Structural characterization of strained oxacycles by ^{13}C NMR spectroscopy

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Dedicated to Professor Manuel González Sierra in honor of his leading work in the field of NMR spectroscopy

Abstract
The ^{1}H and ^{13}C NMR data of a series of epoxy- and epidioxy-bridged tetrahydropyran derivatives containing the same basic carbon skeleton, are reported. ^{13}C NMR spectroscopy was shown to be useful for structural determination of both substructures allowing facile distinction of otherwise similar compounds.

Keywords: NMR, ^{1}H, ^{13}C, oxacycles, catalytic hydrogenation

Introduction

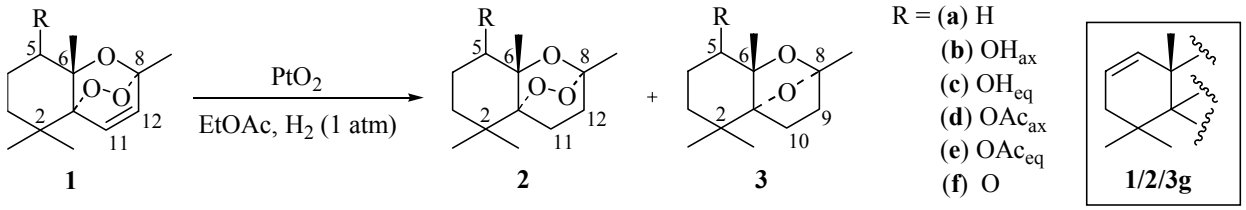
As part of our investigations on the photochemical reactivity of dienone systems, we have established an easy approach for the preparation of a series of bridged unsaturated 1,2,4-trioxanes **1a–g** by irradiation of the corresponding *β*-ionone derivatives in the presence of oxygen.[1,2] Due to their peroxidic nature, analogous to the pharmacophore of the potent antimalarial compound artemisinin, 1,2,4-trioxanic compounds have been the focus of great synthetic activity and several aspects of their fundamental chemical reactivity are currently under investigation.[3,4]

During our studies directed to identifying mild and synthetically useful transformations of **1**,[5] heterogeneous catalytic hydrogenation conditions were used to examine the chemoselectivity of the reduction process and to test primarily peroxy bond compatibility. The reduction of **1a–g** affords products containing the 2,3,5-trioxabicyclo[2.2.2]octane and 2,7-dioxabicyclo[2.2.1]heptane units **2a–g** and **3a–g**, respectively, that can not readily be distinguished by means of spectroscopic techniques. As far as we know, there are no reports in the literature concerning NMR spectral studies for the two sets of oxygen-bridged pyran

derivatives having similar ^{1}H and ^{13}C spectra. Herein we report the characterization of the reduced products and the application of ^{13}C NMR comparative data for the unambiguous structural assignment.

Results and Discussion

The reduction of **1a–g** using platinum oxide as catalyst in ethyl acetate under atmospheric pressure of hydrogen furnished a set of compounds containing the 2,3,5-trioxabicyclo[2.2.2]octane and 2,7-dioxabicyclo[2.2.1]heptane units, **2a–g** and **3a–g**, respectively (Scheme 1). Depending on reaction conditions (mainly amount of catalyst and reaction times) and on substrate structure, reaction products consisted of mixtures of compounds **2** and **3**, or solely the over-reduced products **3**. In order to study the chemoselectivity of the reaction[6,7] and due to the fact that ^{1}H and ^{13}C spectral data for both compounds are too similar, we initially faced the problem of identifying the structures unambiguously. After chromatographic separation, compounds **2** and **3** were isolated in pure form and an exhaustive NMR study was carried out in order to attempt the complete ^{1}H and ^{13}C signal assignments and to ascertain whether the data could be used to unequivocally distinguish the structures.



Scheme 1. Hydrogenation of unsaturated 1,2,4-trioxanes derived from *β*-ionone.

^{1}H NMR assignments for compounds **2a–g** and **3a–g** were not straightforward because of overlapping in the aliphatic region, making determination of any correlation between chemical shifts and epoxy or epidioxy bridged structures problematic.

Comparison of the similarities and differences in the ^{13}C NMR data between **1**, **2** and **3** revealed several trends leading to useful generalizations. During our study, we could realize that the ^{13}C chemical shift values of the oxygenated quaternary carbons change in a regular manner on going from the unsaturated **1** to the saturated systems **2**. The changes involved were low-frequency shift (above 1 ppm) of C-1 signal, high-frequency shift (above 2 ppm) for C-8, while resonance of C-6 remained unaltered.

On the other hand, a similar analysis of the ^{13}C data for the [2.2.2] and [2.2.1] oxacyclic series **2** and **3**, showed significant differences. All carbons corresponding to the pyran skeleton [C-1, C-6, C-8, C-9(12) and C-10(11)] experienced a high-frequency shift on going from the epidioxy-bridged systems to the contracted epoxy-bridged unit. The resonance position of carbons C-1, C-8, C-9(12) and C-10(11) in **3** appeared shifted to higher frequencies by 5 to 11

ppm while for C-6 differences were small (*ca*. 3 ppm) if compared with the same carbons in **2** (see Table 1). Particularly, the ^{13}C chemical shifts of the oxa-bridge-bearing carbons C-1 and C-8 can be used to distinguish the [2.2.2] series **2** from the [2.2.1] series **3** without any further analysis of other spectral data. These two ^{13}C signal values experienced a high-frequency shift (90–95 *vs*. 80–85 ppm for C-1 and 107–108 *vs*. 96–98 ppm for C-8) comparing the contracted system **3** with **2**. This simple rule facilitated our work aimed at finding reaction conditions for chemoselective control.

Table 1. $\Delta\delta_c$ values (in ppm) of carbons 1, 6, 8, 9(12) and 10(11) for series **3** and **2**[a]

Compounds	C-1	C-6	C-8	C-9(12)	C-10(11)
3a, **2a**	11.4	3.6	10.7	7.4	5.3
3b, **2b**	12.1	3.0	10.7	7.1	5.2
3c, **2c**	11.7	4.6	11.2	7.5	5.5
3d, **2d**	12.4	2.7	11.3	7.3	5.0
3e, **2e**	11.8	4.3	11.5	7.5	5.4
3f, **2f**	11.5	3.2	9.8	7.7	4.5
3g, **2g**	11.2	3.3	8.5	7.3	4.3

[a] $\Delta\delta = \delta_c$ **3** $- \delta_c$ **2**

The nature and stereochemistry of the substituents at C-5 appeared to have no influence upon the chemical shift of those diagnostic signals. Considering that we have also observed a slight effect on position 1 and 8 by saturation of the C-C double bond on going from **1** to **2**, the large deshielding effect observed in the chemical shifts of C-1 and C-8 carbon atoms in compounds **3** probably results from the enhancement of the annular strain due to the contraction of the oxygenated bridge,[8] following the same trend as in the carbocyclic frameworks being the norbornyl system more strained than the bicyclo[2.2.2]octyl unit.[9]

For all the examples shown the trend is uniform, variations of chemical shifts were large enough (*ca*. 10 ppm) and the corresponding signals were clearly separated from others in the spectrum so that both systems **2** and **3** could be easily distinguished providing a diagnostic method for the structural elucidation of epoxy and epidioxy bridged pyran systems by application of conventional one-dimensional ^{13}C NMR. The results disclosed herein may offer a practical reference for future structure elucidation of analogous bridged bicyclic ketal units containing compounds.

Experimental Section

General. NMR spectra were recorded in chloroform-d at room temperature at 7.05 Tesla using a 300.13 MHz Fourier transform NMR spectrometer (Bruker Avance II) equipped with a 5 mm multinuclear BBO probehead with a Z-shielded gradient. For the ^{1}H NMR analyses, 16 transients

were acquired with a 1 s relaxation delay, using 16 k data points. The 90º pulse duration was of 10 μs and the spectral width was 3000 Hz. The ^{13}C NMR and DEPT spectra were obtained with a spectral width of 18029 Hz, using 32 k data points. Their 90º pulse duration was of 8 μs. The pulse programs for the 2D experiments (HSQC and HMBC) were the standard sequences taken from the Bruker software library. Chemical shifts for ^{1}H NMR spectra are reported in parts per million relative to the signal of tetramethylsilane at 0 ppm (internal standard). Chemical shifts for ^{13}C NMR spectra are reported in parts per million relative to the center line of the $CDCl_3$ triplet at 76.9 ppm.

For all compounds, assignment of C-6, C-8 and C-2 methyl groups were made by analysis of their HSQC and HMBC 2D experiments except for compounds **3a**, **2g**, **1c**, **1f** and **1g**. For the latter, assignments were made by analogy with other compounds of the same series. For all compounds, stereo-differentiation between C-2 methyl groups (axial and equatorial) was made by analysis of NOE experiments (NOE between C-6 Me and C-2 Me_{ax}; or absence of NOE between C-2 Me_{eq} and C-6 Me) except for compounds **3a**, **2g**, **1g**, **1c** and **1e**. In this case, assignments were made by analogy with other compounds of the same series based on proton chemical shifts of methyl groups.

2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodec-11-ene (1a). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.53 (d AB, J = 8.4 Hz, 1H, 11-H), 6.44 (d AB, J = 8.4 Hz, 1H, 12-H), 2.18 (td, J = 12.6, 3.6 Hz, 1H, 5-H_{ax}), 1.79 (td, J = 13.2, 3.9 Hz, 3-H_{ax}), 1.71–1.42 (m, 3H, 5-H_{eq}, 4-H), 1.49 (s, 3H, 8-CH_3), 1.26–1.18 (dm, J = 13.2 Hz, 1H, 3-H_{eq}), 1.14 (d, J = 1 Hz, 3H, 6-CH_3), 1.12 (s, 3H, 2-CH_{3ax}), 1.01 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 133.3 (d, C-12), 128.5 (d, C-11), 94.6 (s, C-8), 82.1 (s, C-1), 78.0 (s, C-6), 35.5 (s, C-2), 34.5 × 2 (t, C-3, C-5), 26.5 (q, C-2-CH_{3eq}), 25.4 (q, C-6-CH_3), 24.3 (q, C-2-CH_{3ax}), 20.8 (q, C-8-CH_3), 19.2 (t, C-4).

syn-**2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodec-11-en-5-ol (1b).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.53 (d AB, J = 8.4 Hz, 1H, 11-H), 6.42 (d AB, J = 8.4 Hz, 1H, 12-H), 3.72 (t, J = 2.9 Hz, 1H, 5-H_{eq}), 3.54 (bs, 1H, OH), 2.00 (td, J = 13.0, 4.2 Hz, 1H, 3-H_{ax}), 1.95–1.68 (m, 2H, 4-H), 1.52 (s, 3H, 8-CH_3), 1.08 (dt, J = 13.0, 3.9 Hz, 3-H_{eq}), 1.08 (s, 3H, 6-CH_3), 1.07 (s, 3H, 2-CH_{3ax}), 0.96 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 133.2 (d, C-12), 128.9 (d, C-11), 94.8 (s, C-8), 82.8 (s, C-1), 78.4 (s, C-6), 71.1 (d, C-5), 35.1 (s, C-2), 28.8 (t, C-3), 26.05 (q, C-2-CH_{3eq}), 26.00 (q, C-2-CH_{3ax}), 25.5 (t, C-4), 24.1 (q, C-6-CH_3), 20.4 (q, C-8-CH_3).

anti-**2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodec-11-en-5-ol (1c).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.52 (d AB, J = 8.6 Hz, 11-H), 6.44 (d AB, J = 8.6 Hz, 12-H), 4.34 (dd, J = 12.1, 4.6 Hz, 1H, 5-H_{ax}), 1.91 (td, J = 13.5, 4.4 Hz, 1H, 3-H_{ax}), 1.89–1.81 (m, 1H, 4-H_{ax}), 1.62–1.50 (m, 1H, 4-H_{eq}), 1.51 (s, 3H, 8-CH_3), 1.32 (ddd, J = 14.0, 4.8, 3.1 Hz, 1H, 3-H_{eq}), 1.12 (s, 3H, 2-CH_{3ax}), 1.07 (s, 3H, 6-CH_3), 1.00 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 133.3 (d, C-12), 128.6 (d, C-11), 94.9 (s, C-8), 83.1 (s, C-1), 80.8 (s, C-6), 73.7 (d, C-5), 35.5 (s, C-2), 33.6 (t, C-3), 26.7 (t, C-4), 26.0 (q, C-2-CH_{3eq}), 24.5 (q, C-2-CH_{3ax}), 20.7 (q, C-8-CH_3), 19.4 (q, C-6-CH_3).

***syn*-2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodec-11-en-5-yl Acetate (1d).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.55 (d AB, J = 8.4 Hz, 1H, 11-H), 6.43 (d AB, J = 8.4 Hz, 1H, 12-H), 5.12 (t, J = 3.0 Hz, 1H, 5-H_{eq}), 2.18 (s, 3H, $COCH_3$), 2.12 (td, J = 14.0, 4.3 Hz, 1H, 3-H_{ax}), 1.93 (tdd, J = 15.0, 4.0, 3.2 Hz, 1H, 4-H_{ax}), 1.73 (ddt, J = 15.1, 4.5, 2.8 Hz, 1H, 4-H_{eq}), 1.45 (s, 3H, 8-CH_3), 1.26–1.12 (m, 1H, 3-H_{eq}), 1.17 (s, 3H, 6-CH_3), 1.14 (s, 3H, 2-CH_{3ax}), 1.04 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 171.4 (s, COO), 133.3 (d, C-12), 128.6 (d, C-11), 94.2 (s, C-8), 80.9 (s, C-1), 77.3 (s, C-6), 70.7 (d, C-5), 34.9 (s, C-2), 29.6 (t, C-3), 26.1 × 2 (q, C-2-CH_{3eq}, C-6-CH_3), 24.0 (q, C-2-CH_{3ax}), 23.5 (t, C-4), 21.4 (q, $COCH_3$), 20.5 (q, C-8-CH_3).

***anti*-2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodec-11-en-5-yl acetate (1e).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.50 (d AB, J = 8.5 Hz, 1H, 11-H), 6.45 (d AB, J = 8.5 Hz, 1H, 12-H), 5.46 (dd, J = 12.0, 4.5 Hz, 1H, 5-H_{ax}), 2.08 (s, 3H, $COCH_3$), 2.05–1.85 (m, 2H, 3-H_{ax}, 4-H_{ax}), 1.51 (td, J = 14.5, 4.2 Hz, 1H, 4-H_{eq}), 1.47 (s, 3H, 8-CH_3), 1.28 (dm, J = 13.8 Hz, 1H, 3-H_{eq}), 1.13 (s, 6H, 6-CH_3, 2-CH_{3ax}), 1.01 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.2 (s, COO), 133.8 (d, C-12), 128.0 (d, C-11), 94.7 (s, C-8), 83.0 (s, C-1), 78.8 (s, C-6), 76.2 (d, C-5), 35.3 (s, C-2), 33.2 (t, C-3), 26.0 (q, C-2-CH_{3eq}), 24.9 (t, C-4), 24.3 (q, C-6-CH_3), 21.3 (q, $COCH_3$), 20.5 (q, C-8-CH_3), 20.4 (q, C-2-CH_{3ax}).

2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodec-11-en-5-one (1f). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.52 (d AB, J = 8.5 Hz, 1H, 11-H), 6.51 (d AB, J = 8.5 Hz, 1H, 12-H), 2.73 (ddd, J = 15.1, 13.5, 6.5 Hz, 1H, 4-H_{ax}), 2.46 (ddd, J = 15.2, 5.1, 2.6 Hz, 1H, 4-H_{eq}), 2.18 (td, J = 13.8, 5.0 Hz, 1H, 3-H_{ax}), 1.63 (ddd, J = 13.8, 6.6, 2.7 Hz, 1H, 3-H_{eq}), 1.59 (s, 3H, 8-CH_3), 1.36 (s, 3H, 6-CH_3), 1.26 (s, 3H, 2-CH_{3ax}), 1.10 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 207.6 (s, C-5), 134.8 (d, C-12), 126.1 (d, C-11), 95.2 (s, C-8), 85.1 (s, C-1), 82.9 (s, C-6), 35.5 (s, C-2), 34.7 (t, C-3), 34.5 (t, C-4), 25.5 (q, C-2-CH_{3eq}), 24.4 × 2 (q, C-6-CH_3, C-2-CH_{3ax}), 20.4 (q, C-8-CH_3).

2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodeca-4,11-diene (1g). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.61 (d AB, J = 8.4 Hz, 1H, 11-H), 6.47 (d AB, J = 8.4 Hz, 1H, 12-H), 5.79–5.66 (m, 2H, 5-H, 4-H), 2.34 (bd, J = 17.1 Hz, 1H, 3-H$_\alpha$), 1.79 (dd, J = 18.1, 3.7 Hz, 1H, 3-H$_\beta$), 1.53 (s, 3H, 8-CH_3), 1.22 (s, 3H, 6-CH_3), 1.13 (s, 3H, 2-CH_{3ax}), 1.10 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 133.3 (d, C-12), 129.1 (d, C-5), 127.4 (d, C-11), 125.4 (d, C-4), 95.5 (s, C-8), 81.7 (s, C-1), 77.1 (s, C-6), 37.3 (t, C-3), 33.9 (s, C-2), 27.5 (q, C-6-CH_3), 27.2 (q, C-2-CH_{3ax}), 25.2 (q, C-2-CH_{3eq}), 20.9 (q, C-8-CH_3).

2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodecane (2a). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.21 (td, J = 13.9, 5.2 Hz, 1H, 5-H_{ax}), 2.15–1.95 (m, 4H, 11-H, 12-H), 1.72 (td, J = 13.2, 4.1 Hz, 1H, 3-H_{ax}), 1.48–1.43 (m, 3H, 5-H_{eq}, 4-H), 1.40 (s, 3H, 6-CH_3), 1.26 (s, 3H, 8-CH_3), 1.12 (dm, J = 13.2 Hz, 1H, 3-H_{eq}), 0.98 (s, 3H, 2-CH_{3ax}), 0.96 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 96.7 (s, C-8), 80.6 (s, C-1), 77.9 (s, C-6), 37.2 (s, C-2), 36.4 (t, C-5), 35.7 (t, C-3), 30.0 (t, C-12), 25.9 (q, C-2-CH_{3eq}), 25.7 (q, C-6-CH_3), 24.6 (q, C-2-CH_{3ax}), 23.3 (q, C-8-CH_3), 19.7 (t, C-11), 19.2 (t, C-4).

***syn*-2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodecan-5-ol (2b).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.70 (bs, 1H, 5-H_{eq}), 3.66 (bs, 1H, OH), 2.19–2.00 (m, 5H, 11-H, 12-H, 3-H_{ax}),

1.88 (bddd, J = 14.6, 7.0, 3.2 Hz, 1H, 4-H_{eq}), 1.72 (tdd, J = 14.6, 3.8, 2.5 Hz, 1H, 4-H_{ax}), 1.39 (s, 3H, 6-CH_3), 1.37 (s, 3H, 8-CH_3), 1.02 (s, 3H, 2-CH_{3ax}), 1.01 (dt, J = 13.5, 3.6 Hz, 1H, 3-H_{eq}), 0.99 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 97.2 (s, C-8), 81.5 (s, C-1), 78.3 (s, C-6), 73.0 (d, C-5), 36.8 (s, C-2), 29.8 (t, C-3), 29.6 (t, C-12), 26.0 (q, C-6-CH_3), 25.6 (q, C-2-CH_{3eq}), 25.4 (t, C-4), 24.7 (q, C-2-CH_{3ax}), 23.1 (q, C-8-CH_3), 20.3 (t, C-11).

anti-**2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodecan-5-ol (2c).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.36 (dd, J = 12.4, 4.6 Hz, 1H, 5-H_{ax}), 2.15–1.74 (m, 6H, 11-H, 12-H, 4-H_{eq}, 3-H_{ax}), 1.56–1.43 (m, 1H, 4-H_{ax}), 1.35 (s, 3H, 6-CH_3), 1.29 (s, 3H, 8-CH_3), 1.23 (ddd, J = 14.1, 4.5, 2.5 Hz, 1H, 3-H_{eq}), 1.00 (s, 3H, 2-CH_{3ax}), 0.95 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 97.1 (s, C-8), 81.8 (s, C-1), 80.8 (s, C-6), 74.1 (d, C-5), 37.3 (s, C-2), 34.4 (t, C-3), 29.7 (t, C-12), 26.4 (t, C-4), 25.5 (q, C-2-CH_{3eq}), 24.8 (q, C-2-CH_{3ax}), 23.2 (q, C-8-CH_3), 20.3 (t, C-11), 19.3 (q, C-6-CH_3).

syn-**2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodecan-5-yl Acetate (2d).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.05 (t, J = 3.0 Hz, 1H, 5-H_{eq}), 2.16 (s, 3H, $COCH_3$), 2.20–1.66 (m, 7H, 11-H, 12-H, 4-H, 3-H_{ax}), 1.43 (s, 3H, 6-CH_3), 1.23 (s, 3H, 8-CH_3), 1.04 (t, J = 3.2 Hz, 1H, 3-H_{eq}), 1.02 (s, 3H, 2-CH_{3ax}), 1.01 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 171.3 (s, CO), 96.2 (s, C-8), 79.5 (s, C-1), 77.0 (s, C-6), 72.6 (d, C-5), 36.6 (s, C-2), 30.5 (t, C-3), 29.8 (t, C-12), 26.3 (q, C-6-CH_3), 25.6 (q, C-2-CH_{3eq}), 24.5 (q, C-2-CH_{3ax}), 23.5 (t, C-4), 23.0 (q, C-8-CH_3), 21.5 (q, $COCH_3$), 20.4 (t, C-11).

anti-**2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodecan-5-yl Acetate (2e).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.51 (dd, J = 12.3, 4.8 Hz, 1H, 5-H_{ax}), 2.09 (s, 3H, $COCH_3$), 2.15–1.85 (m, 6H, 11-H, 12-H, 4-H_{eq}, 3-H_{ax}), 1.50–1.38 (m, 1H, 4-H_{ax}), 1.41 (s, 3H, 6-CH_3), 1.25 (s, 3H, 8-CH_3), 1.24–1.17 (m, 1H, 3-H_{eq}), 1.01 (s, 3H, 2-CH_{3ax}), 0.97 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.4 (s, CO), 96.9 (s, C-8), 81.9 (s, C-1), 79.0 (s, C-6), 76.5 (d, C-5), 37.1 (s, C-2), 34.0 (t, C-3), 29.7 (t, C-12), 25.5 (q, C-2-CH_{3eq}), 24.9 (t, C-4), 24.5 (q, C-2-CH_{3ax}), 23.0 (q, C-8-CH_3), 21.3 (q, $COCH_3$), 20.3 (q, C-6-CH_3), 20.0 (t, C-11).

2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodecan-5-one (2f). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.66–2.49 (m, 2H, 4-H), 2.21–2.12 (m, 2H, 11-H), 2.11–1.98 (m, 3H, 12-H, 3-H_{eq}), 1.61 (ddd, J = 13.9, 11.5, 5.7 Hz, 1H, 3-H_{ax}), 1.50 (s, 3H, 6-CH_3), 1.38 (s, 3H, 8-CH_3), 1.20 (s, 3H, 2-CH_{3ax}), 1.06 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 208.8 (s, C-5), 98.1 (s, C-8), 84.0 (s, C-1), 82.3 (s, C-6), 36.9 (s, C-2), 34.8 (t, C-3), 34.6 (t, C-4), 29.7 (t, C-12), 25.2 (q, C-2-CH_{3ax}), 24.8 (q, C-2-CH_{3eq}), 23.8 (q, C-6-CH_3), 22.8 (q, C-8-CH_3), 19.8 (t, C-11).

2,2,6,8-Tetramethyl-7,9,10-trioxatricyclo[6.2.2.0^{1,6}]dodec-4-ene (2g). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.69 (ddd, J = 10.3, 4.7, 2.1 Hz, 1H, 4-H), 5.59 (dd, J = 10.3, 2.7 Hz, 1H, 5-H), 2.31 (bd, J = 18.0 Hz, 1H, 3-H_β), 2.26–2.02 (m, 4H, 11-H, 12-H), 1.63 (dd, J = 18.0, 4.6 Hz, 1H, 3-H_α), 1.47 (s, 3H, 6-CH_3), 1.32 (s, 3H, 8-CH_3), 1.05 (s, 3H, 2-CH_{3ax}), 1.02 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 130.4 (d, C-5), 125.2 (d, C-4), 98.2 (s, C-8), 80.3 (s, C-1), 75.9 (s, C-6), 37.2 (t, C-3), 35.5 (s, C-2), 30.0 (t, C-12), 26.6 (q, C-6-CH_3), 26.3 (q, C-2-CH_{3eq}), 24.6 (q, C-2-CH_{3ax}), 23.4 (q, C-8-CH_3), 19.6 (t, C-11).

2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecane (3a). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 1.94–1.43 (m, 8H, 10-H, 9-H, 5-H, 4-H_{eq}, 3-H_{ax}), 1.54 (s, 3H, 8-CH_3), 1.37 (s, 3H, 6-CH_3), 1.36 (tt, J = 13.2, 3.0 Hz, 1H, 4-H_{ax}), 1.32–1.25 (dm, J = 14.5 Hz, 1H, 3-H_{eq}), 1.08 (s, 3H, 2-CH_{3eq}), 0.96 (s, 3H, 2-CH_{3ax}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 107.4 (s, C-8), 92.0 (s, C-1), 81.5 (s, C-6), 39.1 (t, C-3), 37.8 (t, C-5), 37.4 (t, C-12), 34.3 (s, C-2), 26.0 (q, C-2-CH_{3eq}), 25.0 (t, C-11), 24.0 (q, C-2-CH_{3ax}), 22.9 (q, C-6-CH_3), 19.7 (q, C-8-CH_3), 19.6 (t, C-4).

syn-**2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-5-ol (3b).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.44 (bs, 1H, 5-H_{eq}), 2.96 (bs, 1H, OH), 1.98 (td, J = 13.8, 3.6 Hz, 1H, 3-H_{ax}), 1.91–1.52 (m, 6H, 10-H, 9-H, 4-H), 1.53 (s, 3H, 8-CH_3), 1.27 (s, 3H, 6-CH_3), 1.04 (dt, J = 13.8, 3.3 Hz, 1H, 3-H_{eq}), 1.02 (s, 3H, 2-CH_{3eq}), 0.91 (s, 3H, 2-CH_{3ax}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 107.9 (s, C-8), 93.6 (s, C-1), 81.3 (s, C-6), 72.9 (d, C-5), 36.7 (t, C-9), 33.6 (s, C-2), 30.4 (t, C-3), 25.8 (q, C-2-CH_{3eq}), 25.6 (t, C-4), 25.5 (t, C-10), 24.1 (q, C-2-CH_{3ax}), 22.6 (q, C-6-CH_3), 18.9 (q, C-8-CH_3).

anti-**2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-5-ol (3c).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 3.86 (dd, J = 12.3, 4.2 Hz, 1H, 5-H_{ax}), 2.01–1.60 (m, 6H, 10-H, 9-H, 4-H_{eq}, 3-H_{ax}), 1.54 (s, 3H, 8-CH_3), 1.44 (td, J = 12.8, 3.1 Hz, 1H, 4-H_{ax}), 1.37 (dt, J = 12.9, 3.2 Hz, 1H, 3-H_{eq}), 1.31 (s, 3H, 6-CH_3), 1.07 (s, 3H, 2-CH_{3eq}), 0.96 (s, 3H, 2-CH_{3ax}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 108.3 (s, C-8), 93.5 (s, C-1), 85.4 (s, C-6), 76.5 (d, C-5), 37.2 (s, C-9), 36.1 (t, C-3), 34.3 (s, C-2), 26.8 (t, C-4), 25.8 (t, C-10), 25.7 (q, C-2-CH_{3eq}), 24.0 (q, C-2-CH_{3ax}), 19.7 (q, C-8-CH_3), 15.1 (q, C-6-CH_3).

syn-**2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undec-5-yl Acetate (3d).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 4.82 (t, J = 3.0 Hz, 1H, 5-H_{eq}), 2.12 (s, 3H, $COCH_3$), 2.05–1.96 (m, 1H, 3-H_{ax}), 1.92–1.60 (m, 6H, 10-H, 9-H, 4-H), 1.52 (s, 3H, 8-CH_3), 1.39 (s, 3H, 6-CH_3), 1.36 (dt, J = 13.4, 3.3 Hz, 1H, 3-H_{eq}), 1.12 (s, 3H, 2-CH_{3eq}), 0.99 (s, 3H, 2-CH_{3ax}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.4 (s, CO), 107.5 (s, C-8), 91.9 (s, C-1), 79.7 (s, C-6), 73.4 (d, C-5), 37.1 (t, C-9), 33.6 (s, C-2), 31.1 (t, C-3), 25.8 (q, C-2-CH_{3eq}), 25.4 (t, C-10), 23.8 (t, C-4), 23.7 (q, C-2-CH_{3ax}), 23.2 (q, C-6-CH_3), 21.5 (q, $COCH_3$), 18.9 (q, C-8-CH_3).

anti-**2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undec-5-yl Acetate (3e).** ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.00 (dd, J = 12.3, 4.2 Hz, 1H, 5-H_{ax}), 2.06 (s, 3H, $COCH_3$), 2.01–1.59 (m, 6H, 10-H, 9-H, 4-H_{eq}, 3-H_{ax}), 1.54 (s, 3H, 8-CH_3), 1.48–1.40 (m, 1H, 4-H_{ax}), 1.38 (s, 3H, 6-CH_3), 1.35–1.31 (m, 1H, 3-H_{eq}), 1.08 (s, 3H, 2-CH_{3eq}), 0.97 (s, 3H, 2-CH_{3ax}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 170.4 (s, CO), 108.4 (s, C-8), 93.7 (s, C-1), 83.3 (s, C-6), 78.7 (d, C-5), 37.2 (t, C-9), 35.6 (t, C-3), 34.1 (s, C-2), 25.6 (q, C-2-CH_{3eq}), 25.4 (C-10), 24.7 (t, C-4), 23.8 (q, C-2-CH_{3ax}), 21.3 (q, $COCH_3$), 19.4 (q, C-8-CH_3), 16.2 (q, C-6-CH_3).

2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undecan-5-one (3f). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 2.63 (td, J = 14.7, 5.7 Hz, 1H, 4-H_{ax}), 2.35 (ddd, J = 14.7 3.9, 2.7 Hz, 1H, 4-H_{eq}), 2.09 (td, J = 14.7, 3.9 Hz, 1H, 3-H_{ax}), 2.01–1.64 (m, 4H, 10-H, 9-H), 1.63 (ddd, J = 13.7, 5.7, 2.8 Hz, 1H, 3-H_{eq}), 1.55 (s, 3H, 8-CH_3), 1.43 (s, 3H, 6-CH_3), 1.19 (s, 3H, 2-CH_{3ax}), 1.15 (s, 3H, 2-CH_{3eq}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 210.6 (s, C-5), 107.9 (s, C-8), 95.5 (s, C-1), 85.5 (s, C-

6), 37.4 (t, C-9), 36.4 (t, C-3), 35.2 (t, C-4), 33.9 (s, C-2), 25.2 (q, C-2-CH_{3eq}), 24.3 (t, C-10), 22.9 (q, C-2-CH_{3ax}), 20.1 (q, C-6-CH_3), 18.7 (q, C-8-CH_3).

2,2,6,8-Tetramethyl-7,11-dioxatricyclo[6.2.1.0^{1,6}]undec-4-ene (3g). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 5.53 (ddd, J = 10.2, 5.4, 2.1 Hz, 1H, 4-H), 5.36 (dd, J = 10.3, 3.0 Hz, 1H, 5-H), 2.29 (bdt, J = 17.4, 2.2 Hz, 1H, 3-H$_\beta$), 2.00–1.76 (m, 4H, 10-H, 9-H), 1.74 (dd, J = 17.4, 5.4 Hz, 1H, 3-H$_\alpha$), 1.52 (s, 3H, 8-CH_3), 1.37 (s, 3H, 6-CH_3), 1.13 (s, 3H, 2-CH_{3eq}), 0.97 (s, 3H, 2-CH_{3ax}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ = 131.1 (d, C-5), 123.6 (d, C-4), 106.7 (s, C-8), 91.5 (s, C-1), 79.2 (s, C-6), 37.6 (s, C-3), 37.3 (t, C-9), 33.1 (s, C-2), 25.2 (q, C-2-CH_{3eq}), 24.15 (q, C-6-CH_3), 24.12 (q, C-2-CH_{3ax}), 23.9 (t, C-10), 19.4 (q, C-8-CH_3).

Supplementary Material

Table of ^{13}C NMR chemical shifts and assignments for compounds **1a–g**, **2a–g** and **3a–g**. ^{1}H NMR and ^{13}C NMR spectra of compounds **2a–g** and **3a–g**.

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