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The Formation of Two New Ring-Enlargement Products in the Lead Tetraacetate Oxidation of *l*-2(10)-Pinene[1)]

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(Received March 6, 1991)

Synopsis. The oxidation of *l*-2(10)-pinene with lead tetraacetate in glacial acetic acid at 60 °C afforded, besides fifteen known other products, (1*S*,6*S*)-7,7-dimethylbicyclo[4.1.1]octan-3-one (**2**) and (1*R*,6*S*)-2-one isomer (**3**), whose structures were established on the basis of their spectroscopic data. A possible reaction pathway for the formation of these new compounds **2** and **3** involving novel ring-enlargement is described.

One of us (Y. M.) and his co-worker[2)] have studied the lead tetraacetate oxidation of *l*-2(10)-pinene (**1**) by employing trilead tetraoxide in a mixture of acetic acid and acetic anhydride at 60 °C. Hydrolysis of the oily reactant with aqueous potassium hydroxide afforded six major products [mirtenol (**4**), 1-*p*-menthene-7,8-diol (**5**), *trans*- and *cis*-1(7),8-*p*-menthadien-2-ol (**6**,**7**), *trans*- and *cis*-1(7)-*p*-menthene-2,8-diol (**8**,**9**)] and nine minor products [*trans*-pino-carveol (**10**), α-terpineol (**11**), *n*-borneol (**12**), 1(7),4(8)-*p*-menthadien-2-ol (**13**), periryl alcohol (**14**), *p*-cymen-7-ol (**15**), carvacrol (**16**), 1,4(8)-*p*-menthadien-7-ol (**17**), 1,4(8)-*p*-menthadien-9-ol (**18**)]. All of the major products can easily be converted into periryl alcohol which is useful as flavor. Meanwhile, the lead tetraacetate oxidation was performed on other terpene hydrocarbons such as camphene[3)] and longifolene[4)] that have a terminal methylene group between a quaternary carbon and tertiary carbon. The oxidation was found to give ring-enlargement products (*R*-homocamphenilone and longi-homocamphenilone) in good yields.

If the terminal methylene group of *l*-2(10)-pinene (**1**) undergoes a similar ring-enlargement reaction, the corresponding products are expected to become highly important synthetic intermediates for preparation of β- and γ-thujaplicins.[5)] We wish to report herein our detailed reinvestigation on the oxidation of **1** with lead tetraacetate, which enabled us to isolate two unique ring-enlargement compounds.

When the trilead tetraoxide oxidation of *l*-2(10)-pinene (**1**) was carried out in glacial acetic acid alone at 60 °C for 2.5 h and then the reaction mixture was hydrolyzed, we found that two minor compounds (**2** and **3**) were produced beside the fifteen, already identified compounds[2)] **4**—**18** on the evidence of GLC and GC-MS analyses. Yields of these products based on GLC analysis are summarized in Table 1. Compounds **2** and **3** were purified by silica-gel column chromatography, followed by removal of alcoholic compounds by employing phthalic anhydride,[6)] and finally by the use of preparative GLC.

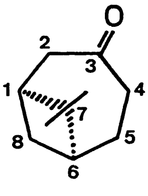
Table 1. Yield/% of the Oxidation Products from **1** with Trilead Tetraacetate[a)]

Product	Yield/%	Product	Yield/%
2	3	**11**	4
3	0.1	**12**	1
4	14	**13**	3
5	25	**14**	9
6	5	**15**	0.3
7	0.2	**16**	0.2
8	15	**17**	0.2
9	0.5	**18**	2
10	11	Others	6

a) Yields (based on GLC analysis) represent the result of several runs of the same experiment.

Compound **2** was a colorless oil, and its EI-MS showed the molecular ion peak at *m/z* 152. The molecular formula of **2** was found to be $C_{10}H_{16}O$ by HR-MS. The IR spectrum showed the presence of a carbonyl group (1697 cm^{-1}) and methylene group(s) (1470 and 1454 cm^{-1}) in compound **2**. The ^{1}H NMR spectrum of **2** exhibited two methyl proton signals at δ=0.75 and 1.28, but no signals due to terminal methylene protons. The complex signals at δ=1.75—2.90 in the spectrum were studied by examining the cross peaks of the 2D ^{1}H NMR (H–H COSY) and 2D ^{13}C NMR (C–H COSY) spectra, as well as by proton–proton decoupling experiments. The assignment of each proton signal was made as follows. First, the interrelations between carbon and proton signals were established by the analysis of the C–H COSY spectrum, thus disclosing that compound **2** consisted of one carbonyl group, one quaternary carbon, two methine groups, and four methylene groups (A, B, C, and D), besides the two methyl groups. Then, one of the methine protons (δ=2.06) was shown to have vicinal couplings with four protons of two methylene groups A (δ=1.79, 2.552) and B (δ=2.42, 2.61). Another methine proton (δ=2.20) had vicinal couplings with four protons of two methylene groups A and C (δ=1.82, 1.84). The latter methylene protons (C) were further coupled with two protons of another methylene group D (δ=2.550, 2.82). Therefore, combination of these NMR spectral data and the mode of the formation pathways (see later) has led to the structure, 7,7-dimethylbicyclo[4.1.1]octan-3-one, for compound **2**. The precise δ and J values of all proton signals, which have been confirmed by a computer-assisted simulation analysis, are shown in the Experimental section.

Compound **3** was also a colorless oil, whose EI-MS showed the molecular ion peak at *m/z* 152. The molecular formula of **3** was identical with **2** ($C_{10}H_{16}O$, by HR-MS). The IR spectrum of **3** similarly showed the presence of a carbonyl (1687 cm^{-1}) and methylene groups (1469, 1455 cm^{-1}). The analysis of ^{1}H and ^{13}C NMR spectra (including their 2D NMR) of compound **3** was carefully made in a manner similar to the case of **2**. It was noted that the methine proton signal at lower field (δ=2.68) showed vicinal couplings only with two, methylene protons (δ=1.96, 2.46) besides a long-range coupling with another methine proton (δ=2.25); this indicated the position of the carbonyl group adjacent to the former methine group. As a result, the isomeric structure, 7,7-dimethylbicyclo[4.1.1]octan-2-one, is assigned to **3**. The δ and J values of all signals for compound **3** are shown in the Experimental section.



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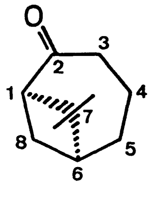

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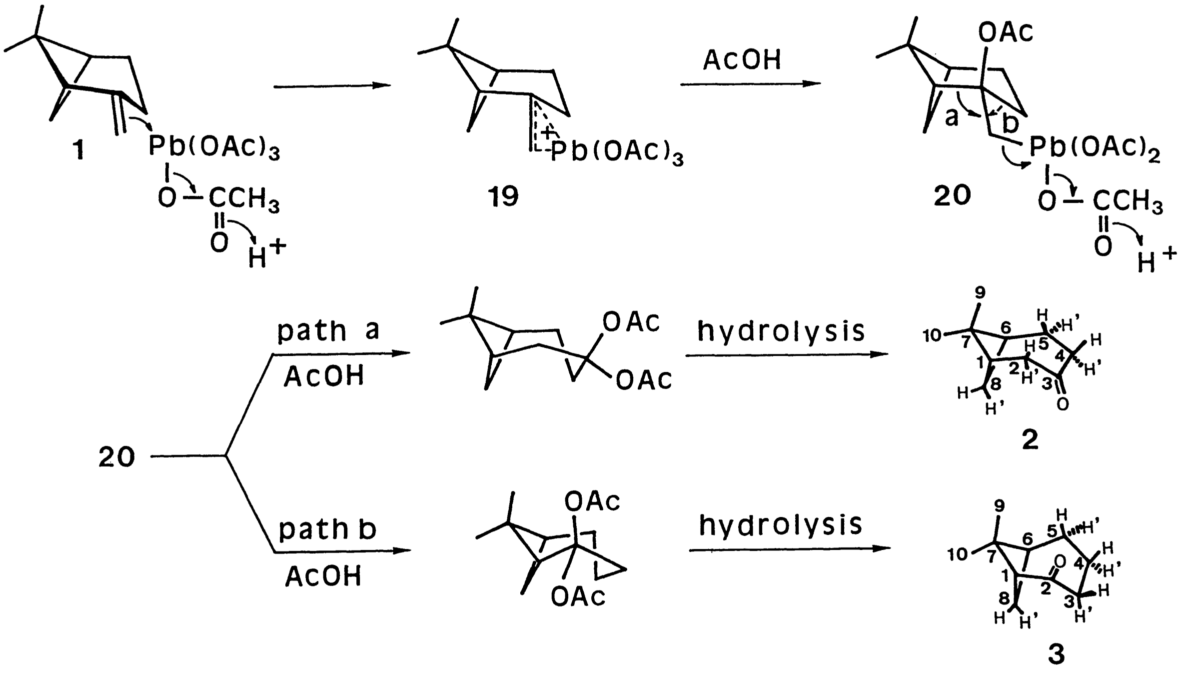
The most likely pathways for the formation of compounds **2** and **3** from **1** are illustrated in Scheme 1. The initial lead intermediate **19** is presumed to undergo a heterolytic cleavage accompanied by two, competitive 1,2-anionotropic shifts (path 'a' and 'b' in **20**).[7] The relative yield between **2** and **3** suggests a predominant migration of the tertiary carbon (C$_1$) (path 'a') compared with that of the secondary carbon (C$_3$) (path 'b') of intermediate **20**. Because no inversion of the configuration of the bridge-head carbon (C$_1$) in **20** is considered to take place, the absolute configuration of compounds **2** and **3** are assigned to be (1*S*,6*S*) and (1*R*,6*S*), respectively, as shown in the formulas.[8]

Experimental

Commercially available *l*-2(10)-pinene (**1**) was washed with dilute aq Na$_2$CO$_3$, then with water, and dried (Na$_2$SO$_4$). This was distilled through a spinning band precision distillation column under a reduced pressure to provide freshly distilled **1**: Bp 70—75 °C/111 mmHg (1 mmHg=133.322 Pa), n_D^{25}=1.4715, d_4^{25}=0.8722, $[\alpha]_D^{25}$=−18.6° (neat) [lit,[9] $[\alpha]_D$=−22.1° (neat) for (1*S*,5*S*) form].

Column chromatography was performed with Wako C-300 silica-gel. Preparative GLC was carried out with a Yanaco G1800 gas liquid chromatograph system equipped with a TCD (thermal conductivity detector) and PEG 20M steel column (ϕ 3 mm×5 m). GLC analysis was conducted with a Yanaco G2800 gas liquid chromatograph system equipped with a HFID (hydrogen flame ionization detector) and PEG 20M glass capillary column (ϕ 0.28 mm×20 m, column temp. 60—180 °C/2 °C min^{-1}). Optical rotations were measured with a JASCO DIP-140 spectrophotometer. IR spectra were taken on a JASCO IR-A-202 Grating spectrometer. Mass spectra were taken on a JEOL JMS-HX100 (with a JEOL JMA-DA5000 mass data system) high-resolution instrument and are given in terms of m/z (rel intensity) compared with the base peak. NMR spectra were recorded in CDCl$_3$ with a JEOL GX-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) at 27 °C. The assigments of all signals were made by employing a first-order analysis with the aid of decoupling, H-H COSY and C-H COSY techniques, and the parameters were confirmed by a computer-assisted simulation analysis.

Oxidation of *l*-2(10)-Pinene (1) with Lead Tetraacetate. A solution of **1** (136 g, 1.0 mol) in glacial acetic acid (1.8 l) was stirred at 60±2 °C. Trilead tetraoxide (690 g, 1.0 mol) was slowly added to the above solution during a period of 90 min and the stirring was continued for further 1 h. The reactant was carefully neutralized with aq Na$_2$CO$_3$. The precipitated solid of PbCO$_3$ was removed by filtration and the filtrate was extracted with hexane (3×1 l). The combined extracts were washed with water, dried (Na$_2$SO$_4$), and evaporated in vacuo to give an almost colorless oil (145.9 g): n_D^{25}=1.4676, d_4^{25}=1.0012, $[\alpha]_D^{22}$=−47.1° (neat), EV (ester value)=324. Hydroly-



Scheme 1. Possible reaction pathways for the formation of 2 and 3.

sis of the reactant oil was performed by following a general method,[2] affording hydrolytic products (107.9 g). Their structures were confirmed by comparing the GLC and GC-MS data with those of the authentic samples **4**—**18**.[2] The yields of these compounds based on GLC analysis are summarized in Table 1. The new minor products **2** and **3** were carefully separated by silica-gel column chromatography, followed by removal of alcoholic compounds by employing phthalic anhydride,[6] and then preparative GLC.

(1*S*,6*S*)-7,7-Dimethylbicyclo[4.1.1]octan-3-one (2): A colorless oil; $n_D^{25}=1.4810$; $d_4^{25}=0.9818$; $[\alpha]_D^{25}=-57°$ (c 0.11, $CHCl_3$); IR (neat) 1697 (C=O), 1470, 1454 cm^{-1} (CH_2); EI-MS m/z 152 (M^+; 25.1%), 137 (3.9), 111 (51.4), 95 (8.0), 93 (8.1), 83 (89.0), 69 (97.8), 55 (100), 41 (49.3); ^{1}H NMR $\delta=0.75$ (Me-9), 1.28 (Me-10), 1.79 (H-8′), 1.82 (H-5), 1.84 (H-5′), 2.06 (H-1), 2.20 (H-6), 2.42 (H-2), 2.550 (H-4), 2.552 (H-8), 2.61 (H-2′), 2.82 (H-4′), $J_{1,2}=3.5$, $J_{1,2'}=4.3$, $J_{1,6}=4.0$, $J_{1,8}=8.0$, $J_{1,8'}=1.5$, $J_{2,2'}=-17.0$, $J_{2',4}\approx J_{2',8}\approx 1.5$, $J_{4,4'}=-13.5$, $J_{4,5}\approx 2$, $J_{4,5'}\approx 6.5$, $J_{4',5}=12$, $J_{4',5'}=7.5$, $J_{4',6}\approx 0.5$, $J_{5,5'}=-14.5$, $J_{5,6}\approx 5.5$, $J_{5',6}\approx 3$, $J_{6,8}=8.0$, $J_{6,8'}\approx 1$, $J_{8,8'}=-12.0$ Hz; ^{13}C NMR $\delta=19.95$ (C-9), 23.40 (C-5), 24.59 (C-8), 30.42 (C-10), 38.51 (C-1), 40.07 (C-7), 41.87 (C-6), 41.90 (C-4), 45.30 (C-2), 214.62 (C-3). Found: m/z 152.1185. Calcd for $C_{10}H_{16}O$: M, 152.1168.

(1*R*,6*S*)-7,7-Dimethylbicyclo[4.1.1]octan-2-one (3): A colorless oil; $n_D^{25}=1.4831$; $[\alpha]_D^{22}=+50°$ (c 0.24, $CHCl_3$); IR (neat) 1687 (C=O), 1469, 1455 cm^{-1} (CH_2); EI-MS m/z 152 (M^+; 14.3%), 137 (7.1), 123 (4.3), 110 (22.4), 98 (20.7), 83 (100), 82 (94.3), 67 (42.1), 55 (38.6), 41 (29.3); ^{1}H NMR $\delta=1.01$ (Me-9), 1.35 (Me-10), 1.90 (H-4), 1.93 (H-5), 1.96 (H-8′), 2.02 (H-5′), 2.03 (H-4′), 2.25 (H-6), 2.46 (H-8), 2.52 (H-3′), 2.68 (H-1), 2.84 (H-3), $J_{1,3}\approx 0.5$, $J_{1,6}=4.3$, $J_{1,8}=7.5$, $J_{1,8'}\approx 1$, $J_{3,3'}=-16.5$, $J_{3,4}=4.0$, $J_{3,4'}=7.5$, $J_{3',4}=10.0$, $J_{3',4'}=4.5$, $J_{4,4'}\approx -12$, $J_{4,5}\approx 2$, $J_{4,5'}\approx 7$, $J_{4',5}\approx 4$, $J_{4',5'}\approx 4$, $J_{5,5'}\approx -12$, $J_{5,6}\approx 5.5$, $J_{5',6}\approx 2.5$, $J_{6,8}=8.0$, $J_{6,8'}\approx 1.5$, $J_{8,8'}=-12.5$ Hz; ^{13}C NMR $\delta=20.30$ (C-5), 21.51 (C-9), 23.38 (C-8), 26.34 (C-4), 31.00 (C-10), 40.13 (C-7), 42.06 (C-3), 42.71 (C-6), 60.38 (C-1), 214.92 (C-2). Found: m/z 152.1191. Calcd for $C_{10}H_{16}O$: M, 152.1168.

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8) Optimization of the yields of compounds **2** and **3** from **1** by the present method or by the use of other methods is currently under intensive investigation.

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