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The Baeyer-Villiger Reaction of Pinanones (Bicyclo[3.1.1]heptanones)

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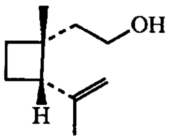
Key Words: Baeyer-Villiger; pinanes; cyclobutanes; lactones; conformational control.

Abstract: The Baeyer-Villiger reaction of bicyclo[3.1.1]heptanones yields the expected lactones, but with some difficulty. These lactones readily react with alcohols, including the ethanol present in commercial chloroform, to give the corresponding hydroxy esters. Pinocamphone and isopinocamphone exhibit conformational control in the Baeyer-Villiger reaction, the trans-*isomer yielding mainly the expected lactone, the* cis-*isomer (isopinocamphone) yielding hydroxyisopinocamphone. The use of this pathway as a synthetic route to cyclobutane monoterpenoids is discussed.*

INTRODUCTION

There are a number of simple naturally occurring cyclobutane monoterpenoids which could be derived from pinanes, for example, grandisol (1)[1], fragranol (2),[2] junionone (3),[3] and the citrus mealybug pheromone, *cis*-planococcyl acetate (4).[4] Some of these have been synthesized from pinane derivatives, for example grandisol (1) from *trans*-pinan-2-ol,[5] and (4) from α-pinene.[6,7]



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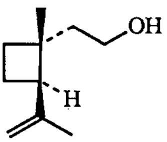

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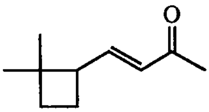

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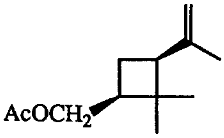

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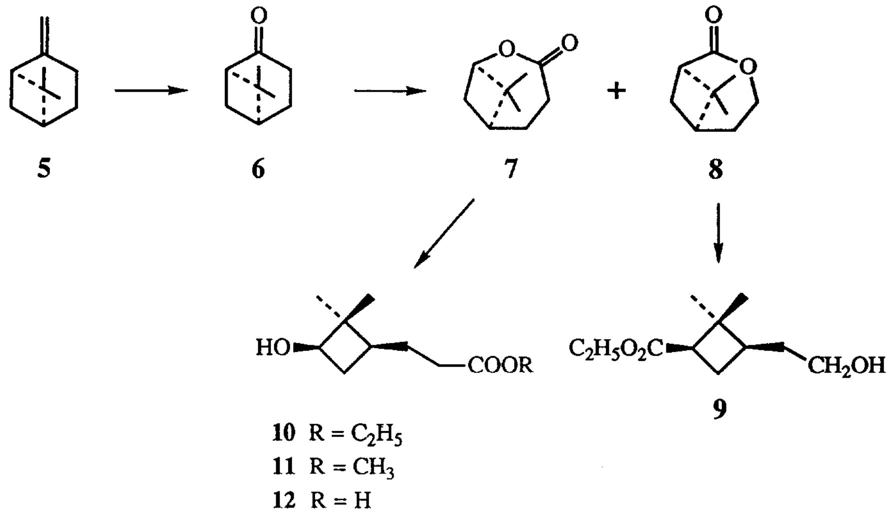
In order to convert pinane derivatives such as β-pinene (5) to monocyclic cyclobutanes, fission of the C_3 chain between the bridgehead atoms is needed. A potential method would be the *Baeyer-Villiger* oxidation of pinane ketones, but this route has not been exploited because of the supposed unreactivity of nopinone (6). We now describe the successful *Baeyer-Villiger* reaction of (6) and other 6,6-dimethylbicyclo[3.1.1.]heptanones.

At the outset of our work, there had only been one report of the *Baeyer-Villiger* reaction of nopinone (6), (prepared by ozonolysis of β-pinene (5)) when the expected lactone (7) was obtained as the only product.[8] An isomeric lactone (8) was suggested to be a byproduct from the ozonolysis of β-pinene (5),[9] but neither of these papers gave full spectral characterization of the lactones claimed.[10]



SCHEME 1

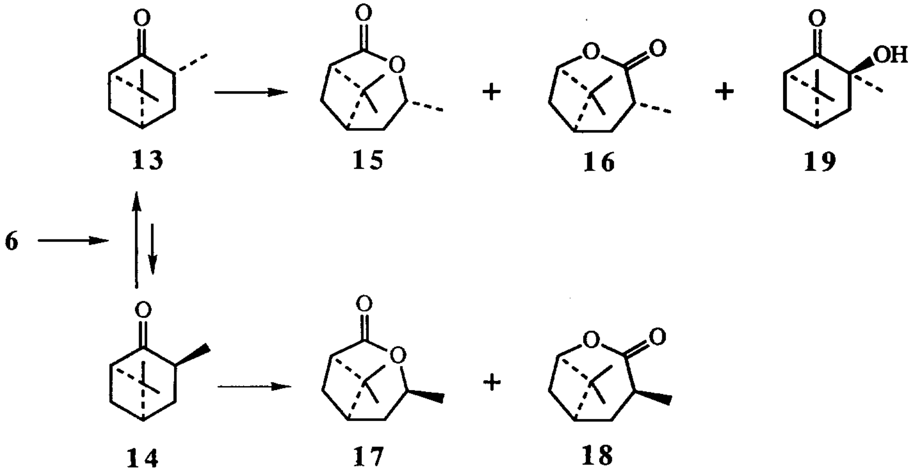
RESULTS AND DISCUSSION

The reaction of nopinone (6) with 3-chloroperbenzoic acid (MCPBA) in chlorinated solvents is very slow,[10] and several weeks at room temperature are necessary to have a reasonable yield of products. For example, *Joulain* and *Rouessac* used 4-nitroperbenzoic acid for three weeks to obtain the lactone (7).[8] In our conditions (more than 3 weeks with MCPBA) we obtained two lactones (7) and (8), in the ratio of about 9:1; their structures were secured by the ^1H- and ^{13}C-NMR spectra, discussed below. Measurement of the ^1H-NMR spectrum of (7) in CCl_4 solution gave data very close to those of *Joulain*,[8] but the ^1H-NMR spectrum of (8) did not fit with the data of the Japanese workers,[9] and we conclude that the latter must have isolated a different compound.

Isolation of the minor lactone (8) is not easy. If there is a trace of ethanol in the chloroform or methylene chloride used as solvent, this lactone is ethanolyzed to the cyclobutane (9), and we could only be sure of obtaining (8) by rigorous removal of the ethanol present in the commercial solvents. The major lactone (7) is more resistant to alcoholysis, but when we added trifluoroacetic acid to the oxidizing medium in the hope of accelerating the reaction,[11] with unpurified commercial chloroform as solvent, not only was the minor lactone (8) converted to the ethyl ester (9), but a small amount of the major lactone (7) was also ethanolyzed to (10). Boiling the major lactone (7) in methanol overnight converts it completely to the methyl ester (11), a compound which has been isolated from the ozonolysis of β-pinene (5) in methanol.[12] We also observed that the minor lactone (8) was largely decomposed on thin-layer chromatography, although we had successfully isolated it by flash column chromatography.

Fringuelli et al. have described *Baeyer-Villiger* reactions with MCPBA in water.[13] Under their conditions (80° for several hours) nopinone (6) undergoes the reaction, but the product is a mixture of lactone (7) and its hydrolysis product (12). (See scheme 1 for the products arising from the nopinone reaction.)

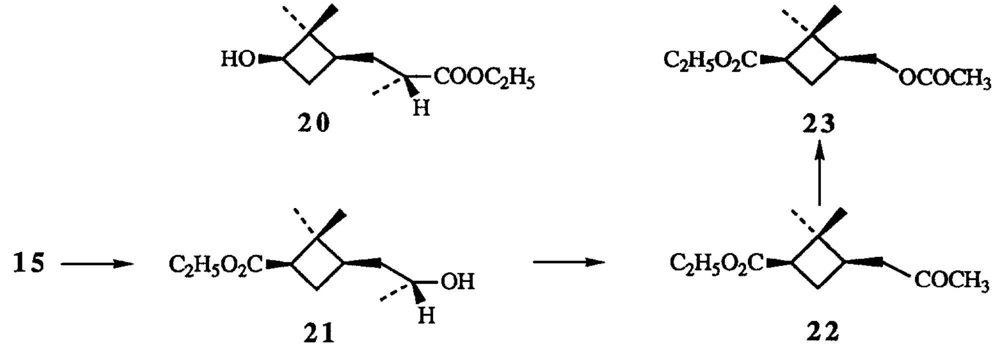
Using an aqueous suspension of magnesium monoperoxyphthalate[14] at 80°, we only achieved a maximum of 0.5% yield of the lactone (7), about the same as we observed using aqueous peracetic acid.



SCHEME 2

The reaction was extended to methylnopinone, which exists at equilibrium mainly as the *cis*-isomer (**13**) containing about 12% of the *trans*-isomer (**14**).[15,16] After treatment with MCPBA in dichloromethane for 5 weeks, there was 20% of unchanged methylnopinones accompanied by 60% of the *cis*-lactone (**15**), readily identified from the spectra. Chromatography on siliga gel gave a fraction of shorter retention time from which we were able to isolate 8% yield of the alternative *cis*-lactone (**16**), and a mixture of the two lactones (**17**) and (**18**), resulting from the *trans*-methylnopinone (**14**) in the starting material. Using our carefully purified chloroform as solvent, the conversion of the methylnopinones was lower (45%), with the product mixture containing, in addition to 55% of recovered methylnopinones, 21% of the lactone (**15**) and 15% of the lactone (**16**), with 4% of the mixture of (**17**) and (**18**). A trace of a hydroxy ketone, to which we attribute structure (**19**) was also isolated from this experiment. *Fringuelli's* aqueous conditions gave a rapid reaction, but after 24h at 80°, there was no further change, and the mixture then consisted of 68% of unchanged methylnopinones, 10% of lactone (**15**) and 5% of lactone (**16**).

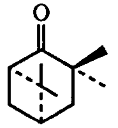
The problem of reaction of the lactones formed in the *Baeyer-Villiger* reaction with the ethanol in commercial chlorinated solvents was also encountered with the methylnopinone reaction. An attempt to raise the yield from the methylnopinone reaction was made by adding the MCPBA in small amounts periodically to the oxidizing mixture over some weeks. The only products detected from this experiment arose from intervention of the ethanol in the solvent: the cyclobutanol (**20**) resulting from ethanolysis of (**16**), a trace of the cyclobutane (**21**), and another cyclobutane (**23**) resulting from, successively, ethanolysis of lactone (**15**) to the hydroxy ester (**21**), oxidation to the corresponding ketone (**22**), and a second *Baeyer-Villiger* reaction (scheme 3). Subsequently a stepwise synthesis of (**23**) confirmed the intermediacy of (**21**) and (**22**). The cyclobutanol structure (**20**) was confirmed by its formation from lactone (**16**) and ethanol. The methyl ester corresponding to (**22**) was prepared from norpinic acid by a long route by *Trave* and *Garanti* in 1960.[17]



SCHEME 3

Dimethylnopinone (24)[18] was inert to the oxidizing conditions in chlorinated solvents.

Isonopinone (6,6-dimethylbicyclo[3.1.1]heptan-3-one (25))[19] underwent the *Baeyer-Villiger* reaction, yielding the racemic lactone (26), identified by its NMR spectra. When it was somewhat later submitted to elemental analysis, the figures showed that there had been uptake of one equivalent of water. The ^{1}H-NMR spectrum of this sample clearly showed that the lactone (26) had been largely converted to the hydroxy acid (27). An attempted reconversion of this acid back to the lactone (26) resulted only in extensive decomposition.



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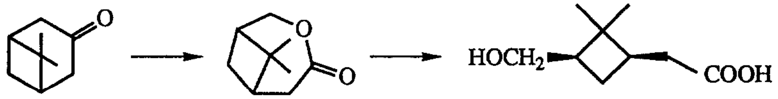
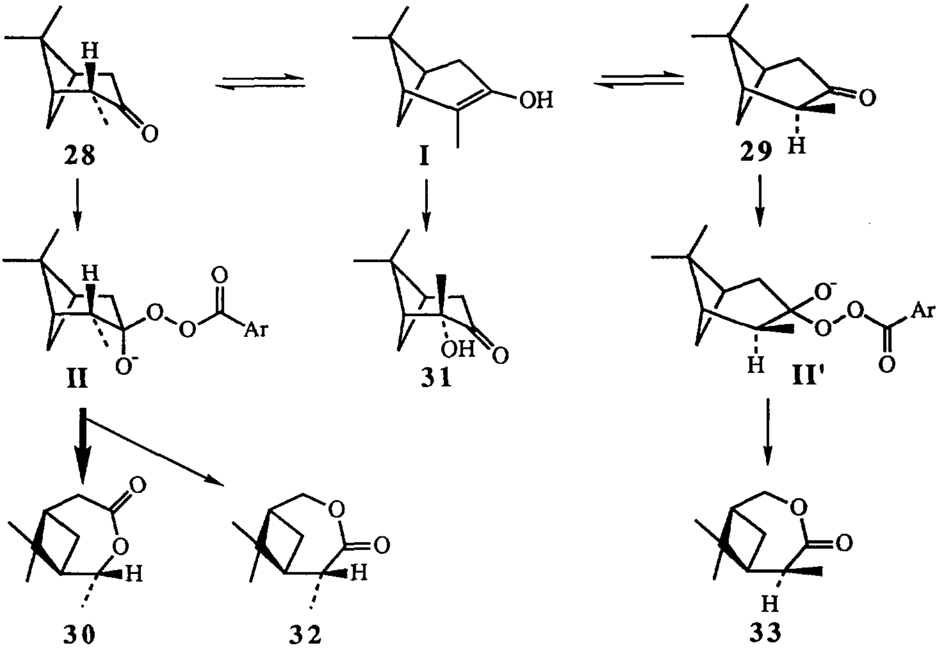


25 26 27

Treatment of the 4:1 equilibrium mixture pinocamphone (28) and isopinocamphone (29)[20] with 3-chloroperbenzoic acid using *Fringuelli's* aqueous conditions[13] yielded the expected lactone (30) as the major product (27%), readily identified by its ^{1}H- and ^{13}C-NMR spectra and mass spectrum. There was also about 5% of the hydroxy ketone (31) whose spectra were identical with those described in the literature[21]. In contrast, when (29) (>95% pure) was treated with peracid under identical conditions, the only major product isolated was (31) (27%), with *ca.* 35% of unchanged starting material. Two minor peaks in the gas chromatogram were identified as the two isomeric lactones (32) and (33) which could not be completely separated, but which amounted together to less than 10% of the total product mixture.

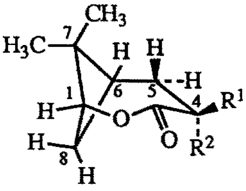
These results may be rationalized using the *Criegee* intermediate[22] on the assumption that the direct precursor of (31) is the tetrasubstituted enol (I), with the peracid acting as an electrophilic oxidizing reagent[23] (scheme 4). It follows that, under the reaction conditions, there is no equilibration between (28) and (29), and that the formation of (31) from (29), rather than from (28), indicates that the tautomerism of (29) to (I) is more rapid than the corresponding tautomerism of (28).[24] In support of this hypothesis are the observed lower thermodynamic stability of (29) compared with (28) and the close structural resemblance of (29) and (I). Another important contributing factor may involve the relative rates of 1,2-addition of the peracid to the carbonyl group in (28) and (29). Thus, the chair-like conformation of (28)[25] presumably favours nucleophilic attack from the sterically less hindered equatorial face of the molecule and subsequent rearrangement of the resulting intermediate (II) then leads to (30) and minor amounts of (32). In contrast, the flattened boat-like conformation of (29) disfavours 1,2-addition by imposing a sterically unfavourable pseudoaxial approach of the nucleophile. Apparently, the resulting intermediate (II') preferentially rearranges to (33) rather than to the undetected C-2 epimer of (30); the reason for this migratory selectivity is unclear.



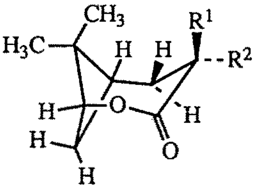
SCHEME 4

The structures of the lactones are supported by the NMR spectra. The ^{1}H-NMR spectra are given in table 1, and for each lactone there are two conformations (A and B) which can be considered. In the major lactone (7) from nopinone, the signals of the methylene group C-5 are at 1.88 and 1.95 ppm (assignments confirmed by ^{13}C-^{1}H-correlation spectra), but only the proton at 1.88 ppm is coupled with the bridgehead proton at 2.28 ppm, and so it must be the *trans*-proton in conformation (7A). Models show that for the *cis*-proton to have a low dihedral angle with the bridgehead proton the conformation would have to be (B); this would involve severe steric interaction between the *cis*-methyl group and the lactone ring. MM2 calculations also support conformation (7A) (44.6 kcal.) over conformation (7B) (47.6 kcal).[26] Calculation of the coupling constants shows that the *cis*-proton on C-4 should be (in Hz) 6.1 + 1.4 + $J_{geminal}$ in conformation (A), and 10.5 + 7.7 + $J_{geminal}$ for conformation (B). The measured values are 5.5 + 2 + 16 for the proton centred on 2.83 ppm, and 11 + 9 + 16 for the one centred on 2.94 ppm, so we attribute the former values to the *cis*-proton at C-4, and the latter to the *trans*-proton.

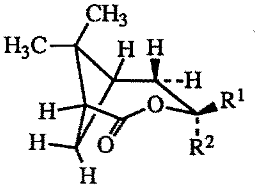
Similar reasoning was used to attribute the signals of the other lactones. Thus the bridgehead proton at C-6 in the *cis*-methyl analogue (16) of lactone (7) at 2.27 ppm is coupled (J = 7 Hz) with the proton at 2.04 ppm (in this case there is also a weak coupling with the proton at 1.72 ppm). There is, however, no doubt that the *cis*-proton at C-5 is at 1.72 ppm, because of the strong nuclear *Overhauser* effect (nOe) observed between it and the *cis*-methyl group (0.84 ppm). A nOe was also observed between the proton (2.96 ppm) next to the carbonyl group and the characteristic pinane doublet of the *cis*-proton in the cyclobutane ring at C-8 (2.17 ppm). The conformation of lactone (**16**) is, therefore very similar to that of (**7**), with the carbonyl group directed up towards the *gem*-dimethyl group and causing a marked shielding of the *cis*-methyl group and the *cis*-proton on C-5.



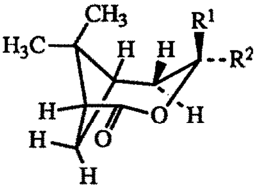
(**7A**) $R^1=R^2=H$
(**16A**) $R^1=Me$, $R^2=H$
(**18A**) $R^1=H$, $R^2=Me$



(**7B**) $R^1=R^2=H$
(**16B**) $R^1=Me$, $R^2=H$
(**18B**) $R^1=H$, $R^2=Me$



(**8A**) $R^1=R^2=H$
(**15A**) $R^1=Me$, $R^2=H$
(**17A**) $R^1=H$, $R^2=Me$



(**8B**) $R^1=R^2=H$
(**15B**) $R^1=Me$, $R^2=H$
(**17B**) $R^1=H$, $R^2=Me$

Table 1: ^{1}H-NMR signals of lactones (**7**), (**8**), (**15**), (**16**), (**17**), (**18**)

Proton on:	(**7**)	(**16**)	(**18**)	(**8**)	(**15**)	(**17**)
C-1	4.33[1] (dd)	4.33 (dd)	4.32 (dd)	2.94[3]	2.94	3.02
C-4 (R^1)	2.83[2]	1.42 (d)	3.22	4.32[4]	1.42 (d)	4.92
C-4 (R^2)	2.94[2]	2.96	1.44 (d)	4.70[4]	4.97	1.48 (d)
C-5 (*cis*)	1.95	1.72	2.20	2.49	2.15	2.32
C-5 (*trans*)	1.88	2.04	1.63	1.87	1.98	1.96
C-6	2.28	2.27	2.3	2.26	2.19	2.29
C-8 (*cis*)	2.11 (d)	2.17 (d)	1.70 (d)	2.31 (d)	2.29 (d)	1.82 (d)
C-8 (*trans*)	2.65	2.62	2.71	2.45	2.44	2.49
Me (*cis*)	0.89 (s)	0.84 (s)	1.01 (s)	1.04 (s)	1.04 (s)	1.20 (s)
Me (*trans*)	1.30 (s)	1.28 (s)	1.29 (s)	1.39 (s)	1.37 (s)	1.37 (s)

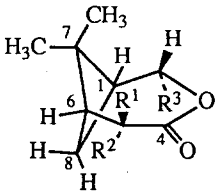
[1] shifted to 4.20 ppm in CCl_4
[2] shifted to 2.74 and 2.79 in CCl_4
[3] shifted to 2.83 in CCl_4
[4] shifted to 4.21 and 4.63 in CCl_4

The conformation of the minor lactone (**8**) from nopinone, and the major lactone (**15**) from *cis*-methylnopinone are also clearly of the (A) type, as shown by the chemical shifts of the *cis*-proton at C-8. The particularly high deshielding of the *cis*-proton on C-5 arises because it is directly behind the carbonyl group. This is indeed the *cis*-proton, because in compound (**15**) there is a nOe between this proton and the *cis*-methyl group, but also between the proton on C-4 (*trans*) at 4.97 ppm and the adjacent C-5 (*trans*) proton at 1.98 ppm.

The assignments for the mixture of the two lactones (17) and (18) are based on the more reliable data of (15) and (16), but the clear doublets of the *cis*-proton of the cyclobutane ring (C-8) are consistent with the alternative conformation (B) for these compounds, as is the downfield shift of the *cis*-methyl group.

The mass spectrum of (17) was similar to that of (15) but without the fragment at m/z 111, while the mass spectrum of (18) resembled that of (16); these similarities support the gross structure of the lactones.

In the ^{1}H-NMR spectrum of the racemic lactone (26) derived from isonopinone (25) (table 2), there is a long-range coupling between the C-5-(*cis*)- and the C-8-(*trans*)-proton, and between the C-5-(*trans*)-proton and the *trans*-methyl group, thus supporting the configurations assigned to the C-5 protons. The major lactone (30) from the pinocamphone (28) reaction is similar, the *trans* orientation of the additional methyl group being confirmed by the observation of a nOe between it and the *cis*-proton at C-8. Despite the fact that the lactones (32) and (33) were only obtained as a mixture, the former was preponderant to the extent that it was possible to observe a nOe between the *cis*-(C-9)-methyl group and the quartet at 2.83 ppm, which we attributed to the proton on C-5 carrying the extra methyl group (table 2), and thus supporting the conclusion that this extra methyl group was *trans* to the *gem*-dimethyl bridge.



(26) R^1=R^2=R^3=H
(30) R^1=R^2=H, R^3=Me
(32) R^1=R^3=H, R^2=Me
(33) R^1=Me, R^2=R^3=H

Table 2: ^{1}H-NMR signals of lactones (26), (30), (32), (33)

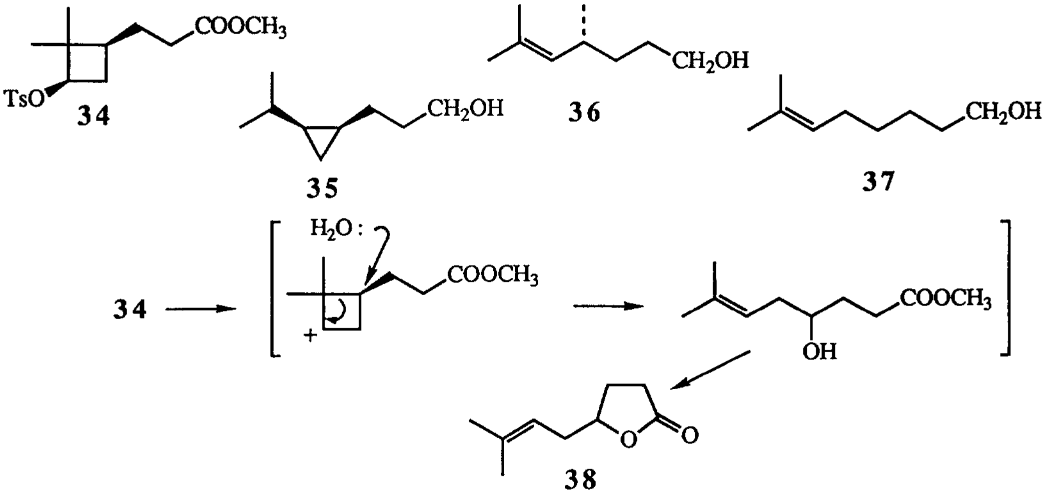
Proton on:	(26)	(30)	(32)	(33)*
C-1	2.28	2.10	2.24	
C-2	4.40	4.70	4.33, 4.37	
C-5	2.89	2.82-2.86	2.83 (q+)	2.76 (dq)
C-6	1.87	1.95	1.82	1.99
C-8(*cis*)	1.58 (d)	1.61 (d)	1.61 (d)	
C-8 (*trans*)	2.60	2.53	2.51	
Me (*cis*)	0.95 (s)	0.97 (s)	0.94 (s)	0.98 (s)
Me (*trans*)	1.32 (s)	1.30 (s)	1.33 (s)	1.34
R^{1,2,3}(Me)	–	1.32 (d)	1.32 (d)	

*observed as impurity in (32)

The ^{13}C-NMR spectra of the lactones we have described are shown in table 3. Correlation spectra (^{1}H-^{13}C) were measured for all lactones except those in the mixture (**18** and **25**).

Table 3: ^{13}C-NMR spectra of oxabicyclo[4.1.1]octanones (n.v. = not visible, * = interchangable)

Carbon	**7**	**16**	**18**	**8**	**15**	**17**	**26**	**30**	**32**	**33**
1	84.0	84.0	83.8	53.3	53.5	54.0	43.8	48.8	44.7	44.7*
2	–	–	–	174.4	174.2	177.5	71,5	78.2	40.5	43.4*
3	174.7	177.2	178.4	–	–	–	–	–	178.1	178.3
4	34.0	38.3	39.8	66.2	73.5	75.3	174.5	173.8	–	–
5	22.1	32.1	32.8	27.5	35.2	37.5	36.7	37.3	71.4	71.4
6	41.2	41.1	42.3	40.8	40.8	42.1	37.1	37.4	43.6	43.5*
7	43.1	42.9	n.v.	40.4	40.3	n.v.	38.7	38.4	38.6	39.2
8	26.4	26.8	30.8	19.7	20.4	27.5	25.4	23.3	23.2	26.3
Me*cis*	18.4	18.3	23.2	20.7	20.6	25.0	19.8	19.5	19.5	20.8
Me*trans*	27.3	27.2	27.8	28.4	28.5	30.3	28.5	28.9	29.0	29.8
Me(CH)	–	17.6	19.1	–	22.4	17.6	–	21.2	18.8	18.5



SCHEME 5

Although the *Baeyer-Villiger* reactions described here render dimethylcyclobutanes such as (10) readily available in moderate yield, access to the natural product (3) is restricted because of the difficulty of economically removing the oxygen function from the cyclobutane ring. Thus reduction of the *p*-toluenesulphonate (34) with lithium aluminium hydride led to the rearranged alcohols (35, 36, 37) in accord with a similar reduction of a cyclobutyl tosylate described by *Karpf* and *Djerassi*.[27] *Conia* has reported the elimination of unsubstituted cyclobutyl tosylate using potassium *t*-butoxide,[28] but in our case, the tosylate (34) yielded only a small amount of the lactone (38), presumably *via* a mechanism (scheme 5) analogous to one again described by *Karpf* and *Djerassi*.[27] *) The only syntheses of junionone (3) do not start from α-pinene[30] and our own conversion of caryophyllene to (3) encountered the same problem of cyclobutanol-cyclobutane reduction.[3]

If satisfactory yields could be obtained, the diester (23) we report would constitute a relay for the synthesis of the citrus mealybug pheromone (4).

EXPERIMENTAL

General Methods

M.p.s. were measured on a *Büchi* type 530 melting point apparatus. NMR spectra were measured in $CDCl_3$ unless otherwise stated, at 360 MHz for ^{1}H-NMR spectra and 90 MHz for ^{13}C-NMR spectra, using the *Bruker* Software Library DISN 89. Attributions were generally confirmed by 2D COSY and ^{1}H-^{13}C correlation spectra. Mass spectra were obtained using a *Finnigan* quadrupole spectrometer coupled with a gas chromatograph containing a 30m glass capillary column coated with either SPB-1 or Supelcowax stationary phase. Exact mass measurements were made with a VG 70SE mass spectrometer with 2000 Da resolution. Results are given in *m/z* (rel. abundance). Infra-red data were measured with a *Hewlett-Packard* model GC-FTIR 5965B spectrometer. Column ("flash") chromatography was carried out on *Merck* silica gel 60 (230–400 mesh). $[\alpha]_D$ were measured in $CHCl_3$ at 20° on a *Perkin-Elmer* model 241 polarimeter.

Elemental analyses were carried out by Dr. *H. Eder*, Service de Microchimie, University of Geneva.

(1R,6S)-7,7-Dimethyl-2-oxabicyclo[4.1.1]octan-3-one (7). (*cf.* [8,10]) A. Using unpurified chloroform and no acid catalyst. (+)-Nopinone ((6), 5g, 36.2 mmol) and 3-chloroperbenzoic acid (85%, 8.33g, 40.6 mmol) in chloroform (120ml) were stirred for 4 weeks in the dark. Gas chromatography showed the presence of 68% unchanged nopinone (retention time 2.89 min on the Supelcowax column) followed by 24% of the title lactone (retention time 9.35 min) and 6.5% of another substance (retention time 10.74 min). Column chromatography enabled the nopinone to be recovered, followed by the title lactone, $[\alpha]_D$ −99.7°

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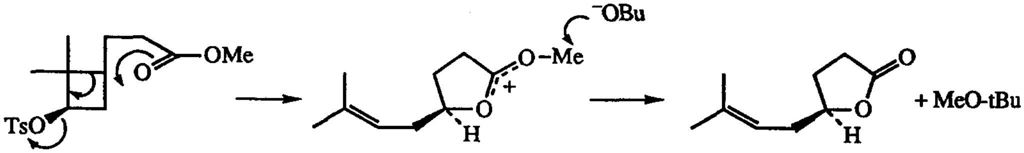
*) A referee has pointed out that the lactonization of 34 could result from acetoxy participation leading to an acetoxonium ion intermediate (cf.[29]) neutralized by *t*-butoxy anion (38 could have *R* configuration). This mechanism does not involve water.



(c=2%); FTIR: 1757 cm^{-1} (C=O). MS: 154 ($M^{+\cdot}$, trace), 125 (2), 111 (28), 83 (50), 82 (9), 72 (10), 69 (100), 55 (73), 43 (11), 41 (20). Found: C 69.7, H 8.9% $C_9H_{14}O_2$ requires C 70.1, H 9.1%. The other substance of retention time 10.75 min was eluted after lactone (7) (200 mg) and was identified as **ethyl (1R,3R)-3-(2-hydroxyethyl)-2,2-dimethyl-1-cyclobutanecarboxylate (9).** Purified by preparative GC on Carbowax, this substance had $[\alpha]_D$ +3° (c=3%). ^{1}H-NMR: 0.94, 1.20 (each 3H, s); 1.25 (3H, t), 1.51 and 1.64 (each 1H, mult., CH_2CH_2OH); 1.84–1.90 (1H, mult) and 1.96–2.08 (3H, mult., cyclobutane CH_2CH); 2.68 (1H, dxd, $COCHCH_2$); 3.51–3.61 (2H, mult, CH_2OH); 4.05–4.19 (2H, mult., OCH_2). ^{13}C-NMR: q at 14.5, 17.6, 30.3; t at 24.6 (cyclobutane CH_2), 33.5, 60.0, 61.2; d at 39.1, 46.3; s at 42.7, 173.2. MS: 200 ($M^{+\cdot}$, 1), 185 (–Me, 3), 156 (22), 128 (80), 101 (83), 100 (85), 83 (85), 82 (85), 73 (50), 69 (100), 67 (52), 57 (68), 55 (92), 41 (97). Found: C 65.8, H 10.0% $C_{11}H_{20}O_3$ requires C 66.0, H 10.1%.

B. Using commercial dichloromethane without purification and acid catalysis. (+)-Nopinone ((6), 5g, 36.2 mmol) in dichloromethane (120ml) was treated with 3-chloroperbenzoic acid (85%, 16g, 78.8 mmol) and trifluoroacetic acid (4g, 35 mmol) over 10 days. The solution was filtered, then washed with aqueous sodium sulphite, dried and concentrated. The residue was taken up in ether, washed with sodium bicarbonate solution, dried and concentrated to yield 4.33g of material which was chromatographed on silica gel. Elution with cyclohexane/ether (4:1) gave in order 3-chlorobenzoic anhydride (50 mg, 0.1 mmol), nopinone (1.24 g, 9 mmol), the title product (3.04g, 37% yield or 72% conversion) and a trace of **ethyl (1'S,3'R)-3-(2'2'-dimethyl-3'-hydroxycyclobutyl)propionate** (10), identified by the similarity of the NMR spectrum with that of the methyl ester (described below). ^{1}H-NMR of (10): 0.96 and 1.07 (each 3H, s); 1.26 (3H, t); 2.21 (2H, t); 3.71 (1H, t); 4.12 (2H, q). MS: 200 ($M^{+\cdot}$, 0), 182 (–H_2O, trace), 156 (20), 95 (15), 88 (15), 85 (20), 83 (20), 82 (100), 72 (40), 69 (30), 57 (23), 55 (27), 43 (23), 41 (25).

C. Using chloroform purified by washing with water, drying, distilling, and passing through a column of alumina (activity 1) immediately before use. A mixture of (+)-nopinone ((6), 20g, 145 mmol), 3-chloroperbenzoic acid (85%, 33g, 162 mmol) in purified chloroform (300ml) was stirred in the dark for 4 weeks. Gas chromatography showed the presence of 30% of unchanged nopinone, 60% of the (main) title lactone, and 9% of **(1R,6R)-7,7-dimethyl-3-oxabicyclo[4.1.1]octan-2-one** (8). Flash chromatography yielded fractions containing a majority of this substance, from which it could be purified by preparative gas chromatography (Carbowax). The anlytical sample still contained 1% of the lactone (7). $[\alpha]_D$ –7.1°, (c=2.8%). FTIR: 1756 cm^{-1} (C=O). MS: 154 ($M^{+\cdot}$, 0), 139 (–Me, 3), 111 (18), 83 (100), 82 (35), 67 (32), 54 (27), 41 (18). Direct introduction into the source of the high resolution mass spectrometer revealed an ion at *m/z* 155.08873 ($M+1^+$ calc. for $C_9H_{15}O_2$ 155.10720), and the ion at *m/z* 111.05214 agreed with $C_6H_7O_2$ (calc. 111.04460). Found: C 69.3, H 9.10%; $C_9H_{14}O_2$ requires C 70.1, H 9.1%.

Methyl (1'S,3'R)-3-(2',2'-dimethyl-3'-hydroxycyclobutyl)propionate (11). A solution of the lactone (7) in methanol was heated at reflux for 16h. After concentration the title product was obtained pratically quantitatively in over 98% purity. $[\alpha]_D \pm 0°$. ^{1}H-NMR: 0.95, 1.07, 3.67 (each 3H, s); 1.41 (1H, mult., cyclobutane HCH_{trans} C-4'); 1.57 and 1.70 (each 1H, mult., H_2C-3); 2.21 (2H, t, H_2C-2); 2.32 (1H, mult., cyclobutane HCH_{cis} C-4'); 3.71 (1H, dxd, J=7 and 7 Hz, cyclobutane HC-3'). ^{13}C-NMR: q at 15.1, 28.2, 51.4; t at 25.4, 32.5, 33.8; d at 36.6, 71.5; s at 43.8, 174.2. MS: 186 ($M^{+\cdot}$, 0), 142 (–C_2H_4O, 22), 82

(100), 74 (39), 72 (48), 69 (43), 57 (32), 55 (22), 43 (31), 41 (29). Found: C 64.3, H 9.8% $C_{10}H_{18}O_3$ requires C 64.5, H 9.7%.

The **p-toluenesulphonate (34)** was made following Kabalka et al.[31] The alcohol ((**11**), 1.86g, 10 mmol) in chloroform (10ml) was cooled to 0°, then pyridine (1.62ml, 20 mmol) and *p*-toluenesulphonyl chloride (2.85g, 15 mmol) were added slowly while stirring. After stirring for 3 days, ether was added and the mixture was washed with hydrochloric acid (10%) and water. The crude material obtained after the usual workup was purified by flash chromatography, and gave 2.77g (80%) of the liquid toluenesulphonate. ^{1}H-NMR: 1.00 (6H, s); 2.45 and 3.64 (each 3H, s); 2.17 (2H, t) superimposed on 2.19 (1H, mult.); 7.33 and 7.77 (each 2H, d). Found: C 60.1, H 7.1, S 9.5% $C_{17}H_{24}O_5S$ requires: C 60.0, H 7.1, S 9.4%.

(1'S,3'R)-3-(2',2'-Dimethyl-3'-hydroxycyclobutyl)propionic acid (12) (*cf.* [13]). (+)-Nopinone ((**6**), 15g, 108 mmol) was stirred in demineralized water (270ml), and 3-chloroperbenzoic acid (50% with 3-chlorobenzoic acid, 50g, 145 mmol) was added. The mixture was heated to 80° for 3h, then allowed to cool to ambient temperature overnight. The crystalline 3-chlorobenzoic acid was filtered off, and the product extracted from the filtrate with ether. The ethereal solution was washed with sodium bicarbonate solution (3 times), then with water, and dried and concentrated to give 4.3g of a mixture consisting of the lactone (**7**) (68%) and unchanged nopinone (32%). The acids were precipitated from the bicarbonate solution with sulphuric acid (20%) and the precipitate filtered off. By extraction of this precipitate with water at 50°, much of the title acid was separated from the chlorobenzoic acid (crystalline at this temperature), and extraction of the filtrate from this treatment with ether yielded 4.2g of acids, mostly the title product still contaminated with chlorobenzoic acid. From the aqueous filtrate of the first precipitation, a further 4.5g of material could be extracted. Two crystallizations of the combined extracts gave 0.5g of the pure title acid (**12**), m.p. 65–66°. ^{1}H-NMR: 0.96, 1.07 (each 3H, s); 1.42 coupled with 2.33 (both mult., cyclobutane CH_2); 2.25 (2H, t, CH_2COOH); 3.73 (1H, mult., CHOH). ^{13}C-NMR: q at 14.9, 28.1; t at 25.1, 32.5, 34.2 (cyclobutane CH_2); d at 36.6, 71.9; s at 43.9, 179.1. MS: 172 ($M^{+\cdot}$, 0), 154 ($-H_2O$, 5), 139 ($-H_2O$–Me, 3), 128 ($-CO_2$, 62), 85 (45), 82 (47), 72 (50), 69 (100), 57 (37), 55 (40), 41 (58). Found: C 62.7, H 9.4% $C_9H_{16}O_3$ requires: C 62.8, H 9.4%.

Reaction of 3-chloroperbenzoic acid with methylnopinone. Method A. A solution of methylnopinone ((**13**), containing *ca.* 15% (**14**), 10g, 65.8 mmol) and 3-chloroperbenzoic acid (85%, 16g, 78.8 mmol) in dichloromethane (100ml, purified by passage over aluminium oxide) was allowed to stand for 5 weeks in the dark at room temperature. During this time, 3-chlorobenzoic acid precipitated. The excess peroxides were removed by washing with sodium sulphite solution, then the mixture was washed with saturated aqueous sodium bicarbonate and water. Drying and concentration yielded 4g of material which was purified by flash chromatography. There was obtained, in order, recovered methylnopinone (0.85g), then a mixture (0.55g) containing 61% of *cis*-4,7,7-trimethyl-2-oxabicyclo[4.1.1]octan-3-one (**16**), 12% of *trans*-4,7,7-trimethyl-2-oxabibyclo[4.1.1]octan-3-one (**18**), 14% of *trans*-4,7,7-trimethyl-3-oxabicyclo[4.1.1]octan-2-one (**17**), and 8% of *trans*-3,6,6-trimethyl-3-hydroxynorpinan-2-one (**19**). Finally, *cis*-4,7,7-trimethyl-3-oxabicyclo[4.1.1.]octan-2-one (**15**) (2.58g) was eluted. This crystallized, and was sublimed at 0.1mm, m.p. 81°, $[\alpha]_D$ −12.6° (c=3%). MS: 168 ($M^{+\cdot}$, 0), 153 (–Me, 1), 111 (40), 96 (15), 83 (100), 82 (18), 81 (32), 69

(27), 68 (24), 67 (25), 55 (65), 43 (19), 41 (25). The high resolution MS showed a small fragment $M^{+\cdot}$ at 168.11476, calc. for $C_{10}H_{16}O_2$ 168.11502. Found: C 70.9, H 9.5% $C_{10}H_{16}O_2$ requires C 71.4, H 9.6%.

The secondary products from this reaction visible on a Supelcowax column were **(19)**, **(17)**, **(18)**, **(16)**, **(15)**. There was sufficient difference in retention times on Carbowax for all compounds except **(17)** and **(18)** to be separated preparatively. The properties of the secondary products are: for the hydroxyketone **(19)**: ^{1}H-NMR: 0.80, 1.37, 1.46 (each 3H, s); 2.27 (1H, d, J=11 Hz, HC-7); 2.51 (1H, mult., HC-4); 2.67 (1H, dxd, J=4 and 4 Hz, HC-1). ^{13}C-NMR: q at 22.8, 25.4, 26.5; t at 26.0 (C-7), 37.8 (C-4); d at 40.6 (C-5), 57.1 (C-1); s at 43.7 (C-6), 72.3 (C-3), 213.3 (C-2). MS: 168 ($M^{+\cdot}$, 10), 107 (10), 95 (60), 85 (85), 84 (90), 83 (25), 82 (28), 71 (39), 69 (27), 67 (42), 43 (100). $M^{+\cdot}$ found: 168.11520, calc. for $C_{10}H_{16}O_2$ 168.11502. The lactone **(16)** had MS: 168 ($M^{+\cdot}$, trace), 140 (1), 125 (4), 124 (5), 97 (27), 70 (17), 69 (100), 67 (15), 55 (28), 43 (15), 41 (57). Found: C 70.7, H 9.6% $C_{10}H_{16}O_2$ requires C 71.4, H 9.6%. For the lactones **(17)** and **(18)**, the NMR spectra given in the theoretical part were attributed from a fraction containing **(17)**/**(18)**=1:2. The MS of **(17)** was: 168 ($M^{+\cdot}$, 0), 153 (–Me, 3), 127 (4), 96 (30), 83 (100), 82 (13), 81 (42), 69 (21), 68 (24), 67 (28), 55 (66), 41 (24). The MS of **(18)** was: 168 ($M^{+\cdot}$, trace), 140 (1), 125 (12), 98 (16), 97 (45), 70 (16), 69 (100), 67 (13), 55 (28), 43 (15), 41 (40).

Method B. A solution of methylnopinone (**(13)**, containing *ca.* 15% **(14)**, 20g, 131.6 mmol), 3-chloroperbenzoic acid (85%, 32g, 157.7 mmol) in chloroform (unpurified, 250ml) was kept in the dark. After 10 days 3-chloroperbenzoic acid (6.5g, 32 mmol) was added, and a further quantity (5g, 24.6 mmol) 7 days later. After 9 more days, the precipitated benzoic acid was filtered off, and the solution washed with sodium hydroxide. The residue (15.6g) was flash chromatographed on silica gel. There was obtained in order, ethyl (1R,3S)-2,2-dimethyl-3-acetoxymethyl-1-cyclobutanecarboxylate **(23)**, 3g, identical with that prepared from the lactone **(15)**, fractions containing mostly impure lactone **(16)** (2.8g), then a mixture of ethyl (1'R,2R,3'R)-3-(3'-hydroxy-2',2'-dimethylcyclobutyl)-2-methylpropionate **(20)**. The two latter products were identified by MS and co-injection with authentic samples prepared as in the following experiments.

Ethyl (1'S,2R,3'R)-3-(3'-hydroxy-2',2'-dimethylcyclobutyl)-2-methylpropionate (20) was prepared from the methyllactone (**(16)**, 0.2g, 1.2 mmol) as described for the ester **(21)**. The product was purified for analysis by preparative gas chromatography on Carbowax. ^{1}H-NMR: 0.95, 1.06 (each 3H, s); 1.13 (3H, d, J=7 Hz); 1.26 (3H, t); 2.29 (1H, mult, cyclobutane H_{cis}C-4) superimposed on 2.33 (1H, mult, HC-2); 3.70 (1H, dxd, CHOH), 4.13 (2H, q). ^{13}C-NMR: q at 14.3, 14.9, 17.6, 28.1; t at 34.2, 34.9, 60.2; d at 35.0, 38.5, 72.2; s at 44.1, 176.9. MS: 214 ($M^{+\cdot}$, 0), 171 (10), 170 (25), 151 (5), 143 (6), 123 (10), 115 (29), 102 (100), 97 (30), 96 (85), 81 (28), 74 (50), 72 (60), 69 (82), 57 (36), 55 (43), 43 (41), 41 (57). Found: C 67.4, H 10.1%. $C_{12}H_{22}O_3$ requires C 67.2, H 10.3%.

Ethyl (1R,2'R,3R)-3-(2'-hydroxypropyl)-2.2-dimethyl-1-cyclobutanecarboxylate (21). A solution of the methyllactone (**(15)**, 11g, 6.5 mmol) and *p*-toluenesulphonic acid (0.1g) in ethanol (100ml) was heated at reflux for 48h. The ethanol was concentrated and the residue taken up in ether. The ethereal solution was washed ($NaHCO_3$, water) and concentrated to yield pratically pure title product (10.7g). $[\alpha]_D$ – 5.7° (c=3%). ^{1}H-NMR: 0.93, 1.22 (each 3H, s); 1.18 (3H, d, J=7 Hz); 1.26 (3H, t); 2.69 (1H, dxd, J=7 and 8 Hz); 3.78 (1H, 6 lines, CHOH); 4.13 (2H, mult., $COOCH_2$). ^{13}C-NMR: q 14.5, 17.6, 23.8, 30.3; t 25.4, 39.9, 59.9; d 39.3, 46.6, 67.1; s 42.9, 173.0. MS: 214 ($M^{+\cdot}$, 0), 196 (7), 171 (10), 170 (25), 102 (100), 97 (29), 96 (66), 95 (55), 74 (45), 69 (70), 55 (32), 43 (41). Found: C 66.6, H 10.1% $C_{12}H_{22}O_3$ requires C 67.2, H 10.3%.

Ethyl (1R,3R)-2,2-dimethyl-3-(2'-oxopropyl)-1-cyclobutanecarboxylate (22). A mixture of sodium dichromate dihydrate (185g, 621 mmol) and sulphuric acid (conc., 280g, 2.7 moles) was prepared in 600ml water. The alcohol ((21), 10g, 46.7 mmol) in ether (30ml) was added over 30 min, maintaining the temperature below 26°. After a futher 30 min, the product was isolated in ether, and after the usual washings and concentration, there was obtained 2.2g of nearly pure title product, $[\alpha]_D$ +1.8° (c=3%). ^{1}H-NMR: 0.90, 1.24, 2.13 (each 3H, s); 1.25 (3H, t); 2.74 (1H, dxd, J=7 and 8 Hz, cyclobutane HC-1); 4.12 (2H, mult. $COOCH_2$). ^{13}C-NMR: q at 14.5 17.8, 30.2, 30.3; t at 24.7 (cyclobutane), 44.9, 60.0; d at 37.5, 46.5; s at 42.7, 172.9, 207.9. MS: 212 ($M^{+\cdot}$, 1) 166 ($-C_2H_5OH$, 5), 129 (34), 128 (50), 123 (22), 112 (20), 101 (41), 100 (30), 83 (37), 82 (22), 69 (38), 55 (34), 43 (100), 41 (22). This material was used without further purification.

Ethyl (1R,3S)-3-acetoxymethyl-2,2-dimethyl-1-cyclobutanecarboxylate (23). The ketone ((22), 2.1g, 10 mmol) and 3-chloroperbenzoic acid (85%, 3.6g, 17.7 mmol) were stirred in chloroform (50ml) for 2 days at room temperature in the dark, then shaken with a solution of sodium sulphite (10%), sodium bicarbonate (3 times) and water. Drying and concentration gave 1.93g of pratically pure title material. ^{1}H-NMR: 0.99, 1.25, 2.04 (each 3H, s); 1.26 (3H, t, J=7 Hz); 1.97–2.04 (2H); 2.27 (1H, mult., HC-3); 2.72 (1H, dxd, J=8 and 9 Hz, HC-1); 3.98 (1H, dxd, J=8 and 11 Hz); 4.10–4.20 (3H, mult). ^{13}C-NMR: q at 14.5, 17.4, 20.9, 30.6; t at 21.3, 60.1, 64.7 (CH_2OAc); d at 40.4 (C-3), 45.8 (C-1); s at 42.0, 170.9, 172.7. MS: 228 ($M^{+\cdot}$, 0), 183 ($-C_2H_5O$, trace), 168 ($-CH_3CO_2H$, 1), 141 (15), 128 (29), 100 (38), 95 (42), 94 (29), 83 (34), 69 (27), 68 (100), 67 (38), 55 (34), 43 (75). Found: C 62.8, H 8.8% $C_{12}H_{20}O_4$ requires C 63.1, H 8.8%.

(±)-7,7-Dimethyl-3-oxabicyclo[4.1.1]octan-4-one (26). Isonopinone ((25),[18] 3g, 21.7 mmol) and 3-chloroperbenzoic acid (85%, 9g, 44.3 mmol) in chloroform (purified by passage through a column of alumina, 100ml) were allowed to stand in the dark for two weeks. Concentration of the filtrate yielded 3.84g of material, from which the title product was recovered by preparative gas chromatography on Carbowax. MS: 154 ($M^{+\cdot}$, 0), 139 (–Me, 3), 113 (8), 95 (13), 94 (16), 69 (100), 68 (40), 67 (32), 41 (90), 39 (26). After standing in air for some weeks, crystals of the following substance were obtained.

(±)-Cis-3-Hydroxymethyl-2,2-dimethyl-1-cyclobutaneacetic acid (27). A solution of the preceding lactone was chromatographed on silica gel. On concentration of the eluate in air, crystals formed, which, after recrystallization from hexane were the title product, m.p. 81°. ^{1}H-NMR: 0.93, 1.10 (each 3H, s); 1.28 (1H, mult.) and 2.06 (1H, mult., CH_2 of cyclobutane); 2.11–2.35 (4H); 3.97 (2H, mult., CH_2OH). ^{13}C-NMR: q at 16.6, 30.3; t at 26.6 (C-4), 35.4 (CH_2CO), 64.7 (CH_2O); d at 38.7 (C-1), 41.0 (C-3); s at 39.9, 172.9. MS: 172 ($M^{+\cdot}$, 0), 154 ($M-H_2O$, 4), 125 (6), 111 (45), 85 (20), 83 (51), 70 (16), 69 (100), 55 (90), 43 (22), 41 (48), 39 (22). Found: C 62.7, H 9.2% $C_9H_{16}O_3$ requires C 62.8, H 9.4%.

(+)-(1R,2R)-2,7,7-Trimethyl-3-oxabicyclo[4.1.1]octan-4-one (30). A suspension of (–)-pinocamphone (the equilibrium mixture of (**28**) and (**29**) (8:2) prepared from (–)-α-pinene,[20] 75g, 490mmol) and 3-chloroperbenzoic acid (55%, 158g, 504mmol) in water (500ml) was stirred at 80° for 3h.[13] The precipitate was filtered off and washed with a small amount of water, followed by ether (50ml). The aqueous phase was extracted with ether and the combined ethereal phases washed with saturated aqueous sodium bicarbonate and water. After checking that peroxides were absent, the organic phases were dried and concentrated to yield 33g of material. A further 7g was obtained from a second extraction of the original precipitate. After flash chromatography, 9.9g of the title lactone was obtained (still containing *ca.* 5% of 2-hydroxypinocamphone (see below), and 1.9g of nearly pure hydroxypinocamphone (**31**). The pure lactone was obtained by preparative gas chromatography on Carbowax. $[\alpha]_D$ +25.4° (c=3%). MS: 168 ($M^{+\cdot}$, 2), 153 (–Me, 5), 114 (20), 83 (81), 82 (36), 81 (35), 69 (93), 67 (53), 55 (100), 43 (33), 41 (29). Found: C 71.0, H 9.6% $C_{10}H_{16}O_2$ requires C 71.4, H 9.6%. When the experiment was repeated with (+)-pinocamphone (ent-**27**) made from (+)-α-pinene, the product (ent-**30**) had $[\alpha]_D$ –24.0° (c=2.7%).

(+)-(1R,2R)-2-hydroxy-2,6,6-trimethylnorpinan-3-one (31). A suspension of (–)-isopinocamphone ((**29**), 82g, 540mmol, prepared from (–)-α-pinene[20]) and 3-chloroperbenzoic acid (55%, 190g, 606mmol) was stirred in water (600ml) at 80° for 3h, then treated as described in the foregoing experiment. From this was obtained 46g of material directly, with a further 3.5g from a second extraction of the precipitate. Flash chromatography yielded the title product (14.3g, 16%) and 32g (39%) of unreacted isopinocamphone. $[\alpha]_D$ +24.7° (c=2.5%). ^{1}H-NMR: 0.90, 1.38, 1.40 (each H, s); 1.70 (1H, d J=11 Hz); 2.13 (2H, mult.); 2.46 (1H, 5 lines); 2.63 (2H, narrow t); in CCl_4: 0.89, 1.32, 1.38 (each 3H, s), corresponding to values given by *Carlson* and *Pierce*[21] for this isomer. ^{13}C-NMR: q at 22.8, 25.3, 27.3; t at 28.5, 43.0; d at 38.4, 49.8; s at 39.3, 77.2, 214. MS: 168 ($M^{+\cdot}$, 3), 150 ($-H_2O$, 2), 126 (10), 99 (86), 71 (100), 69 (24), 43 (73), 41 (32).When the experiment was carried out with (+)-isopinocamphone (ent-**29**) made from (+)-α-pinene, the product (ent-**31**) had $[\alpha]_D$ –27.5° (c=3%).

(+)-(1'S,2'S)-3-(2'-isopropylcyclopropyl)-1-propanol (35). To a solution of lithium aluminium hydride (0.61g, 16mmol) in dry ether (20ml) was added dropwise at 0° a solution of the toluenesulphonate ((**34**), 1.5g, 46.8mmol) in ether (20ml). After stirring for 2h at 0°, the temperature was allowed to rise to 25°, and the mixture was stirred at 25° for 12h. The mixture was poured onto ice, and extracted in ether. After the usual washings there was obtained 0.43g of material consisting of 73% of the title product. This was purified by preparative gas chromatography (Carbowax) and had $[\alpha]_D$ +35° (c=3%). ^{1}H-NMR: –0.28 (1H, "q", J=5); 0.47, 0.58, 0.71 (each 1H, mult.); 0.99, 1.00 (together 6H, each d, J=7 Hz), Me_2CH); 1.04–1.18 (2H, mult.); 1.60–1.75 (3H, mult.); 3.70 (2H, t, J=6 Hz, CH_2O). MS: 142 ($M^{+\cdot}$, trace), 124 ($-H_2O$, 2), 109 (15), 82 (20), 81 (48), 71 (29), 68 (42), 69 (40), 67 (50), 67 (50), 57 (38), 56 (100), 55 (56), 43 (24), 41 (53). Found: C 75.2, H 13.0% $C_9H_{18}O$ requires C 76.0, H 13.0%. Small amounts of two other substances were characterized by their spectra: **4,6-dimethylhept-5-en-1-ol** (presumably (**R**), (**36**)), 8% of the total, eluted just before (**35**). ^{1}H-NMR: 0.93 (3H, d, J=7); 1.61 and 1.69 (each 3H, d, J=1); 1.2, 1.35 (each 1H, mult.); 1.52 (2H, mult.); 2.33 (1H, mult., HC-4); 3.61 (2H, t, HC-1); 4.88 (1H, d+, J=9 and 1, HC-5). MS: 142 ($M^{+\cdot}$, 7), 109 (12), 96 (10), 83 (100), 81 (15), 70 (10), 67 (22), 56 (12), 55 (58), 43 (13), 41 (21). **7-Methyloct-6-en-1-ol** (**37**) was eluted after the title product, and constituted 13% of the total. ^{1}H-NMR: 1.61, 1.69 (each 3H, s); 1.98 (2H, mult.); 3.64 (2H, t, HC-1); 5.12 (1H, t+, HC-6). MS: 142 ($M^{+\cdot}$, 7), 124 ($-H_2O$, 17), 109 (27), 95 (27), 82 (42), 81 (51), 69 (100), 68 (38), 67 (63), 57 (25), 56 (33), 55 (41). Exact mass, found 142.13242, calc. for $C_9H_{18}O$ 142.1357.

7-Methyloct-6-en-4-olide (**38**). Potassium (0.24g, 6mmol) was added to dry *t*-butanol (20ml). When the reaction was finished, the toluenesulphonate ((**34**), 2g, 6.2mmol) was added rapidly, and the mixture heated at 80° for 16h. After cooling, the mixture was poured into ice water and worked up as usual. There was obtained 0.61g of material, which, after flash chromatography yielded 0.32g of the title product, pratically pure by gas chromatography. ^{1}H-NMR: 1.65 and 1.73 (each 3H, s); 1.90 (1H, mult., HC-3); 2.2–2.6 (5H, mult.); 4.54 (1H, 5 lines, HC-4); 5.13 (1H, t+, HC-6). ^{13}C-NMR: q at 18.0, 25.8; t at 27.2 (C-3), 28.8 (C-2), 33.8 (C-5); d at 80.6 (C-4), 117.5 (C-6); s at 135.9 (C-7), 177.2 (C-1). MS: 154 ($M^{+\cdot}$, 12), 85 (100), 69 (14), 57 (13), 41 (17).

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REFERENCES AND NOTES

1. Tumlinson, J.H.; Hardee, D.D; Gueldner, R.C.; Thompson, A.C.; Hedin, P.A.; Minyard, P. *Science*, **1969**, *166*, 1010-1012.
2. Bohlmann, F.; Zdero, C.; Faass, U. *Chem. Ber.*, **1973**, *106*, 2904-2909.
3. Thomas, A.F.; Ozainne, M. *J. Chem. Soc., Chem. Commun.*, **1973**, 746-750.
4. Bierl-Leonhardt, B.A.; Moreno, D.S; Schwarz, M.; Fargerlund, J.; Plimmer, J.R. *Tetrahedron Lett.*, **1981**, *22*, 389-392.
5. Hobbs, P.D.; Magnus, P.D. *J. Chem. Soc., Chem. Commun.*, **1974**, 856; *J. Amer. Chem. Soc.* **1976**, *98*, 4594-4600.
6. Thomas, A.F.; Bessière, Y. in "The Total Synthesis of Natural Products". J.W. ApSimon ed., vol. 7, p. 328, Wiley, New York, **1988**.
7. Barton, D.H.R.; Ozbalik, N; Schmitt, M. *Tetrahedron Lett.*, **1989**, *30*, 3263-3266.
8. Joulain, D. Thèse de docteur de 3ème cycle, Université Le Mans, October 1971. Joulain, D.; Rouessac, F. *C.R. Hebd. Séances Acad. Sci., Ser. C*, **1971**, *273*, 561-564.
9. Tanaka, J.; Takabe, K.; Kawakita, M.; Ito, M.; Katagiri, T. *Nippon Kagaku Kaishi*, **1978**, 284-287.
10. Preliminary communication: Thomas, A.F.; Rey, F. *Chimia*, **1991**, *45*, 964.
11. Sauers, R.R.; Ubersax, R.W. *J. Org. Chem.*, **1965**, *30*, 3939-3941; Koch, S.S.C.; Chamberlin, A.R. *Synth. Commun.*, **1989**, *19*, 829-833.
12. Ozainne, M. (Firmenich SA, personal communication).
13. Fringuelli, F.; Germain, R.; Pizzo, F.; Savelli, G. *Gazz. Chim. Ital.*, **1989**, *119*, 249.

14. Brougham, P.; Cooper, M.S.; Cummerson, D.A.; Heaney, H.; Thompson, N. *Synthesis*, **1987**, 1015-1017. We thank Mr. Reeve, K.M. of Interox research and development for a generous gift of magnesium monoperoxyphthalate.
15. Bessière-Chrétien, Y.; Meklati, B. *C.R. Hebd. Séances Acad. Sci., Ser. C*, **1969**, *269*, 1315-1318; Bessière-Chrétien, Y.; Grison, C. *Bull. Soc. Chim. Fr.*, **1970**, 3103-3111.
16. Mc Murry, J.E.; Musser, J.H.; Ahmad, M.S.; Blaszczak, L.C. *J. Org. Chem.*, **1975**, *40*, 1829-1832.
17. Trave, R.; Garanti, L. *Gazz. Chim. Ital.*, **1960**, *90*, 597-611.
18. Bessière-Chrétien, Y.; ElGaïed, M.M.; Meklati, B. *Bull. Soc. Chim. Fr.*, **1972**, 1000-1008.
19. Chrétien-Bessière, Y., *C.R. Hebd. Séances Acad. Sci., Ser. C*, **1962**, *255*, 943-944.
20. Zweifel, G.; Brown, H.C. *J. Am. Chem. Soc.*, **1964**, *86*, 393-397; Chrétien-Bessière, Y., Bras, J.-P. *C.R. Hebd. Séances Acad. Sci.*, **1969**, *268*, 2221-2224.
21. a) Carlson, R. G.; Pierce, J.K. *J. Org. Chem.*, **1971**, *36*, 2319-2324, give details of the ^{1}H-NMR spectrum of both this and the *cis*-isomer. b) Solladié-Cavallo, A.; Simon, M.C.; Fischer, J.; Decian, A. *Bull. Soc. Chim. Fr.*, **1989**, 544-548 have published full NMR data and a crystal structure for this compound.
22. Hamley, P.; Holmes, A.B.; Marshall, D.R.; MacKinnon, J.W.M. *J. Chem. Soc., Perkin 1*, **1991**, 1793-1802 discuss the behaviour of other bicyclic systems in the light of similar intermediates.
23. Augustine, R.L., "Oxidation", M. Dekker, New York **1969**, p. 86.
24. It is relevant to note that both these tautomerisms are mechanistically similar in that they involve the transfer of either the C-2 axial or pseudoaxial proton to the carbonyl oxygen atom.
25. The epimeric ketones (**28**) and (**29**) are generally considered to adopt a chair-like conformation for the former and a boat-like conformation for the latter epimer, *cf.* Baretta, A.J.; Jefford, C.W.; Waegell, B. *Bull. Soc. Chim. Fr.*, **1970**, 3899-3908, 3985-3993; Bessière-Chrétien, Y.; Grison, C. *ibid.*, **1971**, 1454-1468; Hirata, T. *Bull. Chem. Soc. Jpn.*, **1972**, *45*, 3458-3464. We have carried out MM2 calculations on (**28**) and (**29**) which confirm the conformation of (**28**) but indicate that in (**29**) C-2, C-3 and C-4 are almost coplanar, with the carbonyl group pointing slightly towards the *gem*-dimethyl group.
26. MM2 Calculations were made with Macromodel 3.0 software (Copyright Columbia University) by Mr. Christian Vial.
27. Karpf, M.; Djerassi, C. *J. Amer. Chem. Soc.*, **1981**, *103*, 302-306.
28. Fadel, A.; Salaün, J.; Conia, J.M. *Tetrahedron*, **1983**, *39*, 1567-1573.
29. Winstein, S.-; Grunwald, E.; Ingraham, L.L. *J. Amer. Chem. Soc.*, **1948**, *70*, 821-828.
30. Gaoni, Y. *Tetrahedron Lett.*, **1982**, *23*, 5220; Gaoni, Y.; Tomažič, A. *J. Org. Chem.*, **1985**, *50*, 2948-2957; Ghosh, A.; Banerjee, U.K.; Venkateswaran, R.V. *Tetrahedron*, **1990**, *46*, 3077-3088. This paper describes syntheses of junionone (**3**), grandisol (**1**) and planococcyl acetate (**4**) from α-diazocyclopentanes.
31. Kabalka, G.W.; Varma, M.; Varma, R.S.; Srivastava, P.C.; Knapp, F. F. Jr., *J. Org. Chem.*, **1986**, *51*, 2386-2388.