



## Synthesis of *nor*-Ambreinolide from (+)-*cis*-Abienol

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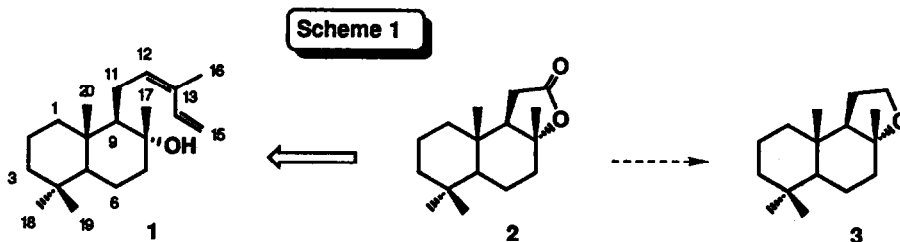
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**Abstract:** The synthesis of *nor*-ambreinolide (2) from *cis*-abienol (1) was carried out by direct treatment with OsO<sub>4</sub>-NaIO<sub>4</sub> or RuO<sub>4</sub>-NaIO<sub>4</sub>. The oxymercuration-demercuration of 1 led to a mixture of 8,12-epoxylabdanes (5-17) which was also converted into *nor*-ambreinolide by treatment with RuO<sub>4</sub>-NaIO<sub>4</sub>. The formation pathways of such epoxy derivatives are discussed.

### INTRODUCTION

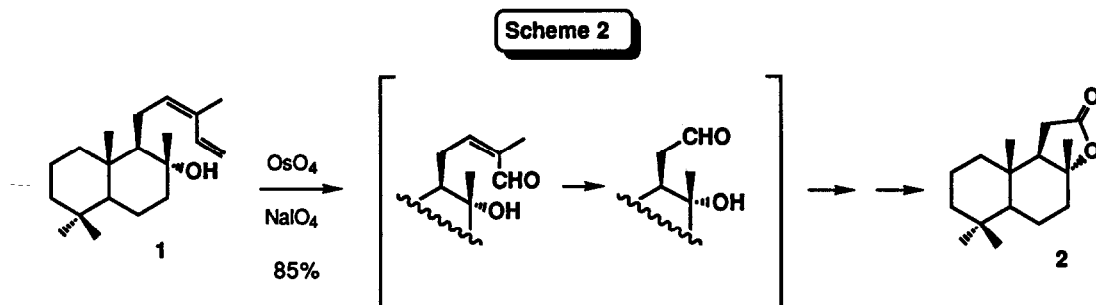
Following the authors' synthesis work on amber-type odorants from labdane diterpenes,<sup>1-4</sup> the naturally-occurring product *cis*-abienol (1) is now used to prepare *nor*-ambreinolide (2), a classic and well-established precursor<sup>5</sup> of *Ambrox*<sup>®</sup> (3) which possesses a powerful and tenacious ambergris-type aroma<sup>6</sup> (scheme 1).

*cis*-Abienol (1) is found in a number of *Abies* resins, specifically in the four species, *Abies amabilis*, *Abies concolor*, *Abies mariesii* and *Abies sachalinensis*, as the major diterpenoid constituent.<sup>7</sup> Furthermore, *cis*-abienol can be readily isolated with up to 13% yield from the commercial Canada balsam, the oleoresin of *Abies balsamea* L. Mill. which provides 1 as an interesting and readily available starting material for the synthesis of *Ambrox*<sup>®</sup> (3). In this context, we have already reported a two-step conversion of *cis*-abienol into *Ambrox*<sup>®</sup> through a reductive ozonolysis followed by the cyclization of the resulting 8,12-dihydroxy-tetranorlabdane.<sup>1,4</sup> This paper reports the synthesis of *nor*-ambreinolide (2) from *cis*-abienol (1), either by direct treatment with degradative combined systems OsO<sub>4</sub>-NaIO<sub>4</sub> and RuO<sub>4</sub>-NaIO<sub>4</sub>, or by previously inducing the tetrahydrofuran ring formation with mercury (II) acetate and then performing the oxidative cleavage of the side chain.

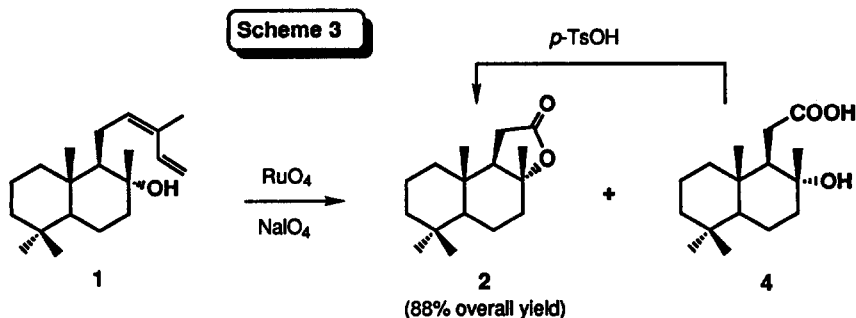


## RESULTS AND DISCUSSION

The one-pot conversion of *cis*-abienol (**1**) into *nor*-ambreinolide (**2**) was performed by oxidative treatments with both OsO<sub>4</sub>-NaIO<sub>4</sub><sup>8</sup> or RuO<sub>4</sub>-NaIO<sub>4</sub>.<sup>9</sup> In the first case, the experimental conditions already established by the authors with other substrates,<sup>1-4,10</sup> were used. This involved stirring **1** with a catalytic amount of OsO<sub>4</sub> and a molar excess of NaIO<sub>4</sub> in Bu<sup>t</sup>OH-H<sub>2</sub>O mixtures, a prolonged treatment (20 days) being required on this occasion to complete the transformation. It should be noted (<sup>1</sup>H NMR monitoring) that the cleavage of the terminal double bond Δ<sup>14</sup> occurred first, as previously observed for the identical side chain of methyl *cis*-communate,<sup>10</sup> and then the subsequent cleavage of Δ<sup>12</sup>. This suggests that **2** is formed from **1** with OsO<sub>4</sub>-NaIO<sub>4</sub> as depicted in scheme 2.

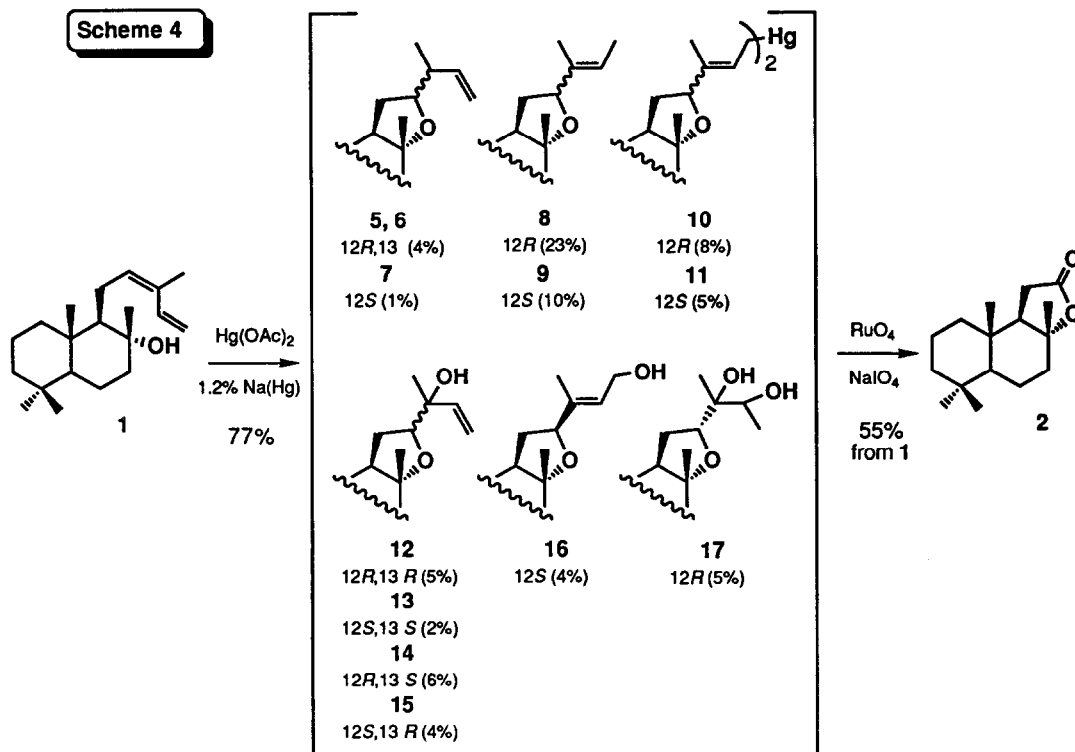


However, the reaction of **1** with the relatively stronger RuO<sub>4</sub>-NaIO<sub>4</sub> system produced *nor*-ambreinolide (**2**) more quickly (12 hours) together with a smaller amount of the hydroxyacid **4** (8:2 ratio). The treatment of this mixture with *p*-TsOH at room temperature finally completed the conversion of **1** into *nor*-ambreinolide in 88% overall yield (scheme 3).<sup>11</sup> The ruthenium tetroxide was initially generated *in situ* from a mixture of ruthenium dioxide and sodium periodate in acetone and was then regenerated throughout the reaction by the addition of portions of sodium periodate.<sup>12</sup>

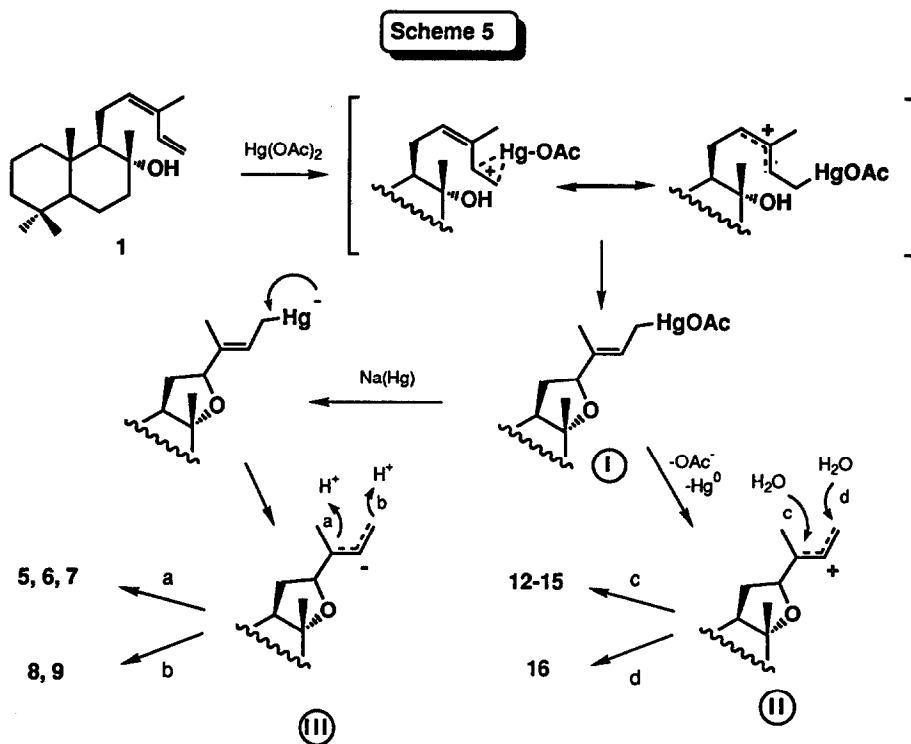


In the authors work on the oxymercuration-demercuration of the labdanes methyl *trans*- and *cis*-communate,<sup>13,14</sup> which bears a conjugated diene in the side chain as in *cis*-abienol, it was observed that the mercuriation ion of the less substituted double bond Δ<sup>14</sup> occurred first. Then, this intermediate underwent, either 1,2-addition, with the subsequent formation of 14-hydroxyderivatives, or 1,4-addition, with the corresponding generation of 12-oxyderivatives. In the case of **1**, the formation of the C<sub>8</sub>-O-C<sub>12</sub> ring was likely in view of the

presence of the neighbouring hydroxyl group. Thus, the oxymercuration-demercuration of *cis*-abienol (**1**) under classic conditions, with mercury (II) acetate in the presence of water and sodium amalgam as reducing agent, basically led to the formation of 8,12-epoxyderivatives (scheme 4), with the preference of the intramolecular attack of the hydroxyl group on the side chain *versus* the addition of water. In view of the efficient formation of the tetrahydrofuran ring (77%) it was worth carrying out the exhaustive side chain degradation of compounds **5-17**, which was performed by direct treatment with  $\text{RuO}_4\text{-NaIO}_4$  of the crude mixture which appeared in the oxymercuration-demercuration reaction of **1** (scheme 4). Thus, after chromatographic purification on silica gel, *nor*-ambreinolide (**2**) was conveniently isolated (55% yield from **1**).



Compounds **5-17** were isolated and their structures and stereochemistries established by spectroscopic analysis and compared with similar or identical compounds previously reported in the literature.<sup>15-18</sup> Thus, the configuration at C-12 may be easily assigned as *S*, or *R*, depending upon whether the  $\delta$  value of C-17 ( $^{13}\text{C}$  NMR) is influenced, or not, respectively, by the deshielding  $\delta$ -*synaxial* effect of the side chain on this methyl group.<sup>19</sup> In a similar way, the *E* configuration around  $\Delta^{13}$  for compounds **8-11** and **16** has been deduced on the basis of the considerably upshifted  $\delta$  values observed in  $^{13}\text{C}$  NMR for C-15 and C-16 as a consequence of the mutual  $\gamma$ -*synperiplanar* effect.<sup>20</sup> Compounds **12-15** were identified by comparison of their spectroscopic features with those of the products obtained in the reactions of *trans*-abienol and *cis*-abienol with *m*-chloroperbenzoic acid<sup>16,18</sup> and *cis*-abienol with singlet oxygen.<sup>17</sup>



In order to explain the formation of these compounds it may be suggested that the course of the oxymercuration-demercuration takes place *via* the formation of an acetoxymercurial I which may generate some of the allyl cation II during the oxymercuration step (scheme 5).<sup>21</sup> The remaining I may be converted to the allyl anion III during the later reducing treatment with sodium amalgam.<sup>22</sup> Then, cation II affords compounds 12-15 and 16 by capturing a molecule of water at C-13 or C-15, while anion III leads to compounds 5-7 and 8, 9 by capturing a proton at the same positions (scheme 5). Glycol 17 is then formed by further hydration of the alcohol 12 (or 14). The isolation of the dialkylmercury compounds 10 and 11 was surprising since it was the first time the authors had observed the formation of such diorganomercurials when sodium amalgam was the reducing agent.<sup>23</sup> The structural assignment of 10 and 11 is supported by the mass spectrum which displays peaks at  $m/z$  289 and 235 corresponding to the initial fragmentation of the C<sub>15</sub>-Hg bond, followed by the loss of the side chain. In addition, it also presents peaks at  $m/z$  198, 199, 200, 201, 202 and 204 according to the relative abundance of the isotopes of mercury.<sup>24</sup> The <sup>1</sup>H NMR spectrum closely parallels that of the mixture of 8 and 9 (Table 1); two new doublets ( $J$  8.9) at  $\delta$  2.60 (for 10) and  $\delta$  2.63 (for 11) are observed, accompanied by the corresponding satellite bands due to the <sup>199</sup>Hg-<sup>1</sup>H coupling.<sup>25</sup>

Table 1. <sup>1</sup>H NMR spectral data<sup>a</sup> of compounds 5-17 (300 MHz, CDCl<sub>3</sub>, TMS as int. standard)

H	5 and 6	7	8	9	10	11	12	13	14	15	16	17	
12	3.92 <i>ddd</i>	3.99 <i>ddd</i>	3.58-3.66 <i>m</i>	4.37 <i>dd</i>	4.25 <i>br t</i>	4.34 <i>br d</i>	4.25 <i>br t</i>	3.92 <i>br t</i>	3.83 <i>dd</i>	3.91 <i>dd</i>	3.78 <i>dd</i>	4.29 <i>br t</i>	4.13 <i>dd</i>
13	2.28 <i>br sext.</i>	2.28 <i>br sext.</i>	2.19 <i>br sext.</i>										
14	5.81 <i>ddd</i>	5.80 <i>ddd</i>	5.66 <i>ddd</i>	5.51 <i>br q</i>	5.54 <i>br q</i>	5.69 <i>t quint.</i>	5.75 <i>t quint.</i>	5.93 <i>dd</i>	5.96 <i>dd</i>	5.87 <i>dd</i>	5.85 <i>dd</i>	5.75 <i>t quint.</i>	3.87 <i>q</i>
15	4.99 <i>m</i>	4.99 <i>m</i>	4.97 <i>ddd</i>	1.59 <i>d</i>	1.59 <i>d</i>	2.60 <sup>#</sup> <i>d</i>	2.63 <sup>#</sup> <i>d</i>	5.11 <i>dd</i>	5.09 <i>dd</i>	5.12 <i>dd</i>	5.10 <i>dd</i>	4.17 <i>d</i>	1.13 <i>d</i>
15'	5.05 <i>m</i>	5.05 <i>m</i>	5.04 <i>ddd</i>					5.29 <i>dd</i>	5.28 <i>dd</i>	5.27 <i>dd</i>	5.28 <i>dd</i>		
16	1.00 <i>d</i>	0.99 <i>d</i>	1.10 <i>d</i>	1.57 <i>s</i>	1.59 <i>s</i>	1.63 <i>d</i>	1.63 <i>d</i>	1.20 <i>s</i>	1.17 <i>s</i>	1.26 <i>s</i>	1.29 <i>s</i>	1.64 <i>d</i>	1.03 <i>s</i>
17	1.11 <i>s</i>	1.11 <i>s</i>	1.10 <i>s</i>	1.11 <i>s</i>	1.09 <i>s</i>	1.09 <i>s</i>	1.07 <i>s</i>	1.12 <i>s</i>	1.17 <i>s</i>	1.13 <i>s</i>	1.15 <i>s</i>	1.11 <i>s</i>	1.14 <i>s</i>
18	0.86 <i>s</i>	0.86 <i>s</i>	0.85 <i>s</i>	0.86 <i>s</i>	0.86 <i>s</i>	0.83 <i>s</i>	0.82 <i>s</i>	0.85 <i>s</i>	0.85* <i>s</i>	0.85 <i>s</i>	0.85 <i>s</i>	0.85 <i>s</i>	0.85 <i>s</i>
19	0.81* <i>s</i>	0.81* <i>s</i>	0.82* <i>s</i>	0.84 <i>s</i>	0.84 <i>s</i>	0.78 <i>s</i>	0.78 <i>s</i>	0.80 <i>s</i>	0.84* <i>s</i>	0.80* <i>s</i>	0.82* <i>s</i>	0.81* <i>s</i>	0.82* <i>s</i>
20	0.80* <i>s</i>	0.80* <i>s</i>	0.81* <i>s</i>	0.84 <i>s</i>	0.84 <i>s</i>	0.78 <i>s</i>	0.78 <i>s</i>	0.80 <i>s</i>	0.81 <i>s</i>	0.79* <i>s</i>	0.80* <i>s</i>	0.80* <i>s</i>	0.81* <i>s</i>

<sup>a</sup> Coupling constants (*J*): Compounds 5 and 6: 11,12= 3.3 Hz; 11',12= 9.0 Hz; 12,13= 6.5 Hz; 13,14= 7.0 Hz; 13,16= 6.8 Hz; 14,15= 10.1 Hz; 14,15'= 17.6 Hz. Compound 7: 12,13=13,14= 7.6 Hz; 13,15= 1.2 Hz; 13,15'= 0.7 Hz; 13,16= 6.7 Hz; 14,15= 10.3 Hz; 14,15'=17.2 Hz; 15,15'= 2.0 Hz. Compound 8: 11,12= 3.9 Hz; 11',12= 8.7 Hz; 14,15= 6.8 Hz. Compound 9: 11,12~11',12= 8.2 Hz; 14,15= 6.9 Hz. Compound 10: 11',12= 9.2 Hz; 14,15= 8.9 Hz; 14,16= 1.2 Hz. Compound 11: 11,12~11',12= 8.2 Hz; 14,15= 8.9 Hz; 14,16= 1.2 Hz. Compound 12: 11,12~11',12= 6.4 Hz; 14,15= 10.8 Hz; 14,15'= 17.4 Hz; 15,15'= 1.5 Hz. Compound 13: 11,12= 5.4 Hz; 11',12= 9.9 Hz; 14,15= 10.7 Hz; 14,15'= 17.3 Hz; 15,15'= 1.4 Hz. Compound 14: 11,12= 3.9 Hz; 11',12= 8.8 Hz; 14,15= 10.9 Hz; 14,15'= 17.4 Hz; 15,15'= 1.6 Hz. Compound 15: 11,12= 5.5 Hz; 11',12= 9.5 Hz; 14,15= 10.9 Hz; 14,15'= 17.4 Hz; 15,15'= 1.6 Hz. Compound 16: 11,12~11',12= 7.8 Hz; 14,15= 6.8 Hz; 14,16= 1.4 Hz. Compound 17: 11,12= 3.8 Hz; 11',12= 9.5 Hz; 14,15= 6.3 Hz.

\* Interchangeable values. # Accompanied by two satellites at 135 Hz from the centre of the doublet.

## EXPERIMENTAL

<sup>1</sup>H NMR (300 MHz) and <sup>13</sup>C NMR (75 MHz) spectra were performed on a Bruker AM 300 spectrometer using TMS as internal standard and CDCl<sub>3</sub> as solvent. Chemical shifts ( $\delta$ ) are expressed in parts per million (ppm) and coupling constants (*J*) in hertz. IR spectra were recorded on a Perkin-Elmer Model 983 G spectrometer with samples between sodium chloride plates (film) or in solution of CHCl<sub>3</sub> in a 0.4 mm thickness sodium chloride cell. All mass spectra were registered on a Hewlett-Packard 5988A mass spectrometer using an ionizing voltage of 70 eV. Analytical TLC was performed on 0.25 mm-thick layers of silica gel 60 G (Merck 7331) and column chromatography over silica gel pads (Merck 7729) using hexane-Bu<sup>4</sup>OMe (H-E) mixtures of increasing polarity.

*cis*-Abienol (1) used in this study was obtained from the neutral fraction of the hexane extract of the leaves of *Abies marocana*<sup>26</sup> and the 1.2% sodium amalgam was prepared according to the literature.<sup>27</sup>

**Table 2.**  $^{13}\text{C}$  NMR chemical shifts<sup>a</sup> of compounds **5-17** (75 MHz,  $\text{CDCl}_3$ )

	5 and 6	7	8	9	10 <sup>#</sup>	11 <sup>#</sup>	12	13	14	15	16	17
C-1	39.90*	40.58*	39.87*	40.69*	39.71*	40.50*	39.74*	40.79*	39.73*	40.81*	40.57*	39.81
C-2	18.40	18.43	18.36	18.36	18.24	18.24	18.31	18.40	18.33	18.41	18.39	18.30
C-3	42.47	42.48	42.43	42.43	42.29	42.29	42.39	42.39	42.41	42.47	42.43	42.31
C-4	33.07	33.10	33.05	33.08	32.94	32.94	33.03	33.09	33.06	33.06	33.10	33.04
C-5	57.32	57.11	57.31	57.12	57.10	56.96	57.24	57.02	57.24	57.07	57.10	57.08
C-6	20.54	20.91	20.51	20.51	20.39	20.39	20.52	21.37	20.54	21.40	20.93	20.48
C-7	39.73*	39.98*	39.73*	40.08*	39.57*	39.94*	39.57*	40.11*	39.63*	40.10*	40.06*	39.81
C-8	80.72	80.37	80.65	80.86	80.86	80.86	81.41	81.27	81.47	81.24	81.23	81.81
C-9	80.62 59.39 59.53	60.93	59.65	59.29	59.29	61.87	60.20	60.69	60.13	60.99	60.96	60.49
C-10	36.21	36.26	36.22	36.12	36.12	36.19	36.29	36.35	36.29	36.40	36.30	36.38
C-11	25.32 25.40	28.17	27.87	28.44	27.94	28.75	23.97	23.97	24.29	24.38	28.73	24.59
C-12	79.26 79.01	82.58	80.47	82.91	79.70	82.26	81.58	85.18	81.66	85.40	81.84	69.87
C-13	42.74 42.93	45.98	136.78	136.78	136.74	136.94	74.46	73.14	74.55	73.34	140.46	74.37
C-14	140.75 140.91	140.87	119.68	117.92	120.63	119.03	143.06	144.22	141.19	141.04	121.81	83.89
C-15	114.45 114.28	114.25	11.73	12.63	29.60	29.81	112.90	112.49	113.58	113.44	59.12	16.60
C-16	15.66 15.29	17.71	12.97	14.86	12.63	13.20	23.39	23.19	24.87	25.91	13.41	20.41
C-17	21.44 21.34	24.84	21.46	24.85	21.41	24.81	21.21	25.34	21.40	25.48	24.73	20.70*
C-18	33.54	33.53	33.51	33.51	33.41	33.41	33.50	33.50	33.51	33.51	33.48	33.45
C-19	21.12	21.07	21.09	21.03	21.00	20.90	21.07	20.95	21.09	20.97	21.01	21.07*
C-20	14.85	15.54	14.86	15.79	14.79	15.70	14.73	15.90	14.77	15.88	15.74	14.70

<sup>a</sup> Referenced to  $\text{CDCl}_3$  as 77.00 ppm relative to TMS. \* Interchangeable values. # Satellite bands corresponding to  $^{199}\text{Hg}$ - $^{13}\text{C}$  couplings were not indicated.

#### Reaction of *cis*-abienol (**1**) with $\text{OsO}_4$ - $\text{NaIO}_4$

To a solution of **1** (260 mg, 0.90 mmol) in  $\text{Bu}^t\text{OH}$  (12 ml)  $\text{H}_2\text{O}$  (2 ml),  $\text{NaIO}_4$  (680 mg, 3.18 mmol) and 0.2%  $\text{OsO}_4$  aq. solution (1.6 ml, 0.0126 mmol) were added. The mixture was stirred for 20 days at room temperature and then was fractionated in  $\text{Bu}^t\text{OMe}$ - $\text{H}_2\text{O}$  and extracted with  $\text{Bu}^t\text{OMe}$ , and the combined organic layers washed with sat.  $\text{K}_2\text{CO}_3$  solution and  $\text{H}_2\text{O}$ . The organic phase was dried over anhyd.  $\text{Na}_2\text{SO}_4$  and the solvent evaporated to afford *nor*-ambreinolide (**2**) (192 mg, 85%).<sup>28</sup> IR ( $\text{CHCl}_3$ ):  $\nu$  1770;  $^1\text{H}$  NMR (80 MHz,  $\text{CDCl}_3$ ):  $\delta$  0.83 (3H, *s*), 0.89 (3H, *s*), 0.92 (3H, *s*), 1.33 (3H, *s*).

#### Reaction of *cis*-abienol (**1**) with $\text{RuO}_4$ - $\text{NaIO}_4$

A solution of **1** (250 mg, 0.86 mmol) in acetone (10 ml) was added dropwise to a yellow  $\text{RuO}_4$  solution, generated by stirring  $\text{RuO}_2$  (50 mg, 0.38 mmol) suspended in acetone (10 ml) with  $\text{NaIO}_4$  (400 mg, 1.87 mmol) in a minimum amount of water. Further portions of  $\text{NaIO}_4$  were added throughout the reaction to

regenerate the RuO<sub>4</sub>. After stirring for 12 h at room temperature the mixture was filtered and the acetone removed *in vacuo*. The crude was dissolved in Bu<sup>t</sup>OMe, washed with water, dried over anh. Na<sub>2</sub>SO<sub>4</sub> and the solvent evaporated to afford a crude mixture (205 mg) comprising an 8:2 mixture of *nor*-ambreinolide (**2**) and 8a-hydroxy-13,14,15,16-tetranorlabdan-12-oic acid (**4**). A solution of this mixture (50 mg) and *p*-TsOH (15 mg) in CH<sub>2</sub>Cl<sub>2</sub> (2 ml) was then stirred at room temperature for 2 h. The crude mixture was diluted with CH<sub>2</sub>Cl<sub>2</sub>, washed with water, dried over anh. Na<sub>2</sub>SO<sub>4</sub> and the solvent evaporated to yield *nor*-ambreinolide (**2**) (48 mg, 88% yield from **1**).

#### Oxymercuration-demercuration (OM-DM) of *cis*-abienol (**1**)

A solution of **1** (2.00 g, 6.89 mmol) in THF (12 ml) was added to a suspension of Hg(OAc)<sub>2</sub> (4.39 g, 13.78 mmol) in a THF-H<sub>2</sub>O mixture (10 ml-11 ml). After stirring for 4 h at room temperature 1.2% Na(Hg) (98.10 g; 3.70 mmol of Na per mmol of Hg(OAc)<sub>2</sub>) and an excess of H<sub>2</sub>O were added. After further stirring for 12 h at room temperature the mixture was extracted with hexane (3x50 ml). The resulting organic phases were dried over anh. Na<sub>2</sub>SO<sub>4</sub> and evaporated to dryness to afford a crude (1.82 g) which after column chromatography on silica gel and 20% AgNO<sub>3</sub>-silica gel yielded the following compounds:

#### (8R,12R,13)-8,12-epoxy-labd-14-ene (**5** and **6**)

A mixture (78 mg) of these epimers was eluted with 98:2 H-E. IR (film):  $\nu$  2928, 2870, 1639, 1455, 1404, 1376, 1122, 1010, 912, 802; MS *m/z* (rel. int.): 290 (M<sup>+</sup>, 1%), 275 (**2**), 235 (**23**), 217 (**16**), 191 (**100**), 137 (**42**), 135 (**12**), 123 (**20**), 121 (**18**), 109 (**44**), 95 (**42**), 93 (**20**), 81 (**53**), 79 (**23**), 69 (**71**), 67 (**36**), 50 (**77**), 53 (**20**), 43 (**50**), 41 (**63**). <sup>1</sup>H NMR data in Table 1. <sup>13</sup>C NMR data in Table 2.

#### (8R,12S)-8,12-epoxy-labd-14-ene (**7**)

25 mg eluted with 93:7 H-E (AgNO<sub>3</sub>-SiO<sub>2</sub>). IR and mass spectra were identical to those of the substances **5** and **6**. <sup>1</sup>H NMR data in Table 1. <sup>13</sup>C NMR data in Table 2.

#### (8R,12R) and (8R,12S)-8,12-epoxy-labd-13E-ene (**8** and **9**)

650 mg (7:3 ratio) eluted with 98:2 H-E. IR (film):  $\nu$  2929, 2860, 1682, 1457, 1378, 1276, 1160, 1124, 1078, 1001, 981, 940, 912, 822.; MS *m/z* (rel. int.): 290 (M<sup>+</sup>, 18%), 275 (**6**), 206 (**10**), 191 (**100**), 137 (**27**), 136 (**19**), 135 (**15**), 123 (**61**), 121 (**24**), 109 (**40**), 107 (**25**), 105 (**15**), 95 (**51**), 93 (**23**), 91 (**23**), 85 (**25**), 83 (**33**), 82 (**33**), 81 (**41**), 79 (**27**), 69 (**47**), 67 (**42**), 55 (**44**), 43 (**31**), 41 (**30**). <sup>1</sup>H NMR data in Table 1. <sup>13</sup>C NMR data in Table 2.

#### Bis-[(8R,12R/S)-8,12-epoxy-labd-13E-ene-15-yl]mercury (**10** and **11**)

259 mg (3:2 ratio) eluted with 85:15 H-E (AgNO<sub>3</sub>-SiO<sub>2</sub>). IR (CHCl<sub>3</sub>):  $\nu$  2933, 2868, 2843, 1657, 1457, 1375, 1265, 1216, 1160, 1121, 1080, 1001, 977, 943, 905, 884, 843, 814; MS *m/z* (rel. int.): 289 (**7%**), 235

(3), 204 (1), 202 (3.7), 201 (1.7), 200 (2.7), 199 (2), 198 (1.2), 191 (30), 137 (9), 135 (6), 123 (12), 121 (9), 109 (16), 95 (23), 93 (16), 91 (18), 83 (21), 81 (41), 79 (27), 69 (48), 55 (100), 43 (71).  $^1\text{H}$  NMR data in Table 1.  $^{13}\text{C}$  NMR data in Table 2.

**(8R,12R,13R) and (8R,12S,13S)-8,12-epoxy-13-hydroxy-labd-14-ene (12 and 13)**

152 mg (7:3 ratio) eluted with 9:1 H-E. IR ( $\text{CHCl}_3$ ):  $\nu$  3681, 3561, 3080, 1605, 1076, 985, 905, 870; MS  $m/z$  (rel. int.): 291 ( $[\text{M}+1]^+$ , 1%), 235 (15), 217 (11), 191 (100), 137 (35), 123 (14), 121 (14), 109 (37), 95 (29), 85 (20), 83 (33), 81 (30), 71 (32), 69 (40), 67 (15), 55 (23), 43 (27), 41 (17).  $^1\text{H}$  NMR data in Table 1.  $^{13}\text{C}$  NMR data in Table 2.

**(8R,12R,13S) and (8R,12S,13R)-8,12-epoxy-13-hydroxy-labd-14-ene (14 and 15)**

200 mg (3:2 ratio) eluted with 9:1 H-E. IR and mass spectra are identical to those of substances 12 and 13.  $^1\text{H}$  NMR data in Table 1.  $^{13}\text{C}$  NMR data in Table 2.

**(8R,12S)-8,12-epoxy-15-hydroxy-labd-13E-ene (16)**

80 mg eluted with 9:1 H-E. IR (film):  $\nu$  3398, 2926, 2867, 1673, 1458, 1378, 1159, 1121, 1080, 1045, 1003, 982, 844, 802; MS  $m/z$  (rel. int.): 306 ( $\text{M}^+$ , 1%), 275 (15), 235 (7), 191 (94), 177 (18), 149 (10), 137 (30), 123 (36), 121 (22), 109 (46), 95 (55), 83 (54), 81 (58), 69 (89), 67 (45), 55 (75), 49 (53), 43 (100).  $^1\text{H}$  NMR data in Table 1.  $^{13}\text{C}$  NMR data in Table 2.

**(8R,12R)-8,12-epoxy-13,14-dihydroxy-labdane (17)**

98 mg eluted with 7:3 H-E. IR (film):  $\nu$  3429, 2925, 2868, 1459, 1378, 1261, 1197, 1121, 1079, 1003, 983, 802; MS  $m/z$  (rel. int.): 288 ( $[\text{M}-2(\text{H}_2\text{O})]^+$ , 1%), 262 (2), 235 (9), 191 (56), 177 (22), 149 (7), 137 (19), 135 (8), 123 (20), 121 (12), 109 (27), 95 (32), 83 (18), 81 (40), 71 (31), 69 (64), 67 (30), 55 (52), 43 (100).  $^1\text{H}$  NMR data in Table 1.  $^{13}\text{C}$  NMR data in Table 2.

**Reaction of the OM-DM crude from *cis*-abienol (1) with  $\text{RuO}_4\text{-NaIO}_4$**

A solution of the resulting crude from the OM-DM of 1 (1.30 g) in acetone (50 ml) was added dropwise to a  $\text{RuO}_4$  solution, generated by stirring  $\text{RuO}_2$  (180 mg) suspended in acetone (40 ml) with  $\text{NaIO}_4$  (1.20 g) in a minimum amount of water. After stirring for 15 h at room temperature the starting material disappeared. Following the same procedure described above a crude (1.11 g) was obtained which after column chromatography (7:3 H:E) yielded *nor*-ambreinolide (2) (675 mg, 55% from 1).



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