The Development of a Unified Enantioselective, Convergent Synthetic Approach Toward the Furanobutenolide-Derived Polycyclic Norcembranoid Diterpenes: Asymmetric Formation of the Polycyclic Norditerpenoid Carbocyclic Core by Tandem Annulation Cascade

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1. X-Ray Crystal Structure Analysis of Diene 34

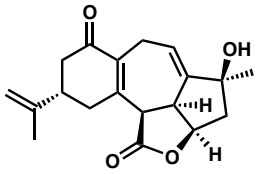

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*Figure S1.1. X-Ray Crystal Structure of Diene **34** (ellipsoids represent 50% probability levels)*

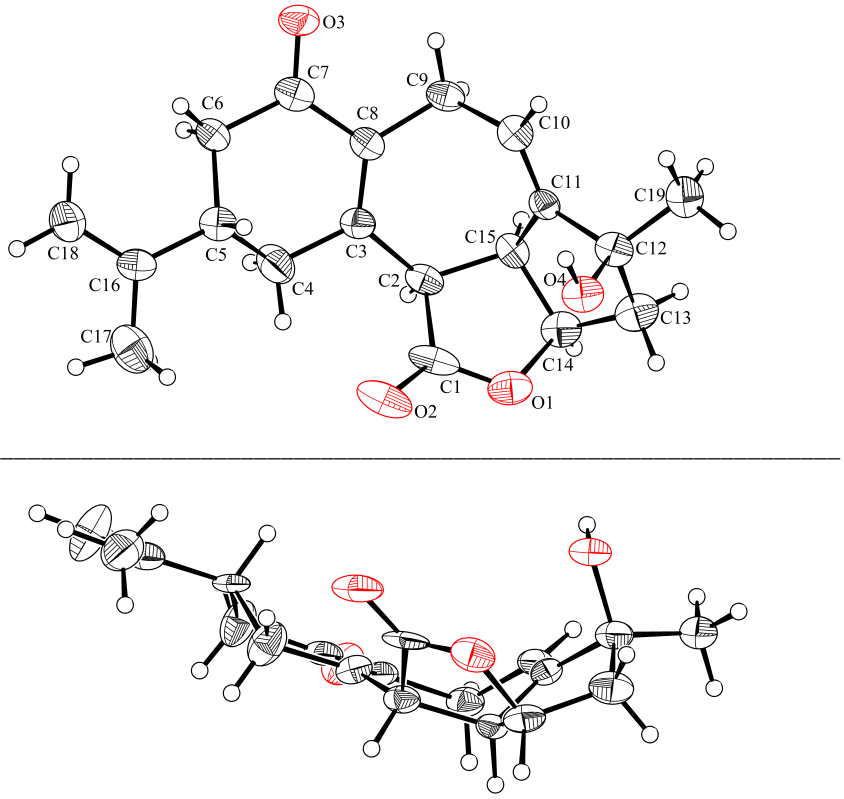


*Table S1.1. Experimental Details for X-Ray Structure Determination of Diene **34**.*

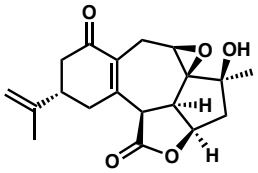
Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS KAPPA APEX II diffractometer coupled to a APEX II CCD detector with graphite monochromated Mo K_α radiation (λ = 0.71073 Å) for the structure of diene **34**. The structure was solved by direct methods using SHELXS[1] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[2] using established refinement techniques.[3] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups).

Diene **34** crystallizes in the monoclinic space group $P2_1$ with one molecule in the asymmetric unit. The coordinates for the hydrogen atom bound to O4 was located in the difference Fourier synthesis and refined semi-freely with the help of a restraint on the O-H distance (0.84(4) Å). The crystal diffracted to 0.93 Å leading to low pond precision. The structure is sufficient to determine the relative stereochemistry of the molecule.

*Table S1.2. Crystal Data and Structure Refinement for Diene **34**.*

Caltech Identification code	rac01	
CCDC Deposition Number	1061010	
Empirical formula	C19 H22 O4	
Formula weight	314.36	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 11.7563(19) Å	α= 90°.
	b = 5.3917(8) Å	β= 104.529(8)°.
	c = 12.861(2) Å	γ = 90°.
Volume	789.2(2) $Å^3$	
Z	2	
Density (calculated)	1.323 Mg/m^3	
Absorption coefficient	0.092 mm^{-1}	
F(000)	336	
Crystal size	0.500 x 0.100 x 0.050 mm^3	
Theta range for data collection	1.636 to 22.464°.	
Index ranges	$-12 \le h \le 11, -5 \le k \le 5, -13 \le l \le 13$	
Reflections collected	8970	
Independent reflections	2037 [R(int) = 0.0848]	
Completeness to theta = 22.464°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2037 / 2 / 213	
Goodness-of-fit on F^2	1.016	
Final R indices [I>2sigma(I)]	R1 = 0.0505, wR2 = 0.1037	
R indices (all data)	R1 = 0.0898, wR2 = 0.1180	
Absolute structure parameter	0.4(10)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.181 and -0.210 $e.Å^{-3}$	

2. X-Ray Crystal Structure Analysis of *ent*-Isoineleganolide A (36)



***ent*-Isoineleganolide A**
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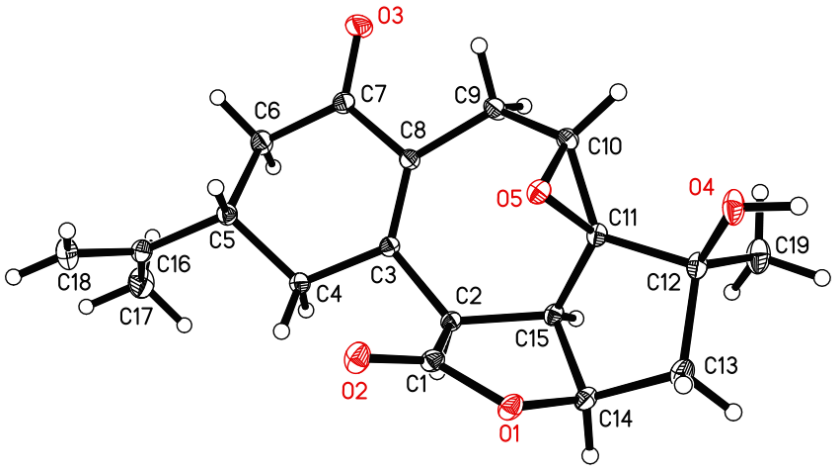
*Figure S2.1. X-Ray Crystal Structure of ent-Isoineleganolide A (**36**) (ellipsoids represent 50% probability levels)*



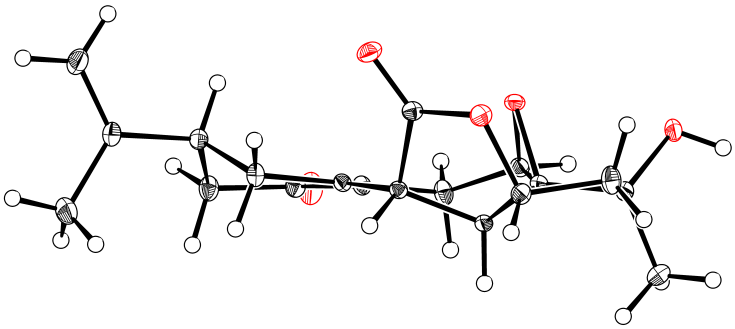


*Table S2.1. Experimental Details for X-Ray Structure Determination of ent-Isoineleganolide A (**36**).*

Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS KAPPA APEX II diffractometer coupled to a APEX II CCD detector with graphite monochromated Mo K_α radiation (λ = 0.71073 Å) for the structure of *ent*-isoineleganolide A (**36**). The structure was solved by direct methods using SHELXS[1] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[2] using established refinement techniques.[3] All non-hydrogen atoms were refined anisotropically. Unless otherwise noted, all hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups).

ent-Isoineleganolide A (**36**) crystallizes in the monoclinic space group $P2_1$ with one molecule in the asymmetric unit. The coordinates for the hydrogen atom bound to O4 was located in the difference Fourier synthesis and refined semi-freely with the help of a restraint on the O-H distance (0.84(4) Å).

*Table S2.2. Crystal Data and Structure Refinement for ent-Isoineleganolide A (**36**).*

Caltech Identification code	rac03	
CCDC Deposition Number	853379 / 1061011	
Empirical formula	C19 H22 O5	
Formula weight	330.36	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 6.9222(2) Å	α= 90°.
	b = 11.1470(4) Å	β= 94.070(2)°.
	c = 10.4409(4) Å	γ = 90°.
Volume	803.61(5) $Å^3$	
Z	2	
Density (calculated)	1.365 Mg/m^3	
Absorption coefficient	0.098 mm^{-1}	
F(000)	352	
Crystal size	0.500 x 0.450 x 0.200 mm^3	
Theta range for data collection	1.955 to 36.317°.	
Index ranges	$-11 \le h \le 11, -18 \le k \le 18, -17 \le l \le 17$	
Reflections collected	30117	
Independent reflections	7796 [R(int) = 0.0404]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7475 and 0.6239	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7796 / 2 / 222	
Goodness-of-fit on F^2	1.067	
Final R indices [I>2sigma(I)]	R1 = 0.0445, wR2 = 0.1109	
R indices (all data)	R1 = 0.0538, wR2 = 0.1198	
Absolute structure parameter	-0.5(3)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.732 and -0.318 $e.Å^{-3}$	

3. X-Ray Crystal Structure Analysis of Bromide 54

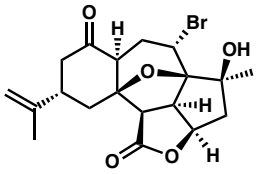


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*Figure S3.1. X-Ray Crystal Structure of Bromide **54** (ellipsoids represent 50% probability levels)*

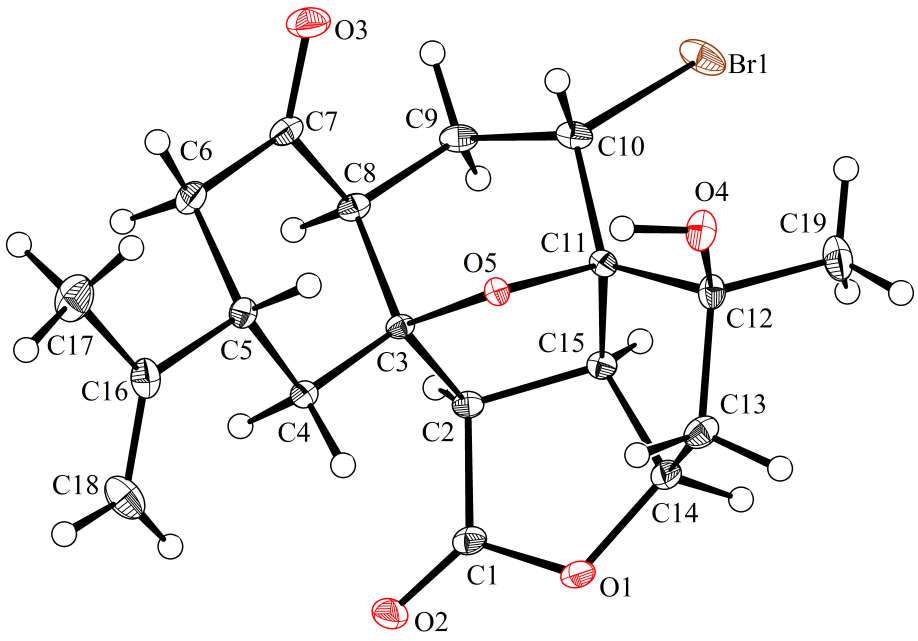

*Table S3.1. Experimental Details for X-Ray Structure Determination of Bromide **54**.*

Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS KAPPA APEX II diffractometer coupled to a APEX II CCD detector with graphite monochromated Mo K_α radiation (λ = 0.71073 Å) for the structure of bromide **54**. The structure was solved by direct methods using SHELXS[1] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[2] using established refinement techniques.[3] All non-hydrogen atoms were refined anisotropically. Unless otherwise noted, all hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups).

Bromide **54** crystallizes in the orthorhombic space group $P2_12_12_1$ with one molecule in the asymmetric unit. The coordinates for the hydrogen atom bound to O4 was located in the difference Fourier synthesis and refined semi-freely with the help of a restraint on the O-H distance (0.84(4) Å).

*Table S3.2. Crystal Data and Structure Refinement for Bromide **54**.*

Caltech Identification code	rac10	
CCDC Deposition Number	1061013	
Empirical formula	C19 H23 Br O5	
Formula weight	411.28	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 7.6137(4) Å	α= 90°.
	b = 9.3584(5) Å	β= 90°.
	c = 24.1592(13) Å	γ = 90°.
Volume	1721.39(16) $Å^3$	
Z	4	
Density (calculated)	1.587 Mg/m^3	
Absorption coefficient	2.416 mm^{-1}	
F(000)	848	
Crystal size	0.500 x 0.450 x 0.100 mm^3	
Theta range for data collection	2.334 to 36.318°.	
Index ranges	$-12 \le h \le 12, -15 \le k \le 14, -39 \le l \le 40$	
Reflections collected	51998	
Independent reflections	8272 [R(int) = 0.0380]	
Completeness to theta = 25.242°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7478 and 0.5973	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	8272 / 1 / 231	
Goodness-of-fit on F^2	1.035	
Final R indices [I>2sigma(I)]	R1 = 0.0251, wR2 = 0.0613	
R indices (all data)	R1 = 0.0297, wR2 = 0.0625	
Absolute structure parameter	0.014(2)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.746 and -0.367 $e.Å^{-3}$	

4. X-Ray Crystal Structure Analysis of Ketopyran 55

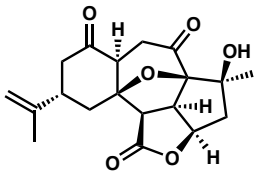

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*Figure S4.1. X-Ray Crystal Structure of Ketopyran **55** (ellipsoids represent 50% probability levels)*

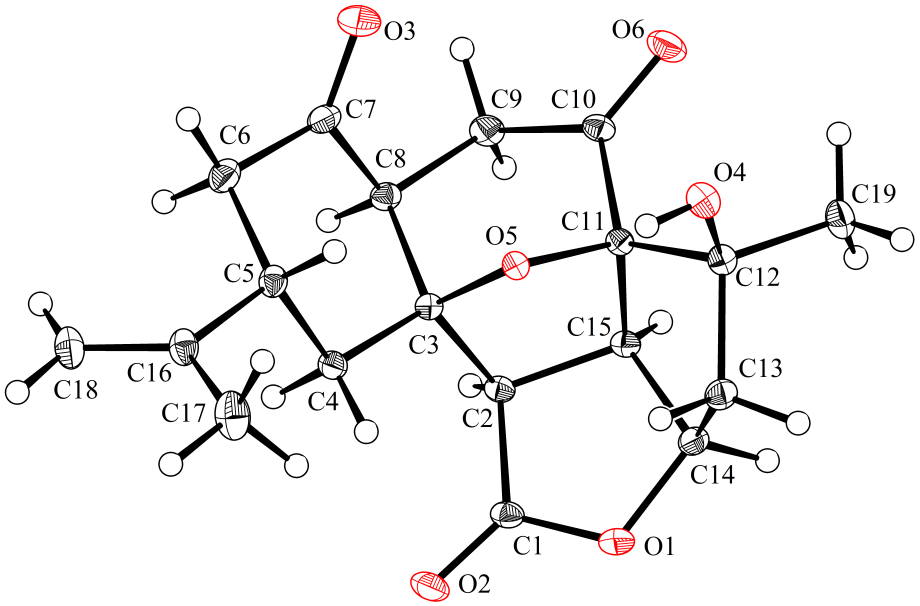

*Table S4.1. Experimental Details for X-Ray Structure Determination of Ketopyran **55**.*

Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS KAPPA APEX II diffractometer coupled to a APEX II CCD detector with graphite monochromated Mo K_α radiation (λ = 0.71073 Å) for the structure of ketopyran **55**. The structure was solved by direct methods using SHELXS[1] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[2] using established refinement techniques.[3] All non-hydrogen atoms were refined anisotropically. Unless otherwise noted, all hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups).

Ketopyran **55** crystallizes in the orthorhombic space group $P2_12_12_1$ with one molecule in the asymmetric unit. The coordinates for the hydrogen atom bound to O4 was located in the difference Fourier synthesis and refined semi-freely with the help of a restraint on the O-H distance (0.84(4) Å). The chirality of the molecule cannot be reliably determined from the diffraction data. The molecule could be the wrong enantiomer or a mixture of both enantiomers.

*Table S4.2. Crystal Data and Structure Refinement for Ketopyran **55**.*

Caltech Identification code	rac06	
CCDC Deposition Number	1061012	
Empirical formula	C19 H22 O6	
Formula weight	346.36	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.2576(3) Å	α= 90°.
	b = 10.4049(4) Å	β= 90°.
	c = 19.0995(8) Å	γ = 90°.
Volume	1641.02(11) $Å^3$	
Z	4	
Density (calculated)	1.402 Mg/m^3	
Absorption coefficient	0.104 mm^{-1}	
F(000)	736	
Crystal size	0.450 x 0.350 x 0.100 mm^3	
Theta range for data collection	2.133 to 43.738°.	
Index ranges	$-16 \le h \le 14, -20 \le k \le 18, -37 \le l \le 37$	
Reflections collected	85501	
Independent reflections	12633 [R(int) = 0.0489]	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7487 and 0.7039	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12633 / 1 / 231	
Goodness-of-fit on F^2	1.060	
Final R indices [I>2sigma(I)]	R1 = 0.0442, wR2 = 0.1107	
R indices (all data)	R1 = 0.0613, wR2 = 0.1176	
Absolute structure parameter	0.35(16)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.468 and -0.291 $e.Å^{-3}$	

5. X-Ray Crystal Structure Analysis of Hemiketal 57

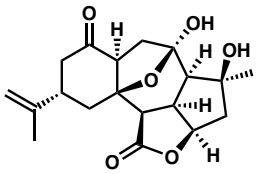

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*Figure S5.1. X-Ray Crystal Structure of Hemiketal **57** (ellipsoids represent 50% probability levels)*

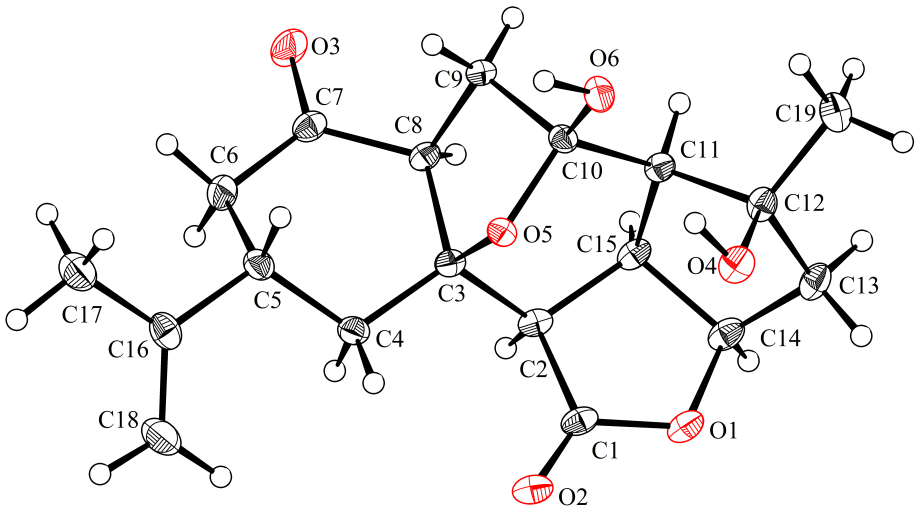


*Table S5.1. Experimental Details for X-Ray Structure Determination of Hemiketal **57**.*

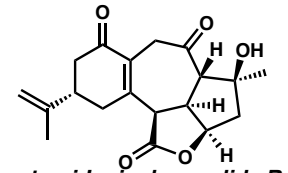
Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS KAPPA APEX II diffractometer coupled to a APEX II CCD detector with graphite monochromated Mo K_α radiation (λ = 0.71073 Å) for the structure of hemiketal **57** and on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON 100 CMOS detector with Cu K_α radiation (λ = 1.54178 Å) from an IμS micro-source for the structure of compound P15149 and P15156. The structure was solved by direct methods using SHELXS[1] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[2] using established refinement techniques.[3] All non-hydrogen atoms were refined anisotropically. Unless otherwise noted, all hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups).

Hemiketal **57** crystallizes in the orthorhombic space group $P2_12_12_1$ with one molecule in the asymmetric unit. The coordinates for all hydrogen atoms were located in the difference Fourier synthesis and refined freely.

*Table S5.2. Crystal Data and Structure Refinement for Hemiketal **57**.*

Caltech Identification code	p15156cu	
CCDC Deposition Number	1061009	
Empirical formula	C19 H24 O6	
Formula weight	348.38	
Temperature	100 K	
Wavelength	1.54178 Å	
Crystal system	Orthorhombic	
Space group	$P2_12_12_1$	
Unit cell dimensions	a = 8.2463(2) Å	α= 90°
	b = 10.3683(3) Å	β= 90°
	c = 19.3151(5) Å	γ = 90°
Volume	1651.44(8) $Å^3$	
Z	4	
Density (calculated)	1.401 Mg/m^3	
Absorption coefficient	0.859 mm^{-1}	
F(000)	744	
Crystal size	0.16 x 0.09 x 0.08 mm^3	
Theta range for data collection	4.578 to 79.097°.	
Index ranges	$-10 \le h \le 10, -13 \le k \le 13, -24 \le l \le 24$	
Reflections collected	40519	
Independent reflections	3557 [R(int) = 0.0399]	
Completeness to theta = 67.000°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0000 and 0.8788	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3557 / 0 / 322	
Goodness-of-fit on F^2	1.070	
Final R indices [I>2sigma(I)]	R1 = 0.0252, wR2 = 0.0607	
R indices (all data)	R1 = 0.0268, wR2 = 0.0619	
Absolute structure parameter	0.03(4)	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.170 and -0.183 $e.Å^{-3}$	

6. X-Ray Crystal Structure Analysis of Enone 59



ent-epi-Isoineleganolide B
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*Figure S6.1. X-Ray Crystal Structure of Enone **59** (ellipsoids represent 50% probability levels)*

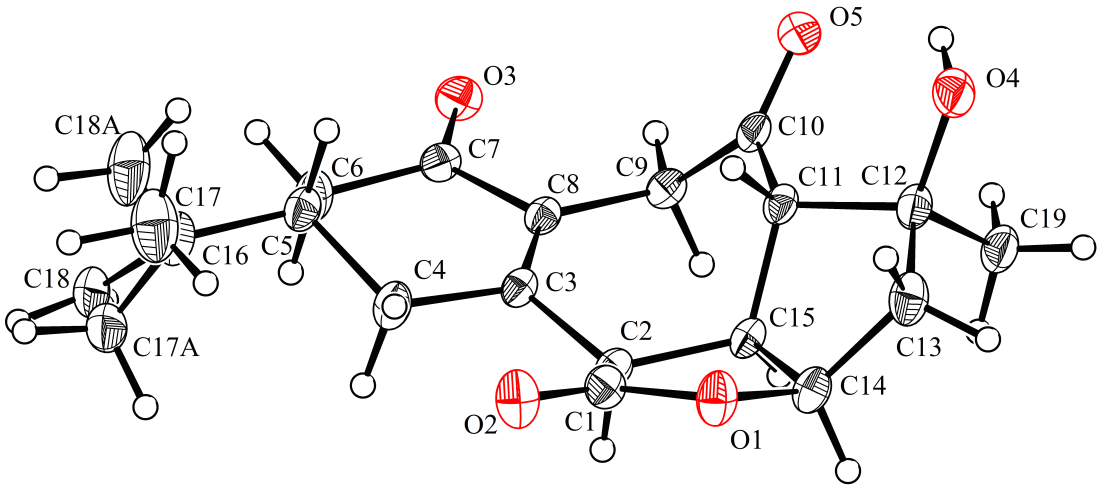

*Table S6.1. Experimental Details for X-Ray Structure Determination of Enone **59**.*

Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON 100 CMOS detector with Cu $K\alpha$ radiation (λ = 1.54178 Å) from an IμS micro-source for the structure of *ent-epi*-Isoineleganolide B (**59**). The structure was solved by direct methods using SHELXS[1] and refined against F^2 on all data by full-matrix least squares with SHELXL-2014[2] using established refinement techniques.[3] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups).

ent-epi-Isoineleganolide B (**59**) crystallizes in the monoclinic space group *C2* with one molecule in the asymmetric unit. The isopropenyl group was disordered in the crystal (51.5:48.5) and the corresponding positions were labeled C17-C18 and C17A-C18A, respectively.

*Table S6.2. Crystal Data and Structure Refinement for Enone **59**.*

Identification code	p17139
Empirical formula	C19 H22 O5
Formula weight	330.36
Temperature	100 K
Wavelength	1.54178 Å
Crystal system	Monoclinic
Space group	C 1 2 1
Unit cell dimensions	a = 22.5468(19) Å α = 90°
	b = 10.4722(9) Å β = 107.751(5)°
	c = 7.3277(5) Å γ = 90°
Volume	1647.8(2) Å3
Z	4
Density (calculated)	1.332 Mg/m3
Absorption coefficient	0.787 mm-1
F(000)	704
Crystal size	0.32 x 0.13 x 0.06 mm3
Theta range for data collection	4.698 to 79.209°.
Index ranges	-28<=h<=28, -12<=k<=13, -9<=l<=9
Reflections collected	19495
Independent reflections	3531 [R(int) = 0.0367]
Completeness to theta =	67.000° 99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	1.0000 and 0.8733
Refinement method	Full-matrix least-squares on F2
Data / restraints / parameters	3531 / 1 / 240
Goodness-of-fit on F2	1.048
Final R indices	[I>2sigma(I)]R1 = 0.0274, wR2 = 0.0697
R indices (all data)	R1 = 0.0277, wR2 = 0.0699
Absolute structure parameter	0.06(4)
Extinction coefficient	n/a
Largest diff. peak and hole	0.212 and -0.159 e.Å-3

7. Notes & References

1. Sheldrick, G. M. *Acta Cryst*. **1990**, A46, 467–473.

2. Sheldrick, G. M. *Acta Cryst*. **2008**, A64, 112–122.

3. Müller, P. *Crystallography Reviews* **2009**, *15*, 57–83.