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

Robert A. Craig, II, Russell C. Smith, Jennifer L. Roizen,
Amanda C. Jones, Scott C. Virgil, and Brian M. Stoltz*

Warren and Katharine Schlinger Laboratory for Chemistry and Chemical Engineering, Division of Chemistry and Chemical Engineering, California Institute of Technology, MC 101-20, Pasadena, CA 91125, U.S.A.

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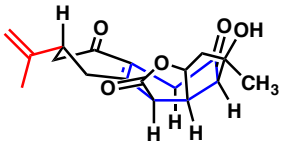
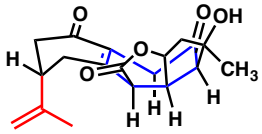
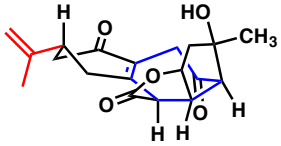
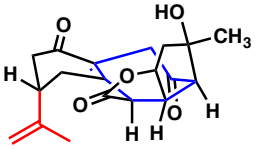
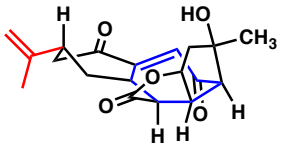
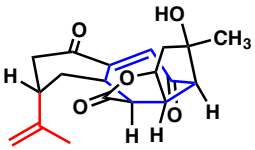
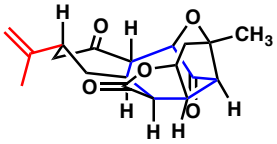
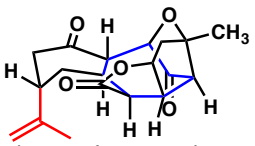
Computational Assessment of Isomerization of ent-Isoineleganolide B (*ent*-9)

As noted in footnote 46 of the manuscript, all calculations were performed with Spartan '10 (Wavefunction, Inc., Irvine, CA). The in vacuo equilibrium geometry for each structure was calculated by a series of sequential calculations as follows: Hartree–Fock computation (equilibrium geometry, 3-21G basis set), DFT (equilibrium geometry, B3LYP/6-31G basis set), DFT (energy, B3LYP/6-311+G** basis set), DFT (equilibrium geometry, B3LYP/6-311+G** basis set). The error from these calculations is ±0.23 kcal/mol, thus all energy differences larger than 0.46 kcal/mol were considered significant. Except for molecular mechanics and semi-empirical models, the calculation methods used in Spartan have been documented in the literature.[1] All ground state energies have been expressed relative to the energy of *ent*-ineleganolide (***ent*-1**) in the naturally occurring conformation (cf. ***ent*-1^{ax}**, Figure 3, Table S1) as determined on the initial isolation by single crystal X-ray diffraction.[2]

Table S7. Calculated Ground State Energies for Enone ***ent-9*** *and Isomers*

entry	*compound*		*relative ground state free energy (kcal/mol)**
1		***ent-9^{equ}***	***0.8***
2		***ent-9^{ax}***	***2.1***
3		***ent-9A^{equ}***	***–1.4***
4		***ent-9A^{ax}***	***0.7***
5		***38^{equ}***	***14.1***
6		***38^{ax}***	***14.2***
7		***ent-1^{equ}***	***1.9***
8		***ent-1^{ax}***	***0.0***

*: Relative ground state free energies are calculated relative to the energy of ***ent-1^{ax}*** (entry 8) where posititve and negative values denote higher and lower relative ground state energies, respectively.

Cartesian Coordinates and Imaginary Frequencies

ent-9^{equ} (entry 1)

Imaginary Frequencies = 0
Total Energy = –698,839.7 kcal mol^{-1}

C	3.350825	-1.350522	-0.163913
C	3.113162	0.063160	0.362455
C	2.059735	0.735914	-0.538993
C	0.775187	-0.066689	-0.663632
C	0.782710	-1.416211	-0.537199
C	2.064173	-2.149590	-0.271385
C	-0.419758	0.769080	-1.099672
C	-1.835385	0.187781	-1.362447
C	-2.481060	-0.833791	-0.368913
C	-1.560331	-1.899935	0.217202
C	-0.420132	-2.330374	-0.686997
C	-0.707707	2.060724	-0.296999
C	-2.745193	1.454941	-1.242559
C	-3.311413	0.002332	0.627567
O	-1.956085	2.484069	-0.610233
C	-3.898866	1.080936	-0.309856
O	2.085864	-3.369994	-0.193317
O	0.018914	2.715163	0.404356
H	-1.873207	-0.217172	-2.376147
C	4.362410	0.921743	0.501859
C	5.532087	0.614809	-0.069246
C	4.209013	2.160588	1.353672
O	-1.754482	-2.411258	1.300316
H	-3.074703	1.852527	-2.206651
C	-4.372314	-0.762236	1.416992
O	-2.336730	0.580155	1.507411
H	-3.199874	-1.414335	-0.969993
H	4.052096	-1.922882	0.450262
H	1.819633	1.730711	-0.164907
H	2.488171	0.873476	-1.546047
H	-0.103520	1.193864	-2.071262
H	-0.107998	-3.337925	-0.406956
H	-4.279723	1.957344	0.225892
H	-4.728918	0.656877	-0.888698
H	6.400425	1.257678	0.050745
H	5.681100	-0.279490	-0.666225
H	3.415506	2.822322	0.983999
H	3.933088	1.892381	2.382698
H	5.138826	2.736084	1.390438
H	-3.892757	-1.501338	2.059956
H	-4.950967	-0.066234	2.037951
H	-5.076284	-1.271764	0.748299
H	-2.766390	1.270821	2.036556
H	-0.758231	-2.351118	-1.732175
H	3.779085	-1.302223	-1.177252
H	2.661942	-0.020648	1.363638

ent-9^{ax} (entry 2)

Imaginary Frequencies = 0
Total Energy = –698,838.4 kcal mol^{-1}

C	3.112859	-0.848771	1.296365
C	3.246176	0.618393	0.841632
C	1.831049	1.206359	0.757249
C	0.817609	0.351114	0.011799
C	1.034190	-0.966705	-0.217301
C	2.245359	-1.645337	0.342901
C	-0.365785	1.143322	-0.524878
C	-1.575754	0.515270	-1.270709
C	-2.206678	-0.833639	-0.797332
C	-1.247027	-1.941346	-0.373826
C	0.126851	-1.881383	-1.018699
C	-1.023566	2.117319	0.480584
C	-2.710567	1.567812	-1.023521
C	-3.329357	-0.452754	0.191489
O	-2.248650	2.458638	0.010519
C	-3.922724	0.790639	-0.503563
O	2.511567	-2.805968	0.065132
O	-0.564071	2.627570	1.467725
H	-1.341334	0.450378	-2.335758
C	4.110162	0.764647	-0.408472
C	3.682586	1.300664	-1.556151
C	5.540088	0.291140	-0.268452
O	-1.570184	-2.833075	0.383354
H	-2.933972	2.184853	-1.898279
C	-4.363353	-1.539972	0.478674
O	-2.634304	-0.075311	1.388964
H	-2.705332	-1.254423	-1.685723
H	4.072308	-1.360760	1.396014
H	2.627564	-0.868210	2.283341
H	3.776471	1.157916	1.640812
H	1.453575	1.369343	1.773904
H	1.860108	2.207457	0.314243
H	0.080996	1.850455	-1.248200
H	0.567064	-2.879867	-1.014954
H	-4.536989	1.406680	0.162612
H	-4.555395	0.477880	-1.343642
H	4.348449	1.408951	-2.408461
H	2.666241	1.652240	-1.701913
H	6.014126	0.715651	0.627043
H	5.601048	-0.800416	-0.170938
H	6.138801	0.578257	-1.137785
H	-3.884851	-2.387694	0.970776
H	-5.153645	-1.143833	1.130016
H	-4.841522	-1.889843	-0.444128
H	-3.264335	0.345468	1.995532
H	0.043049	-1.535946	-2.056793

ent-9A^{equ} (entry 3)

Imaginary Frequencies = 0
Total Energy = –698,841.9 kcal mol^{-1}

C	3.215367	-1.483695	-0.031586
C	3.441522	0.020758	0.144190
C	2.268289	0.774554	-0.514557
C	0.902082	0.235561	-0.145212
C	0.723081	-0.990161	0.393727
C	1.882406	-1.921620	0.552095
C	-0.234972	1.203649	-0.399874
C	-1.503284	0.808529	-1.185392
C	-2.279946	-0.528923	-0.935608
C	-1.588241	-1.731718	-0.284423
C	-0.617217	-1.515329	0.864305
C	-0.794865	1.916807	0.843101
C	-2.483657	1.940697	-0.758595
C	-3.588428	-0.147276	-0.160947
O	-2.031145	2.397576	0.538763
C	-3.857775	1.293048	-0.640823
O	1.758226	-3.007218	1.098216
O	-0.258300	2.110987	1.900337
H	-1.288967	0.872181	-2.255566
C	4.787057	0.534365	-0.347079
C	5.613177	-0.186225	-1.112782
C	5.154430	1.932609	0.095016
O	-1.868245	-2.847261	-0.682968
H	-2.470896	2.805792	-1.430103
C	-4.742249	-1.116821	-0.413670
O	-3.242828	-0.152664	1.231049
H	-2.605075	-0.898323	-1.912807
H	4.002269	-2.079398	0.438670
H	3.383293	0.238652	1.222654
H	2.302246	1.836331	-0.239393
H	2.386048	0.744497	-1.610971
H	0.192337	2.036736	-0.980313
H	-1.065867	-0.821142	1.581606
H	-0.457373	-2.480971	1.346759
H	-4.522525	1.847362	0.031728
H	-4.329689	1.273442	-1.631203
H	6.566346	0.218211	-1.444493
H	5.386656	-1.198299	-1.433600
H	4.436617	2.680898	-0.265711
H	5.160463	2.009903	1.190727
H	6.144740	2.218810	-0.271146
H	-4.459287	-2.128960	-0.112391
H	-5.623676	-0.816115	0.166706
H	-5.027092	-1.138025	-1.471254
H	-3.957948	0.275028	1.727713
H	3.205060	-1.740822	-1.102107

ent-9A^{ax} (entry 4)

Imaginary Frequencies = 0
Total Energy = –698,839.8 kcal mol^{-1}

C	-3.505679	-0.155535	1.250167
C	-3.502826	-0.879562	-0.112949
C	-2.169061	-1.628952	-0.254213
C	-0.935237	-0.835699	0.125109
C	-0.988510	0.270049	0.898887
C	-2.294931	0.743919	1.447102
C	0.369261	-1.427473	-0.365626
C	1.369093	-0.608456	-1.210496
C	1.786892	0.854605	-0.835003
C	0.926609	1.711723	0.104437
C	0.228387	1.077596	1.297535
C	1.265713	-2.065375	0.710011
C	2.658340	-1.463282	-1.053678
C	3.261979	0.776402	-0.307037
O	2.530843	-2.150036	0.214942
C	3.817861	-0.477560	-1.012285
O	-2.381243	1.776313	2.094479
O	0.953731	-2.497849	1.786629
H	1.037184	-0.604096	-2.252250
C	-3.850389	0.060016	-1.265656
C	-2.975400	0.460344	-2.193665
C	-5.292629	0.510085	-1.313897
O	0.860515	2.907818	-0.109081
H	2.770493	-2.229662	-1.828083
C	4.064841	2.049361	-0.574382
O	3.162537	0.549287	1.105587
H	1.825327	1.428152	-1.765592
H	-4.403176	0.446187	1.412079
H	-3.477217	-0.909350	2.051753
H	-4.301075	-1.635548	-0.081960
H	-2.193224	-2.524023	0.388349
H	-2.062082	-2.004044	-1.279970
H	0.110164	-2.287003	-1.002902
H	0.945311	0.448159	1.835417
H	-0.096614	1.889745	1.949577
H	4.699786	-0.891684	-0.510019
H	4.108599	-0.231457	-2.041510
H	-3.275052	1.124128	-3.000381
H	-1.931472	0.163366	-2.183623
H	-5.972945	-0.351638	-1.361226
H	-5.572798	1.082587	-0.420518
H	-5.482874	1.142479	-2.185853
H	3.576091	2.909822	-0.109277
H	5.074789	1.954645	-0.155752
H	4.162173	2.245180	-1.647835
H	4.041654	0.316559	1.442974

38^{equ} (entry 5)

Imaginary Frequencies = 0
Total Energy = –698,826.4 kcal mol^{-1}

C	-3.064381	-1.102350	0.505180
C	-2.524302	-0.096122	-0.528308
C	-1.404759	0.780300	0.105603
C	-0.598005	0.003889	1.194014
C	-0.566757	-1.471306	0.880474
C	-1.959019	-2.075128	0.902238
C	0.730177	0.662520	1.692504
C	2.147334	0.368518	1.136259
C	2.469393	-0.692035	0.066813
C	1.830614	-2.073679	0.142222
C	0.422046	-2.309762	0.513967
C	0.605159	2.187544	1.575049
C	2.599426	1.710231	0.482709
C	2.323359	0.000116	-1.321491
O	1.594253	2.692594	0.789181
C	2.768078	1.461637	-1.030368
O	-2.168884	-3.247483	1.150231
O	-0.245796	2.886439	2.061708
H	2.775995	0.159651	2.006732
C	-3.581346	0.770275	-1.192823
C	-4.843463	0.857743	-0.760238
C	-3.112806	1.554565	-2.396977
O	2.510069	-3.039324	-0.191348
H	3.528339	2.087093	0.919884
C	3.145832	-0.676185	-2.419033
O	0.931104	-0.057323	-1.663677
H	3.541322	-0.899558	0.164934
H	-3.428718	-0.580235	1.402131
H	-3.899513	-1.690554	0.115283
H	-2.047825	-0.688687	-1.325167
H	-0.727382	1.131838	-0.672462
H	-1.857067	1.652096	0.586234
H	0.759736	0.446455	2.765212
H	0.144898	-3.355136	0.392236
H	2.178780	2.178594	-1.610798
H	3.817704	1.597305	-1.312523
H	-5.565170	1.499020	-1.259742
H	-5.210770	0.305947	0.099285
H	-2.322100	2.269201	-2.132987
H	-2.694328	0.887293	-3.163714
H	-3.933627	2.118108	-2.850260
H	2.823640	-1.711953	-2.556372
H	3.022666	-0.141002	-3.370342
H	4.213382	-0.679538	-2.176293
H	0.832840	0.298447	-2.561480
H	-1.238244	0.071765	2.084695

38^{ax} (entry 6)

Imaginary Frequencies = 0
Total Energy = –698,826.3 kcal mol^{-1}

C	2.415399	-1.748296	1.088012
C	2.546440	-0.219546	1.247441
C	1.185852	0.452805	0.906109
C	0.772690	0.082006	-0.543990
C	0.536157	-1.409390	-0.601686
C	1.760929	-2.211508	-0.212195
C	-0.256713	0.980457	-1.297160
C	-1.790913	0.857396	-1.181098
C	-2.510845	-0.347663	-0.562177
C	-2.005738	-1.755981	-0.871351
C	-0.578392	-2.138344	-0.808998
C	-0.006132	2.450297	-0.928825
C	-2.193284	2.047828	-0.280346
C	-2.703999	-0.056699	0.972006
O	-1.109556	2.994600	-0.342316
C	-2.416787	1.472170	1.129728
O	2.125212	-3.204060	-0.813429
O	1.011104	3.077941	-1.079217
H	-2.182359	1.015763	-2.190982
C	3.708424	0.393348	0.471638
C	4.449345	-0.292936	-0.408032
C	3.991601	1.853029	0.748454
O	-2.833810	-2.628733	-1.104492
H	-3.079631	2.569645	-0.650474
C	-4.111513	-0.454050	1.425927
O	-1.744076	-0.840857	1.696726
H	-3.520174	-0.347232	-0.986825
H	3.369850	-2.267906	1.207309
H	2.736876	-0.017277	2.312225
H	0.423574	0.111304	1.611515
H	1.282037	1.536860	1.005431
H	0.010511	0.876384	-2.353432
H	-0.457321	-3.218948	-0.850018
H	-1.498541	1.599915	1.709654
H	-3.218377	1.994175	1.662097
H	5.274001	0.184070	-0.932078
H	4.275087	-1.336454	-0.649849
H	3.210363	2.501058	0.332239
H	4.039873	2.053528	1.827415
H	4.943113	2.158218	0.303201
H	-4.295049	-1.509924	1.204243
H	-4.227479	-0.294235	2.506620
H	-4.877877	0.144884	0.921449
H	-1.992043	-0.811865	2.634744
H	1.690656	0.250587	-1.126125
H	1.746783	-2.113202	1.882712

ent-1^{equ} (entry 7)

Imaginary Frequencies = 0
Total Energy = –698,838.6 kcal mol^{-1}

C	2.771812	-1.524254	0.139160
C	3.101931	-0.030238	0.267683
C	2.054611	0.830325	-0.496571
C	0.641647	0.185408	-0.573810
C	0.347695	-0.737652	0.633630
C	1.416963	-1.841845	0.747603
C	-0.427410	1.284859	-0.816817
C	-1.860337	0.936631	-1.336309
C	-2.475827	-0.494642	-1.141498
C	-1.466773	-1.589609	-0.857703
C	-1.058320	-1.371277	0.601487
C	-0.662131	2.181468	0.403309
C	-2.782265	1.889904	-0.495182
C	-3.180643	-0.405988	0.224717
O	-1.944474	2.610086	0.427955
C	-3.766136	1.003855	0.280938
O	1.192576	-2.891263	1.318165
O	0.144708	2.544100	1.223957
H	-1.913421	1.181134	-2.399190
C	4.517052	0.347058	-0.145723
C	5.332203	-0.473650	-0.816648
C	4.955780	1.738249	0.248351
O	-1.062258	-2.453747	-1.601957
H	-3.286495	2.642837	-1.106261
C	-4.175763	-1.519404	0.541037
O	-2.041194	-0.466218	1.132450
H	-3.127366	-0.753423	-1.979706
H	0.409517	-0.149887	1.561215
H	3.007124	0.225173	1.334639
H	0.011642	1.959033	-1.566843
H	2.738637	-1.821673	-0.920547
H	3.517205	-2.159431	0.625807
H	1.982857	1.807647	-0.016589
H	2.405018	0.990770	-1.524740
H	-1.044582	-2.309717	1.164111
H	-3.894738	1.360376	1.306884
H	-4.748316	1.006002	-0.206101
H	6.332271	-0.158664	-1.103856
H	5.048719	-1.481054	-1.105480
H	4.314475	2.508507	-0.199178
H	4.893996	1.875772	1.336481
H	5.986158	1.934499	-0.062235
H	-4.547539	-1.407256	1.564594
H	-5.029497	-1.490149	-0.145328
H	-3.711031	-2.508235	0.458753
H	0.635978	-0.451113	-1.466907

ent-1^{ax} (entry 8)

Imaginary Frequencies = 0
Total Energy = –698,840.5 kcal mol^{-1}

C	-2.957152	0.273839	1.630853
C	-3.233628	-0.701832	0.467457
C	-1.946916	-1.514907	0.177280
C	-0.752165	-0.607755	-0.171175
C	-0.446718	0.376873	0.994625
C	-1.708093	1.122290	1.454386
C	0.479012	-1.444776	-0.613018
C	1.678576	-0.788986	-1.372676
C	1.956267	0.753374	-1.290509
C	0.786460	1.601046	-0.826687
C	0.703935	1.353191	0.682912
C	1.124391	-2.236756	0.527462
C	2.931458	-1.462839	-0.709145
C	2.897918	0.896823	-0.079970
O	2.460843	-2.328303	0.340426
C	3.794483	-0.339544	-0.118069
O	-1.694082	2.308156	1.729102
O	0.574724	-2.776963	1.456155
H	1.606529	-1.058491	-2.428375
C	-3.811756	-0.052813	-0.785490
C	-3.808561	1.265991	-1.015372
C	-4.435855	-1.007981	-1.778726
O	0.088818	2.338070	-1.484157
H	3.490008	-2.096489	-1.403026
C	3.651672	2.220177	0.030192
O	1.964154	0.750378	1.029137
H	2.366334	1.122329	-2.233756
H	-0.127215	-0.223672	1.860146
H	-3.985788	-1.422230	0.822513
H	0.079007	-2.219286	-1.283340
H	-3.802201	0.939234	1.825225
H	-1.700048	-2.132186	1.046471
H	-2.125070	-2.207206	-0.654150
H	0.552761	2.290559	1.226878
H	4.170378	-0.609032	0.873048
H	4.656700	-0.141315	-0.765665
H	-4.236353	1.672467	-1.928660
H	-3.391046	1.991915	-0.325890
H	-3.716830	-1.748071	-2.154644
H	-5.252625	-1.577219	-1.313671
H	-4.843305	-0.473192	-2.641443
H	4.227009	2.243895	0.961285
H	4.343500	2.350128	-0.809645
H	2.965110	3.073798	0.037494
H	-1.058460	-0.011654	-1.040134
H	-2.794029	-0.327480	2.538047

Notes & References

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