 0.40 (diethyl ether/*n*-pentane, 1:4, v/v). − IR (film): $\tilde{\nu}$ = 3445 cm^{-1},

1727, 1624, 1183, 1161, 1027. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.77−2.10 (m, 8 H, 2-H, 3-H, 4-H, 5-H), 3.15 (s, 1 H, OH), 4.82 (dd, ^3J = 6.49 Hz, ^4J = 1.65 Hz, 2 H, OCH_2), 6.28 (dt, ^3J = 15.85, 6.49 Hz, 1 H, C*H*=CHPh), 6.67 (dt, ^3J = 15.85 Hz, ^4J = 1.65 Hz, 1 H, CH=C*H*Ph), 7.25−7.67 (m, 5 H, Ph). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 25.7 (C-3, C-4), 40.1 (C-2, C-5), 66.6 (OCH_2), 82.3 (C-1), 122.9 (*C*H=CHPh), 127.5, 128.6, 129.0 (CH-*ar.*), 135.2 (CH=*C*HPh), 136.4 (C-*ipso*), 177.6 (*C*O$_2$). − MS (EI, 70 eV): *m*/*z* (%) = 246 (39) [M$^+$], 134 (52), 117 (100) [$C_9H_9^+$], 96 (70), 85 (92), 67 (84), 41 (40). − $C_{15}H_{18}O_3$ (246.31): calcd. C 73.15, H 7.36; found C 73.24, H 7.41.

***trans*-3′-Phenylallyl 1-Hydroxycyclohexanecarboxylate (2c):** This compound (1.87 g, 7.19 mmol, 72%) was obtained from 1-hydroxycyclohexanecarboxylic acid (1.44 g); white solid; m.p. 43 °C; R_f = 0.52 (diethyl ether/*n*-pentane, 1:4, v/v). − IR (KBr): ṽ = 3481 cm^{-1}, 2941, 1717, 1241, 1179, 1161, 1137. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.31−1.86 (m, 10 H, 2-H, 3-H, 4-H, 5-H, 6-H), 2.90 (s, 1 H, OH), 4.80 (dd, ^3J = 6.48 Hz, ^4J = 1.23 Hz, 2 H, OCH_2), 6.28 (dt, ^3J = 15.90, 6.48 Hz, 1 H, C*H*=CHPh), 6.66 (dd, ^3J = 15.90 Hz, ^4J = 1.23 Hz, 1 H, CH=C*H*Ph), 7.25−7.41 (m, 5 H, Ph). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.1 (C-3, C-5), 25.2 (C-4), 37.4 (C-2, C-6), 66.0 (OCH_2), 73.6 (C-1), 122.5 (*C*H=CHPh), 126.6, 128.2, 128.6 (CH-*ar.*), 134.7 (CH=*C*HPh), 136.0 (C-*ipso*), 177.0 (*C*O$_2$). − MS (EI, 70 eV): *m*/*z* (%) = 260 (31) [M$^+$], 242 (15) [M$^+$ − H_2O], 134 (19) [$C_9H_{10}O^+$], 117 (100) [$C_9H_9^+$], 115 (83), 110 (84) [M$^+$ − $C_9H_{10}O_2$; *242* − $C_9H_8O^+$], 91 (62), 81 (97). − $C_{16}H_{20}O_3$ (260.34): calcd. C 73.82, H 7.74; found C 73.80, H 7.66.

***trans*-3′-Phenylallyl 1-Hydroxycycloheptanecarboxylate (2e):** This compound (1.83 g, 6.68 mmol, 67%) was obtained from 1-hydroxycycloheptanecarboxylic acid (1.58 g); colourless viscous oil; R_f = 0.57 (diethyl ether/*n*-pentane, 1:4, v/v). − IR (film): ṽ = 3510 cm^{-1}, 2926, 2859, 1724, 1171, 1111. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20−2.10 (m, 12 H, 2-H, 3-H, 4-H, 5-H, 6-H, 7-H), 2.98 (s, 1 H, OH), 4.80 (dd, ^3J = 6.43 Hz, ^4J = 1.24 Hz, 2 H, OCH_2), 6.27 (dt, ^3J = 15.89, 6.43 Hz, 1 H, C*H*=CHPh), 6.66 (dt, ^3J = 15.89 Hz, ^4J = 1.24 Hz, 1 H, CH=C*H*Ph), 7.25−7.56 (m, 5 H, Ph). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 21.7 (C-3, C-6), 28.6 (C-4, C-5), 38.0 (C-2, C-7), 65.2 (OCH_2), 76.0 (C-1), 121.6 (*C*H=CHPh), 125.7, 127.3, 127.7 (CH-*ar.*), 133.8 (CH=*C*HPh), 135.1 (C-*ipso*), 177.1 (*C*O$_2$). − MS (EI, 70 eV): *m*/*z* (%) = 274 (18) [M$^+$], 256 (7) [M$^+$ − H_2O], 124 (60) [M$^+$ − $C_9H_{11}O_2$; *256* − $C_9H_9O^+$], 117 (100) [$C_9H_9^+$], 115 (80), 95 (89), 86 (56). − $C_{17}H_{22}O_3$ (274.36): calcd. C 74.42, H 8.08; found C 74.48, H 8.03.

3. Synthesis of 3. − General Procedure: A solution of ketenylidenetriphenylphosphorane (**4**) (2.26 g; 7.50 mmol), the respective 1-hydroxy-cycloalkanoic acid ester **2** (5.00 mmol) and a catalytic amount of benzoic acid in dry THF (50 mL) was heated under reflux, with exclusion of air and moisture, for 24 h. After cooling, the solvent was evaporated and the resulting residue was purified by column chromatography (silica gel 60, solvent as indicated).

4-(*trans*-3′-Phenylallyloxy)-1-oxaspiro[4.4]non-3-en-2-one (3a): This compound (1.22 g, 4.53 mmol, 92%) was obtained from **2a** (1.25 g); white needles; m.p. 97 °C; R_f = 0.50 (diethyl ether/hexane, 2:1, v/v). − IR (KBr): ṽ = 2979 cm^{-1}, 2939, 1733, 1623, 1392, 1360, 1200. − ^{1}H NMR (300 MHz, C_6D_6): δ = 1.75−2.09 (m, 8 H, 6-H, 7-H, 8-H, 9-H), 4.70 (dd, ^3J = 6.39, ^4J = 1.14 Hz, 2 H, OCH_2), 5.07 (s, 1 H, 3-H), 6.32 (dt, ^3J = 15.91, 6.39 Hz, 1 H, *H*C=CHPh), 6.72 (dt, ^3J = 15.91, ^4J = 1.14 Hz, 1 H, CH=C*H*Ph), 7.30−7.43 (m, 5 H, Ph). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ= 25.1 (C-7, C-8), 36.3 (C-6, C-9), 73.0 (OCH_2), 88.6 (C-3), 92.3 (C-5-*spiro*), 121.1 (*C*H=CHPh), 126.8, 128.6, 128.8 (CH-*ar.*), 135.5 (C-*ipso*), 135.7 (CH=*C*HPh), 172.0, 182.1 (C-2, C-4). − MS (EI, 70 eV): *m*/*z* (%) = 270 (6) [M$^+$], 257 (11), 157 (42), 117 (100) [$C_9H_9^+$], 91 (29). − $C_{17}H_{18}O_3$ (270.33): calcd. C 75.53, H 6.71; found C 75.47, H 6.70.

4-Allyloxy-1-oxaspiro[4.5]dec-3-en-2-one (3b): This compound (0.89 g, 4.26 mmol; 85%) was obtained from **2b** (0.92 g); white solid; m.p. 43 °C; R_f = 0.69 (diethyl ether/*n*-pentane, 2:1, v/v). − IR (KBr): ṽ = 2938 cm^{-1}, 2862, 1748, 1450, 1337, 1267, 1195, 988. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.61−1.83 (m, 10 H, 6-H, 7-H, 8-H, 9-H, 10-H), 4.52 (dt, ^3J = 5.28 Hz, ^4J = 1.37 Hz, 2 H, OCH_2), 4.94 (s, 1 H, 3-H), 5.35 (dt, ^3J = 11.41 Hz, ^4J = 1.37 Hz, 1 H, CH=C*H*H-*cis*), 5.39 (dt, ^3J = 17.24 Hz, ^4J = 1.37 Hz, 1 H, CH=CH*H*-*trans*), 5.91−6.01 (m, 1 H, C*H*=CH$_2$). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 19.7 (C-7, C-9), 22.4 (C-8), 31.1 (C-6, C-10), 70.8 (OCH_2), 81.9 (C-5-*spiro*), 85.7 (C-3), 117.7 (CH=*C*H$_2$), 128.4 (*C*H=CH$_2$), 170.1, 182.8 (C-2, C-4). − MS (EI, 70 eV): *m*/*z* (%) = 209 (20) [MH$^+$], 196 (13), 167 (19) [M$^+$ − C_3H_5], 152 (16), 140 (14), 125 (36), 113 (31), 99 (47), 82 (70), 69 (100), 55 (83). − $C_{12}H_{16}O_3$ (208.26): calcd. C 69.21, H 7.74; found C 69.19, H 7.79.

4-(*trans*-3′-Phenylallyloxy)-1-oxaspiro[4.5]dec-3-en-2-one (3c): This compound (1.17 g, 4.12 mmol, 82%) was obtained from **2c** (1.33 g); white needles; m.p. 105 °C; R_f = 0.37 (diethyl ether/*n*-pentane, 1:1, v/v). − IR (KBr): ṽ = 2940 cm^{-1}, 2933, 2844, 1739, 1622, 1339, 1187, 965. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.63−1.82 (m, 10 H, 6-H, 7-H, 8-H, 9-H, 10-H), 4.67 (dd, ^3J = 6.35 Hz, ^4J = 1.34 Hz, 2 H, OCH_2), 5.07 (s, 1 H, 3-H), 6.30 (dt, ^3J = 15.91, 6.35 Hz, 1 H, C*H*=CHPh), 6.71 (dt, ^3J = 15.91 Hz, ^4J = 1.34 Hz, 1 H, CH=C*H*Ph), 7.28−7.42 (m, 5 H, Ph). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 21.7 (C-7, C-9), 24.5 (C-8), 33.2 (C-6, C-10), 73.0 (OCH_2), 84.0 (C-5-*spiro*), 87.7 (C-3), 121.2 (*C*H=CHPh), 126.8, 128.6, 128.8 (CH-*ar.*), 135.6 (C-*ipso*), 135.6 (CH=*C*HPh), 172.1, 184.9 (C-2, C-4). − MS (EI, 70 eV): *m*/*z* (%) = 284 (31) [M$^+$], 266 (27) [M$^+$ − H_2O], 56 (5) [M$^+$ − CO], 251 (18), 240 (14), 209 (27), 184 (21), 175 (45), 117 (100) [$C_9H_9^+$], 91 (15) [$C_7H_7^+$]. − $C_{18}H_{20}O_3$ (284.36): calcd. C 76.03, H 7.09; found C 75.96, H 7.02.

4-Allyloxy-1-oxaspiro[4.5]undec-3-en-2-one (3d): This compound (669 mg, 3.00 mmol, 60%) was obtained from **2d** (1.00 g); colourless oil; R_f = 0.73 (diethyl ether/*n*-pentane, 2:1, v/v). − IR (film, NaCl): ṽ = 2929 cm^{-1}, 1861, 1755, 1627, 1337, 1212, 952. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20−1.95 (m, 12 H, 6-H, 7-H, 8-H, 9-H, 10-H, 11-H), 4.51 (dt, ^3J = 5.53 Hz, ^4J = 1.39 Hz, 2 H, OCH_2), 5.34 (s, 1 H, 3-H), 5.36 (dt, ^3J = 11.43 Hz, ^4J = 1.39 Hz, 1 H, CH=C*H*H-*cis*), 5.41 (dt, ^3J = 17.07 Hz, ^4J = 1.39 Hz, 1 H, CH=CH*H*-*trans*), 5.91−5.99 (m, 1 H, C*H*=CH$_2$). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 23.1 (C-7, C-10), 29.7 (C-8, C-9), 37.4 (C-6, C-11), 73.3 (OCH_2), 87.2 (C-3), 87.7 (C-5-*spiro*), 120.1 (CH=*C*H$_2$), 130.9 (*C*H=CH$_2$), 172.6, 186.3 (C-2, C-4). − MS (EI, 70 eV): *m*/*z* (%) = 223 (6) [MH$^+$], 210 (9), 181 (19) [M$^+$ − C_3H_5], 163 (11), 153 (13), 125 (15), 113 (66), 95 (17), 82 (79), 69 (100), 55 (68), 41 (85) [$C_3H_5^+$]. − $C_{13}H_{18}O_3$ (222.29): calcd. C 70.25, H 8.16; found C 70.32, H 8.16.

4-(*trans*-3′-Phenylallyloxy)-1-oxaspiro[4.5]undec-3-en-2-one (3e): This compound (1.36 g, 4.56 mmol; 91%) was obtained from **2e** (1.37 g); white needles; m.p. 54 °C; R_f = 0.66 (diethyl ether/*n*-pentane, 2:1, v/v). − IR (KBr): ṽ = 3114 cm^{-1}, 2929, 1748, 1627, 1211, 1159. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.22−2.10 (m, 12 H, 6-H, 7-H, 8-H, 9-H, 10-H, 11-H), 4.67 (dd, ^3J = 6.32 Hz, ^4J = 1.07 Hz, 2 H, OCH_2), 4.94 (s, 1 H, 3-H), 6.31 (dt, ^3J = 15.91, 6.32 Hz, 1 H, C*H*=CHPh), 6.71 (dt, ^3J = 15.91 Hz, ^4J = 1.07 Hz, 1 H, CH=C*H*Ph), 7.27−7.43 (m, 5 H, Ph). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 22.7 (C-7, C-10), 29.2 (C-8, C-9), 37.0 (C-6, C-11),

73.1 (OCH_2), 86.8 (C-3), 87.4 (C-5-*spiro*), 121.2 (*C*H=CHPh), 126.8, 128.6, 128.8 (CH-*ar.*), 135.6 (CH=*C*HPh), 135.6 (C-*ipso*), 172.3, 186.1 (C-2, C-4). − MS (EI, 70 eV): *m/z* (%) = 298 (12) [M^+], 157 (44), 124 (22), 117 (100) [$C_9H_9^+$], 115 (100), 91 (74), 69 (34). − $C_{19}H_{22}O_3$ (298.39): calcd. C 76.48, H 7.43; found C 76.53, H 7.40.

4. Synthesis of 5. − General Procedure: A solution of the respective 4-allyl spirotetronate **3** (1.00 mmol) in dry acetonitrile (10 mL) was heated under reflux for 48 h (for **3b**: toluene, 24 h) with exclusion of air and moisture. The mixture was then allowed to cool to room temperature and the solvent was evaporated under reduced pressure. Pure tetronic acids **5** were obtained from the remaining residue by column chromatography (silica gel 60; solvent as indicated).

4-Hydroxy-3-(1′-phenylallyl)-1-oxaspiro[4.4]non-3-en-2-one (5a): This compound (151 mg, 0.56 mmol; 56%) was obtained from **3a** (270 mg); yellowish viscous oil; R_f = 0.21 (diethyl ether/hexane, 1:1, v/v). By-products: 1-methyl-2-phenyl-10-oxadispiro[2.1.4.2]undecane-4,11-dione (**6a**) (50 mg; 0.19 mmol, 19%) with R_f = 0.71 (diethyl ether/hexane, 1:1, v/v) and 65 mg (20%) of **3a** recovered, R_f = 0.45 (diethyl ether/hexane, 1:1, v/v). − IR (film, NaCl): $\tilde{\nu}$ = 3445 cm^{-1}, 2956, 2951, 1701, 1650, 1396. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.57−2.04 (m, 8 H, 6-H, 7-H, 8-H, 9-H), 4.55 (d, ^3J = 6.24 Hz, 1 H, 3-CH), 5.08 (d, ^3J = 17.26 Hz, 1 H, CH=C*H*H-*trans*), 5.31 (d, ^3J = 10.14 Hz, 1 H, CH=CH*H*-*cis*), 6.26−6.32 (m, 1 H, C*H*=CH_2), 7.24−7.47 (m, 5 H, Ph). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 25.5 (C-7, C-8), 36.3, 36.4 (C-6, C-9), 43.4 (3-CH), 91.5, 101.9 (C-3, C-5-*spiro*), 118.0 (CH=*C*H_2), 127.7, 128.3, 129.5 (CH-*ar*), 137.72 (*C*H=CH_2), 140.0 (C-*ipso*), 176.0, 176.1 (C-2, C-4). − MS (EI, 70 eV): *m/z* (%) = 270 (17) [M^+], 252 (21) [M^+ − H_2O], 175 (29) [*252* − $C_6H_5^+$], 157 (41), 129 (37), 117 (100) [$C_9H_9^+$], 96 (38), 77 (13) [$C_6H_5^+$]. − $C_{17}H_{18}O_3$ (270.33): calcd. C 75.53, H 6.71; found C 75.48, H 6.77.

3-Allyl-4-hydroxy-1-oxaspiro[4.5]dec-3-en-2-one (5b): This compound (125 mg, 0.60 mmol; 60%) was obtained from **3b** (208 mg); white solid; m.p. 131 °C; R_f = 0.43 (diethyl ether/*n*-pentane, 2:1, v/v). − IR (KBr): $\tilde{\nu}$ = 3425 cm^{-1}, 2932, 2859, 1750, 1710, 1628, 1245. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08−1.93 (m, 10 H, 6-H, 7-H, 8-H, 9-H, 10-H), 2.98 (d, ^3J = 6.12 Hz, 2 H, 3-CH_2), 5.00−5.12 (m, 2 H, CH=CH_2), 5.79−5.92 (m, 1 H, C*H*=CH_2), 10.02 (s, br., 1 H, OH). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 22.2 (C-7, C-9), 24.7, 25.6 (C-8, 3-CH_2), 33.1 (C-6, C-10), 84.1, 97.6 (C-3, C-5-*spiro*), 116.2 (CH=*C*H_2), 134.7 (*C*H=CH_2), 176.3, 180.9 (C-2, C-4). − MS (EI, 70 eV): *m/z* (%) = 208 (29) [M^+], 190 (8) [M^+ − H_2O], 109 (16), 99 (62) [$C_5H_7O_2^+$], 82 (100), 69 (19) [$C_4H_5O^+$] 54 (54), 41 (37) [$C_3H_5^+$]. − $C_{12}H_{16}O_3$ (208.26): calcd. C 69.21, H 7.74; found C 69.24, H 7.78.

4-Hydroxy-3-(1′-phenylallyl)-1-oxaspiro[4.5]dec-3-en-2-one (5c): This compound (154 mg, 0.54 mmol; 54%) was obtained from **3c** (285 mg); white solid; m.p. 149 °C; R_f = 0.17 (diethyl ether/hexane, 1:1, v/v). By-product: 1-methyl-2-phenyl-11-oxadispiro[2.1.5.2]dodecane-4,12-dione (**6c**) (55 mg, 0.20 mmol, 20%) with R_f = 0.71 (diethyl ether/hexane, 1:1, v/v). − IR (KBr): $\tilde{\nu}$ = 3433 cm^{-1}, 2939, 1739, 1700, 1622, 1266, 1230, 980, 696. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18−1.86 (m, 10 H, 6-H, 7-H, 8-H, 9-H, 10-H), 4.52 (dt, ^3J = 6.83 Hz, ^4J = 1.42 Hz, 1 H, 3-CH), 5.07 (dd, ^3J = 17.21 Hz, ^4J = 1.42 Hz, 1 H, CH=C*H*H-*trans*), 5.24 (dd, ^3J = 10.24 Hz, ^4J = 1.42 Hz, 1 H, CH=CH*H*-*cis*), 6.30 (ddd, ^3J = 17.21, 10.24, 6.83 Hz, 1 H, C*H*=CH_2), 7.22−7.32 (m, 5 H, Ph), 8.59 (s, br., 1 H, OH). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 22.1 (C-7, C-9), 24.8 (C-8), 33.1 (C-6, C-10), 43.2 (3-CH), 83.5, 101.2 (C-3, C-5-*spiro*), 117.4 (CH=*C*H_2), 127.4, 128.2, 129.2 (CH-*ar.*), 137.2 (*C*H=CH_2), 140.6 (C-*ipso*), 174.3, 179.9 (C-2, C-4). − MS (EI, 70 eV): *m/z* (%) = 284 (19) [M^+], 266 (28) [M^+ − H_2O], 240 (17) [M^+ − CO_2], 206 (27) [M^+ − C_6H_6], 175 (29), 157 (25), 129 (18), 117 (100) [$C_9H_9^+$], 115 (41). − $C_{18}H_{20}O_3$ (284.36): calcd. C 76.03, H 7.09; found C 76.10, H 7.10.

4-Hydroxy-3-(1′-phenylallyl)-1-oxaspiro[4.6]undec-3-en-2-one (5e): This compound (147 mg, 0.49 mol, 49%) was obtained from **3e** (300 mg); white solid; m.p. 133 °C; R_f = 0.4 (ethyl acetate/hexane, 1:1, v/v). − IR (KBr): $\tilde{\nu}$ = 3434 cm^{-1}, 2930, 1698, 1648, 1577, 1457, 1388, 1299, 1032. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.53−1.98 (m, 12 H, 6-H, 7-H, 8-H, 9-H, 10-H, 11-H), 4.51 (d, ^3J = 6.40 Hz, 1 H, 3-CH), 5.06 (d, ^3J = 17.22 Hz, 1 H, CH=C*H*H-*trans*), 5.26 (d, ^3J = 10.15 Hz, 1 H, CH=CH*H*-*cis*), 6.25−6.31 (m, 1 H, C*H*=CH_2), 7.22−7.33 (m, 5 H, Ph), 8.95 (s, br., 1 H, OH). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 22.7 (C-7, C-10), 29.2 (C-8, C-9), 36.6 (C-6, C-11), 42.7 (3-CH), 86.0, 99.8 (C-3, C-5-*spiro*), 117.3 (CH=*C*H_2), 127.2, 128.9 and 129.0 (CH-*ar.*), 137.4 (*C*H=CH_2), 140.0 (C-*ipso*), 173.4, 180.0 (C-2, C-4). − MS (EI, 70 eV): *m/z* (%) = 298 (12) [M^+], 280 (8) [M^+ − H_2O], 158 (46), 130 (30), 117 (100) [$C_9H_9^+$], 91 (16) [$C_7H_7^+$]. − $C_{19}H_{22}O_3$ (298.39): calcd. C 76.48, H 7.43; found C 76.52, H 7.43.

5. Synthesis of 6. − General Procedure: A solution of the respective 4-allylspirotetronate **3** (1.0 mmol) in toluene (5 mL) was heated under exclusion of air and moisture to 200 °C in a sealed glass tube for 48 h. The mixture was then allowed to cool to room temperature, the solvent was evaporated in a rotary evaporator and the resulting residue was purified by column chromatography (silica gel 60, solvent as indicated).

1-Methyl-2-phenyl-10-oxadispiro[2.1.4.2]undecane-4,11-dione (6a): This compound (200 mg, 0.74 mmol, 74%) was obtained from **3a** (270 mg); white solid; m.p. 78 °C; mixture of diastereoisomers; R_f = 0.84 (diethyl ether/hexane, 1:1, v/v). − IR (KBr): $\tilde{\nu}$ = 3065 cm^{-1}, 2966, 1778, 1735, 1311, 1216, 1160, 1108. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.54 and 1.62 (each d, ^3J = 6.25/6.21 Hz, 3 H, 1-CH_3^{α} and 1-CH_3^{β}), 1.85−2.02 (m, 8 H, 6-$H^{\alpha,\beta}$, 7-$H^{\alpha,\beta}$, 8-$H^{\alpha,\beta}$, 9-$H^{\alpha,\beta}$), 2.85−2.88 and 2.98−3.01 (each m, 1 H, 1-H^{α} and 1-H^{β}), 3.37 and 3.51 (each d, ^3J = 9.24/9.33 Hz, 1 H, 2-H^{α} and 2-H^{β}), 7.05−7.32 (m, 5 H, $Ph^{\alpha,\beta}$). − ^{13}C NMR (125.7 MHz, $CDCl_3$); δ = 11.48, 11.95 (1-$CH_3^{\alpha,\beta}$), 25.17, 25.24, 25.30, 25.31 (C-$7^{\alpha,\beta}$, C-$8^{\alpha,\beta}$), 35.75 (C-$1^{\alpha\text{ or }\beta}$), 36.94, 37.08, 37.35 (C-$6^{\alpha\text{ or }\beta}$ or C-$9^{\alpha\text{ or }\beta}$), 37.50 (C-$1^{\alpha\text{ or }\beta}$), 37.65 (C-$6^{\alpha\text{ or }\beta}$ or C-$9^{\alpha\text{ or }\beta}$), 39.46, 39.61 (C-$3^{\alpha,\beta}$-*spiro*), 51.55, 52.08 (C-$2^{\alpha,\beta}$), 96.53, 96.68 (C-$5^{\alpha,\beta}$-*spiro*), 128.27, 128.32, 128.38, 128.50, 128.96, 129.07 (CH$^{\alpha,\beta}$-*ar.*), 132.39, 132.65 (C$^{\alpha,\beta}$-*ipso*), 171.14, 172.57 (C-$11^{\alpha,\beta}$), 207.16, 209.56 (C-$4^{\alpha,\beta}$). − MS (EI, 70 eV): *m/z* (%) = 270 (46) [M^+], 255 (17), 252 (24) [M^+ − CH_3], 237 (19), 183 (19), 158 (60), 130 (100), 118 (62) [$C_9H_{10}^+$], 115 (70), 105 (15), 95 (32), 91 (29) [$C_7H_7^+$]. − $C_{17}H_{18}O_3$ (270.33): calcd. C 75.53, H 6.71; found C 75.54, H 6.70.

1-Methyl-11-oxadispiro[2.1.5.2]dodecane-4,12-dione (6b): This compound (63 mg, 0.30 mmol; 30%) was obtained from **3b** (208 mg); white solid; m.p. 61 °C; mixture of diastereoisomers; R_f = 0.69 (diethyl ether/*n*-pentane, 1:4, v/v). − IR (KBr): $\tilde{\nu}$ = 2938 cm^{-1}, 2862, 1783, 1739, 1328, 1182, 1119, 1033, 971. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.30 and 1.43 (each d, ^3J = 6.15 Hz, 3 H, 1-$CH_3^{\alpha,\beta}$), 1.67−1.79 (m, 10 H, 6-$H^{\alpha,\beta}$, 7-$H^{\alpha,\beta}$, 8-$H^{\alpha,\beta}$, 9-$H^{\alpha,\beta}$, 10-$H^{\alpha,\beta}$), 1.79−1.97 (m, 2 H, 2-$H^{\alpha,\beta}$), 2.10−2.38 (m, 1 H, 1-$H^{\alpha,\beta}$). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 10.5, 11.1 (1-$CH_3^{\alpha,\beta}$), 20.1, 22.5 (C-$7^{\alpha,\beta}$, C-$9^{\alpha,\beta}$), 28.0, 28.6 (C-$8^{\alpha,\beta}$), 30.89, 30.93, 31.0, 31.3 (C-$2^{\alpha,\beta}$, C-$6^{\alpha,\beta}$, C-$10^{\alpha,\beta}$), 31.5, 31.6 (C-$3^{\alpha,\beta}$-*spiro*), 34.8, 35.2 (C-$1^{\alpha,\beta}$), 88.3, 88.6 (C-$5^{\alpha,\beta}$-*spiro*), 171.9, 173.7 (C-$12^{\alpha,\beta}$), 207.9, 209.1 (C-$4^{\alpha,\beta}$) − MS (EI, 70 eV): *m/z* (%) = 208 (64) [M^+], 190 (21) [M^+ − H_2O],

180 (9) [$M^+ - CO$], 166 (11) [$M - C_3H_6$], 127 (23), 109 (30), 99 (45) [$C_5H_7O_2^+$], 82 (83), 69 (46) [$C_4H_5O^+$], 55 (100), 41 (68) [$C_3H_5^+$]. − $C_{12}H_{16}O_3$ (208.26): calcd. C 69.21, H 7.74; found C 69.27, H 7.77.

1-Methyl-2-phenyl-11-oxadispiro[2.1.5.2]dodecane-4,12-dione (6c): This compound (188 mg, 0.66 mmol, 66%) was obtained from **3c** (283 mg); white solid; m.p. 148−150 °C; mixture of diastereoisomers; separated by column chromatography and recrystallization.

Compound (±)−6c$^{\alpha}$: R_f = 0.68 (diethyl ether/*n*-pentane, 1:4, v/v). − IR (KBr): $\tilde{\nu}$ = 3063 cm^{-1}, 2936, 1775, 1732, 1313, 1279, 1119, 969. − ^1H NMR (500 MHz, $CDCl_3$): δ = 1.25−1.83 (m, 10 H, 6-H, 7-H, 8-H, 9-H, 10-H), 1.52 (d, ^3J = 6.15 Hz, 3 H, 1-CH_3), 2.98 (dq, ^3J = 9.20, 6.15 Hz, 1 H, 1-H), 3.33 (d, ^3J = 9.20 Hz, 1 H, 2-H), 7.25−7.32 (m, 5 H, Ph). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 11.5 (1-CH_3), 21.05, 21.12 (C-7, C-9), 24.5 (C-8), 32.0, 32.8 (C-6, C-10), 37.5 (C-1), 40.0 (C-3-*spiro*), 51.4 (C-2), 88.7 (C-5-*spiro*), 128.3, 128.4, 129.0 (CH-ar.), 132.4 (C-*ipso*), 171.2 (C-12), 208.7 (C-4).

Compound (±)−6c$^{\beta}$: R_f = 0.72 (diethyl ether/*n*-pentane, 1:4, v/v); m.p. 151 °C (from chloroform/*n*-pentane). − IR (KBr): $\tilde{\nu}$ = 3063 cm^{-1}, 2952, 2935, 1773, 1737, 1458, 1447, 1315, 1110, 966, 694. − ^1H NMR (500 MHz, $CDCl_3$): δ = 1.25−1.77 (m, 10 H, 6-H, 7-H, 8-H, 9-H, 10-H), 1.62 (d, ^3J = 6.20 Hz, 3 H, 1-CH_3), 2.83 (dq, ^3J = 9.25, 6.20 Hz, 1 H, 1-H), 3.50 (d, ^3J = 9.25 Hz, 1 H, 2-H), 7.23−7.32 (m, 5 H, Ph). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 11.8 (1-CH_3), 20.8, 21.0 (C-7, C-9), 24.4 (C-8), 31.88, 31.94 (C-6, C-10), 35.7 (C-1), 38.8 (C-3-*spiro*), 51.79 (C-2), 88.8 (C-5-*spiro*), 128.15, 128.20, 128.8 (CH-*ar.*), 132.3 (C-*ipso*), 172.5 (C-12), 206.1 (C-4). − MS (EI, 70 eV): *m/z* (%) = 284 (42) [M^+], 266 (27) [$M^+ - H_2O$], 251 (66) [*266* − CH_3^+], 185 (20), 175 (13) [*266* − $C_7H_7^+$], 158 (41) [*175* − OH^+], 130 (77), 115 (100), 109 (25), 91 (77) [$C_7H_7^+$]. − $C_{18}H_{20}O_3$ (284.36): calcd. C 76.03, H 7.09; found C 76.08, H 7.03.

X-ray Crystal-Structure Analysis of (±)−6c$^{\beta}$:[15] Clear, colourless crystals were obtained from chloroform/*n*-pentane solutions at room temperature. Empirical formula $C_{18}H_{20}O_3$, molecular mass 284.34 g mol^{-1}, crystal size 0.2 × 0.3 × 0.1 mm, *a* = 21.690(4), *b* = 6.9970(10), *c* = 21.276(3) Å, β = 112.280(10)°, *V* = 2987.9(8) $Å^3$, *T* = 293 K; $d_{calcd.}$ = 1.264 g cm^{-3}, μ = 1.0 cm^{-1}, *Z* = 8, monoclinic, space group *C*2/*c*, Siemens P4 diffractometer, λ = 0.71037 Å, Θ range 2.0−25°; ω scans, index ranges $0 \le h \le 25$, $-8 \le k \le 0$, $-25 \le l \le 25$, 2716 collected reflections, 2038 reflections [$I > 2\sigma(I)$], 270 refined parameters, absorption correction with Ψ scans. Structure solution: direct methods (SHELXS86); structure refinement: full-matrix least squares on F^2 (SHELXL93); *R*1 = 0.0392, *wR*2 = 0.1272 (all data), largest diff. peak and hole 0.19 and −0.23 e$Å^{-3}$.

1-Methyl-12-oxadispiro[2.1.6.2]tridecane-4,13-dione (6d): This compound (76 mg, 0.35 mmol; 35%) was obtained from **3d** (222 mg); white solid; m.p. 97 °C; mixture of two diastereomers; R_f = 0.74 and 0.70 (diethyl ether/*n*-pentane, 1:4, v/v). − IR (KBr): $\tilde{\nu}$ = 2931 cm^{-1}, 1784, 1740, 1327, 1168, 1102, 1107. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.30 and 1.42 (each d, ^3J = 6.14, 6.10 Hz, 3 H, 1-$CH_3^{\alpha,\beta}$), 1.66−2.08 (m, 14 H, 2-$H^{\alpha,\beta}$, 6-$H^{\alpha,\beta}$, 7-$H^{\alpha,\beta}$, 8-$H^{\alpha,\beta}$, 9-$H^{\alpha,\beta}$, 10-$H^{\alpha,\beta}$, 11-$H^{\alpha,\beta}$), 2.12−2.40 (m, 1 H, 1-$H^{\alpha,\beta}$). − ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 11.5, 12.7 (1-$CH_3^{\alpha,\beta}$), 22.26, 22.34 (C-$7^{\alpha,\beta}$, C-$10^{\alpha,\beta}$), 28.8, 29.1, 29.2, 29.5 (C-$2^{\alpha,\beta}$, C-$8^{\alpha,\beta}$, C-$9^{\alpha,\beta}$), 31.6, 32.1 (C-$3^{\alpha,\beta}$-*spiro*), 35.7, 35.9 (C-$6^{\alpha,\beta}$, C-$11^{\alpha,\beta}$), 36.0, 36.4 (C-$1^{\alpha,\beta}$), 92.4 (C-$5^{\alpha,\beta}$-*spiro*), 172.9, 174.8 (C-$13^{\alpha,\beta}$), 209.9, 211.2 (C-$4^{\alpha,\beta}$). − MS (EI, 70 eV): *m/z* (%) = 222 (67) [M^+], 207 (16) [$M^+ - CH_3$], 204 (7) [$M^+ - H_2O$], 153 (19) [$M^+ - C_4H_5O$], 127 (21), 113 (35), 95 (25), 82 (100), 68 (37), 54 (100), 41 (79). − $C_{13}H_{18}O_3$ (222.29): calcd. C 70.25, H 8.16; found C 70.17, H 8.11.

1-Methyl-2-phenyl-12-oxadispiro[2.1.6.2]tridecane-4,13-dione (6e): This compound (219 mg, 0.77 mmol, 77%) was obtained from **3e** (285 mg); yellowish viscous oil; mixture of two diastereoisomers; R_f = 0.65 (diethyl ether/hexane, 1:1, v/v).

Mixture of Diastereoisomers: IR (KBr): $\tilde{\nu}$ = 3062 cm^{-1}, 2929, 1781, 1732, 1309, 1215, 1165, 1032, 1109, 697. − ^1H NMR (500 MHz, $CDCl_3$): δ = 1.25−1.99 (m, 12 H, 6-$H^{\alpha,\beta}$, 7-$H^{\alpha,\beta}$, 8-$H^{\alpha,\beta}$, 9-$H^{\alpha,\beta}$, 10-$H^{\alpha,\beta}$, 11-$H^{\alpha,\beta}$), 1.51 (d, ^3J = 6.17 Hz, 3 H, 1-CH_3^{β}), 1.60 (d, ^3J = 6.15 Hz, 3 H, 1-CH_3^{α}), 2.82 (dq, ^3J = 9.15, 6.17 Hz, 1 H, 1-H^{β}), 2.96 (dq, ^3J = 9.23, 6.15 Hz, 1 H, 1-H^{α}), 3.32 (d, ^3J = 9.23 Hz, 1 H, 2-H^{α}), 3.47 (d, ^3J = 9.15 Hz, 1 H, 2-H^{β}), 7.13−7.36 (m, 5 H, $Ph^{\alpha,\beta}$). − ^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 11.4 (1-CH_3^{α}), 11.9 (1-CH_3^{β}), 22.1, 22.3 (C-7^{β}, C-10^{β}), 22.4, 22.5 (C-7^{α}, C-10^{α}), 29.12, 29.16 (C-8^{β}, C-9^{β}), 29.2, 29.3 (C-8^{α}, C-9^{α}), 35.60 (C-6 $^{\beta}$or C-11 $^{\beta}$), 35.65 (C-1 $^{\beta}$), 35.73 (C-6^{α} or C-11^{α}), 35.95 (C-6 $^{\beta}$or C-11 $^{\beta}$), 36.1 (C-6^{α} or C-11^{α}), 37.7 (C-1^{α}), 38.5 (C-3^{β}-*spiro*), 38.6 (C-3^{α}-*spiro*), 51.2 (C-2^{β}), 51.7 (C-2^{α}), 91.57 (C-5^{β}-*spiro*), 91.65 (C-5^{α}-*spiro*), 128.30, 128.38, 128.42, 128.48, 128.9, 129.0 (C$H^{\alpha,\beta}$), 132.4 (C$^{\beta}$-*ipso*), 132.7 (C$^{\alpha}$-*ipso*), 172.2 (C-13^{α}), 172.6 (C-13^{β}), 207.1 (C-4^{β}), 209.6 (C-4^{α}). − MS (EI, 70 eV): *m/z* (%) = 298 (70) [M^+], 280 (22) [$M^+ - H_2O$], 265 (26) [*280* − CH_3^+], 192 (19), 198 (20), 189 (20) [*280* − $C_7H_7^+$], 185 (44), 158 (50), 130 (79), 118 (100) [$C_9H_{10}^+$], 110 (78), 105 (28), 91 (51) [$C_7H_7^+$]. − $C_{19}H_{22}O_3$ (298.39): calcd. C 76.48, H 7.43; found C 76.52, H 7.47.

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[15] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (CCDC-151642). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033, E-mail: deposit@ccdc.cam.ac.uk].

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