206. Functionalisation of Saturated Hydrocarbons

Part XI[1])

Oxidation of Cedrol, β- and γ-Eudesmol, Sclareol, Manoyl Oxide, 1,9-Dideoxyforskolin, Methyl *trans*-Dihydrojasmonate, and Tetrahydrolinalool by the '*Gif* System'

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Dedicated to Professor *Tadeus Reichstein* on the occasion of his 90th birthday

(10. VII. 87)

The oxidation of cedrol (**1**), β- and γ-eudesmol (**6** and **7**, resp.), sclareol (**14**), manoyl oxide (**15**), 1,9-dideoxyforskolin (**22**) (±)-methyl *trans*-dihydrojasmonate (**28**), and tetrahydrolinalool (**32**), nearly all of natural terpenoid origin, by the '*Gif* system' has afforded a number of novel products (**3**, **11**, and **12**, **16**/**17**, **18**/**19**, **26**, **29**–**31**, and ketones corresponding to **34**–**35**, resp.). The structures of these compounds were established by spectroscopic techniques including 2D-NMR and, where appropriate, by comparison with authentic samples.

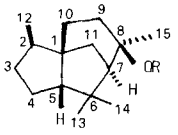
Introduction. – In the preceding parts of this series [1–6], we reported our findings on the oxidation of saturated hydrocarbons by the '*Gif* system'. This process, especially in its most elaborate form (catalytic amounts of iron cluster $Fe_3O(OAc)_6Pyr_{3,5}$, Zn powder, AcOH, pyridine, and air at room temperature) was successfully applied to a variety of simple hydrocarbons [2] [3] and then to more complex molecules such as steroids [4] [5] and terpenoids [1] [6]. As a rule, this oxidising system leads to the formation of ketones as major products, *i.e.* selective attack on secondary positions. This regioselectivity is rather unusual when compared with other oxidising processes. A noticeable exception was observed in the case of cholestane derivatives where the important side-chain cleavage to give 20-ketones competed with the oxidation of the methylenes of the steroidal nucleus [4] [5].

In addition to our fundamental studies on simple substrates, we believed that comparable work on rather more complex substrates could enhance our understanding of the mechanisms involved. It is known that terpenoids display interesting biological activities, particularly organoleptic properties. The selective functionalisation of these compounds could allow access to ketonic derivatives otherwise difficult to obtain by straightforward classical multistep syntheses or even by microbial transformations. In this article, we

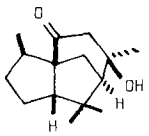
[1]) Part IX and X: [1].

wish to report the results obtained upon oxidising cedrol (**1**), β-eudesmol (**6**), γ-eudesmol (**7**), manoyl oxide (**16**), sclareol (**13**), 1,9-dideoxyforskolin (**21**), methyl dihydrojasmonate (**27**), and tetrahydrolinalool (**39**). The structural assignments of the oxidised products are based on chemical and mainly spectral data, especially those obtained by two-dimensional NMR techniques and, where appropriate, comparison with authentic samples.

Results. – *Oxidation of Cedrol* (**1**). Cedrol is a sesquiterpenoid usually extracted from Texas cedarwood oil *(Juniperus mexicana)*, and widely used as a perfume ingredient. Hydroxylations of **1** or its acetate **2** were effected by dry ozonisation [7], by mammals [8] [5], by microorganisms [10], and by *m*-chloroperbenzoic acid [11]. Dry ozonisation [7] of **2** according to *Mazur*'s procedure afforded the tertiary alcohol at the 2α position, electrophilic oxidation of **1** or **2** with *m*-chloroperbenzoic acid gave a mixture of tertiary alcohols at C(2) and C(7) and some secondary alcohol at C(4) [11]. Biohydroxylations of **1** by *Aspergillus Niger* [10] or 'Fauve de Bourgogne' rabbits [9] afforded alcohols at C(3), whereas dogs [8] were less discriminative, for oxidations, at C(3), C(12), C(4), and C(15) were observed.



1 R = H
2 R = Ac



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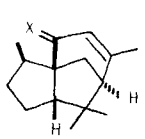
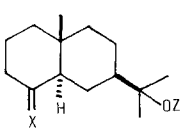


4 X = H_2
5 X = O

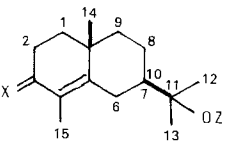
The oxidation of cedrol (**1**) with the '*Gif IV* system' [3] gave, apart from the recovered starting material (68%), a new ketone as the major oxidation product (1.3%, $[\alpha]_D^{20} = -90°$). IR, NMR, and MS data (see below) are in full agreement with structure **3**. The latter was confirmed by chemical correlation: Cedrol (**1**) was dehydrated with $(CF_3CO)_2O$ (20°, 15 min) to 8-cedrene (**4**) [12] which was oxidised with CrO_3/AcOH, (20°) to the known cedrenone **5** [13]; dehydration of **3** afforded an enone identical to **5**. Ketone **3** (or the corresponding alcohols) was never found in either biological or any other chemical oxidation of **1**.

Oxidation of β- and γ-Eudesmols **6** *and* **7**. Eudesmol is a crystalline sesquiterpenoid alcohol first isolated by *Baker* and *Smith* towards the end of the nineteenth century [12] from the essential oil of *Eucalyptus piperita*. Since then it has been found to be uniquitous, and reports concerning its isolation from various sources still abound. In fact, the natural product has been recognised for many years to be an almost inseparable mixture of two and, sometimes, three isomeric alcohols, depending on the source of the material [13]. These alcohols are the olefinic isomers α-, β-, and γ-eudesmols having the structures **8**, **6**, and **7**, respectively. These structures are due to the investigations of *Ruzicka* and coworkers in the thirties. Much work has been devoted to these compounds, including their total syntheses [13a–c]. Recently, β-eudesmol was found to inhibit gastric ulcers and especially to possess a preventive effect against aspirin-induced ulcers [13d].

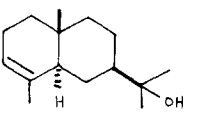
The β- and γ-eudesmols (**6** and **7**, resp.) that we used were obtained by chromatography of a crude extract which gave a mixture **6**/**7** and γ-eudesmol (**8**). The fraction **6**/**7** was esterified (3,5-dinitrobenzoyl chloride, 4-(dimethylamino)pyridine, benzene/pyridine, 20°), and the crystalline 3,5-dinitrobenzoates **9** and **10** [14] were obtained pure by careful chromatography. After alkaline hydrolysis, pure **6** and **7** were isolated. We found this separation more convenient than both the tedious repetitive recrystallisation procedure [14] and that involving expensive chromatography on silver-salt-impregnated columns [15].



6 X = CH_2, Z = H
9 X = CH_2, Z = 3,5-$(NO_2)_2C_6H_3CO$
11 X = O, Z = H



7 X = H_2, Z = H
10 X = H_2, Z = 3,5-$(NO_2)_2C_6H_3CO$
12 X = O, Z = H



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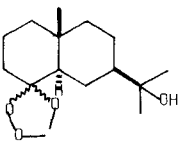


13

The oxidation of β-eudesmol (**6**) by the '*Gif IV* system' gave a mixture which was separated by silica-gel chromatography into 2 fractions, the starting material **6** (60%) and the oxidised products. This latter fraction was subjected to HPLC and gave a major compound (4.5%). Its spectral data (IR: 3490 (OH), 1710 cm^{-1} (CO); ^1H- and ^{13}C-NMR: no olefinic bond, loss of 1 C-atom; MS: *m/z* 224 ($M^{+\cdot}$, $C_{14}H_{24}O_2$)) are strongly indicative of structure **11**. In order to confirm this hypothesis, we undertook a chemical correlation. β-Eudesmol (**6**) was treated with ozone (CH_2Cl_2, −78°). After 5 min, TLC revealed the disappearance of **6** and the formation of 2 new polar compounds in *ca.* equal amounts, presumably the 2 diastereoisomeric ozonides. When the reaction was quenched with excess Me_2S, only one of these 2 derivatives was converted to a more polar compound, *i.e.* **11**. The remaining ozonide was isolated by column chromatography and its structure determined to be **13** on the basis of spectral data (see *Exper. Part*) and because it was converted to **11** upon treatment with Zn/AcOH. Ketone **11** was also obtained as the sole product when the crude ozonolysed mixture was treated directly with Zn/AcOH. The different behaviour of the 2 ozonides towards reduction with Me_2S could be a reflection of the steric congestion due to the angular Me group. What is relevant is the fact that the final product obtained upon ozonolysis of **6** is the same as the major product arising from the '*Gif* oxidation' of **6**.

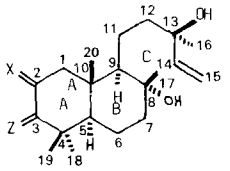
When the isomeric γ-eudesmol (**7**) was oxidised under '*Gif IV* conditions' [3], the same separation procedure as that used after oxidation of **6** afforded the starting material **7** (56%) followed by the major oxidised product (2.7%). This was identified (TLC, HPLC, IR) as carissone **12** [14] [16].

Oxidation of Sclareol (**14**) *and Manoyl Oxide* (**15**). (−)-Sclareol (**14**) and its dehydration derivative (+)-manoyl oxide (**15**) belong to the rich class of labdane diterpenoids. Many compounds of this type display an ambergris odour, the origin of which has been recently discussed [17]. Sclareol is extracted commercially from clary sage (*Salvea sclarea*) and manoyl oxide mainly from the wood oil of pine, the latter being also present in

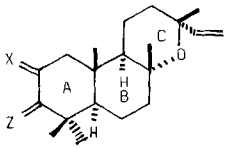
Turkish and Greek tobacco. Although manoyl-oxide analogues oxygenated in the A ring are often found in plant extracts, their counterparts in the sclareol series are unknown. Microbial transformation of sclareol (**14**) results only in C(18) oxidation [18]. The configuration at C(13) of **14** has been shown to be *R* beyond any doubt [19]. Despite this, authors kept drawing the formula of **14** erroneously with 13*S* configuration [20].

When (−)-sclareol (**14**) was oxidised by the '*Gif IV* system', two fractions were isolated by column chromatography, the starting material **14** (62%) and a more polar fraction. The latter was subjected to HPLC and afforded 2 new ketones as oils, the 2-keto derivative **16** (2.5%; $[\alpha]_D^{22} = +9.2°$; IR: 1700 cm^{-1}) and the 3-keto derivative **17** (0.7%; $[\alpha]_D^{20} = -2.5°$; IR: 1695 cm^{-1}). The structures of these compounds were deduced from their IR, MS, and especially NMR data *(vide infra)*.

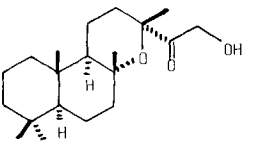
The oxidation of the closely related (+)-manoyl oxide (**15**) led to 2 major oxidised products, *viz.* the known [21] 2-keto derivative **18** (2.1%) and the keto alcohol **19** (0.7%; $[\alpha]_D^{21} = +61.7°$; IR: 1715 cm^{-1}). The structure of **19** was deduced from its spectral data and



14 X = Z = H_2
16 X = O, Z = H_2
17 X = H_2, Z = O



15 X = Z = H_2
18 X = O, Z = H_2
20 X = H_2, Z = O

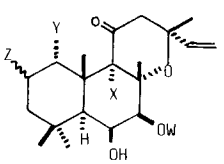


19

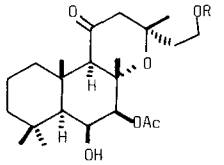
especially from the comparison of the ^{13}C-NMR spectra of **19** and that of manoyl oxide (**15**; *vide infra*). A minor compound which could not be fully characterised was isolated in trace amounts and is suspected to be the 3-keto derivative **20** on the basis of MS, IR, and NMR spectra.

Oxidation of 1,9-Dideoxyforskolin (**22**). Forskolin (**21**) and its 1,9-dideoxy analog **22** also belong to the labdane series of diterpenoids. They are both extracted from the Indian herb *Coleus forskohlii*. Forskolin exhibits a promising potential for the treatment of various diseases [22]. It activates adenylate cyclase and represents a useful tool in the understanding of cyclic AMP-mediated physiological processes [22]. Microbial hydroxylation of 7-*O*-deacetyl-1,9-dideoxyforskolin (**23**) led to 7-*O*-deacetylforskolin (**24**), whereas 1,9-dideoxyforskolin (**22**) gave a mixture of 2-hydroxylated derivatives **25** [22]. In addition to these microbial oxidations, the potential biological usefulness of this class of polyfunctionalised labdane derivatives prompted the interest of chemists to either perform chemical modifications of these compounds or devise their total syntheses [23].

Using our oxidation system, we observed that 1,9-dideoxyforskolin (**22**) gave only one major derivative **26** (4.5%). Close examination of MS and NMR data of **26** and of its monoacetate **27** led to the unambiguous conclusion that its formation is a result of an *anti-Markovnikov* addition of H_2O across the double bond of **22**. The difficulty encountered in acetylating the sterically highly hindered 6β-OH group of **26** is not surprising [24]. By a blank experiment (**22**, Zn, AcOH, pyridine, air, 20°), we showed that no trace of **26** was formed in the absence of the iron catalyst.



21 W = Ac, X = Y = OH, Z = H
22 W = Ac, X = Y = Z = H
23 W = X = Y = Z = H
24 W = H, X = Y = OH, Z = H
25 W = Ac, X = Y = H, Z = OH

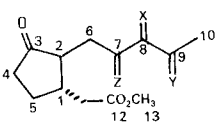


26 R = H
27 R = Ac

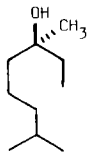
Oxidation of (±)-Methyl trans-*Dihydrojasmonate* (**28**). Methyl *trans*-dihydrojasmonate (**28**) possesses a powerful jasmin-like odour and is widely used as an economic fragrance ingredient. The distinguished organoleptic and plant hormone properties of the jasmonoids and, as a result, their industrial use has provoked an abundant patent literature and the development of many synthetic routes to these molecules [25].

The '*Gif* oxidation' of (±)-methyl *trans*-dihydrojasmonate (**28**) afforded a mixture of products which was separated by silica-gel chromatography followed by HPLC. Besides the starting material **28** (69%), 3 new ketonic products were obtained all exhibiting the same IR absorptions at 1710 and 1735 cm^{-1} (CO). Their MS including high-resolution MS indicate that these keto compounds are isomers and bring additional information on the position of the second keto group (see *Exper. Part*). This and analysis of the NMR spectra led to the assignment of structures **29**–**31** (1.7, 1.4, and 1%, resp.).

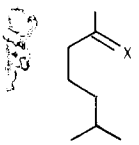
Oxidation of Tetrahydrolinalool **32**. Tetrahydrolinalool **32** is widely used in its racemic form as a perfume ingredient. Apart from the potential modification of its odoriferous properties, the behaviour of this compound in the '*Gif* system' was of interest, since it has the same C framework as the cholesterol-type steroid side-chain [4], but an additional OH group is also present.



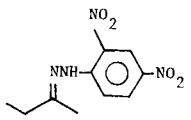
28 X = Y = Z = H_2
29 X = O, Y = Z = H_2
30 X = H_2, Y = O, Z = H_2
31 X = Y = H_2, Z = O



32



33 X = O
34 X = 2,4-$(NO_2)_2C_6H_3$–NHN



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Preliminary experiments showed that (±)-tetrahydrolinalool **32** and especially its oxidation products were too volatile to perform the oxidation under air as was customary. We, therefore, carried out the reaction under an O_2-filled balloon, and the expected

ketone or aldehyde products were extracted into Et_2O and immediately trapped with (2,4-dinitrophenyl)hydrazine. The remaining starting material **32** was removed by evaporation and the residue separated by silica-gel chromatography. Three (2,4-dinitrophenyl)hydrazones were isolated. Their structures were elucidated on the basis of spectral data (MS and NMR) and by the comparison with their known melting points. The first compound to be eluted was shown to be **34** (6.5%), derived from 6-methylheptan-2-one (**33**). The second (12.6%) was easily identified as being the (2,4-dinitrophenyl)hydrazone **35** of acetone, while the third one, **36** (1.55%), was shown to derive from 2-butanone. In order to establish the stability of the tertiary alcohol function under the conditions of (2,4-dinitrophenyl)hydrazone formation [26], the starting material **32** was directly subjected to identical treatment: unchanged **32** was recovered. In the same manner, any β-hydroxy ketone formed would have given rise to a stable (2,4-dinitrophenyl)hydrazone [26].

NMR Spectra. The same strategy [27] [28] base upon one- and two-dimensional ^1H- and ^{13}C-NMR spectroscopy has been used to determine the oxidation sites of all compounds (data in *Exper. Part, Tables 1–12*). Generally, the ^{13}C-NMR spectrum of the oxidation product shows an extra carbonyl function. Only the product from 1,9-dideoxyforskolin (**22**) does not reveal the presence of an extra carbonyl group.

Methyl trans-*Dihydrojasmonate* (**28**). The *J*-modulation of the spin echo spectra [29] of **28**–**31** gives the multiplicities of the ^{13}C-NMR signals. From the number of quaternary C, CH, CH_2, and CH_3 groups, we can assess that a modification of the C skeleton is highly unlikely for **29**–**31** as compared to **28**. Only one CH_2 group is changed into a carbonyl group. In the ^{13}C-NMR spectrum of **28**, CH_3(13), CH_2(4), and CH_3(11) are easily identified because they are deshielded. The $^1H,^{13}C$ chemical-shift correlation spectrum [30a] permits the identification of protons of CH, CH_2, and CH_3 groups and is especially useful for identification of non-equivalent protons of CH_2 groups. The $^1H,^1H$ chemical-shift correlation (COSY) experiment [30b] then gives information about series of coupled protons separated by quaternary C-atoms. For **29** and **31**, the following sequences were determined: Compound **29**: 2 H–C(4)→2 H–C(5)→H–C(1)→2 H–C(11), H–C(1)→H–C(2)→2 H–C(6)→2 H–C(7), Me(10)→2 H–C(9). The oxidation site is at C(8). Compound **31**: Me(10)→2 H–C(9)→2 H–C(8), H–C(1)→H–C(2)→2 H–C(6), 2 H–C(4)→2 H–C(5)→H–C(1)→2 H–C(11). Hence, oxidation occurred at C(7).

In the case of **30**, CH_3(10) is a *s*, therefore, identification of the oxidation site at C(9) is straightforward. The 2D spectra confirm this result.

Cedrol (**1**). The NMR parameters of **1** are well known [31]. The ^{13}C-NMR spectrum of its oxidation product **3** shows that a CH_2 has been transformed into a carbonyl group and the CH signals have not been disturbed. Therefore, oxidation did not occur at C(3), C(4), or C(11). On the other hand, we observe a shift of 1 quaternary C-atom; thus the oxidation site can be either at C(9) or C(10). As the quaternary C(8) bearing an OH function shows a very typical chemical shift (75 ppm), we can easily see that it is not disturbed by the oxidation; hence, cedrol is oxidised at C(10).

Sclareol (**14**). We have clarified the ambiguous ^{13}C-NMR assignments made by *Svenolof et al.* [32] for C(2), C(11), C(7), and C(12) of the starting alcohol **14**, *i.e.* C(2) appears at 19.05, C(7) at 44.28, C(11) at 18.52, and C(12) at 45.07 ppm. Applying the methodology described above, we found the oxidation site for **16** to be at C(2). The ^{13}C-NMR spectrum of **17** shows that the oxidation has occurred in α position to a quaternary C-atom. The oxidation site is not at C(7) or C(12) because the quaternary C(8) and C(13) bearing an OH function have the same typical chemical shifts in **17** as in the starting alcohol **14**. The oxidation is possible at C(1) or C(3), but from the COSY and $^{13}C,^1H$ correlation spectra only, no decision can be made.

However, a 'long-range' $^1H,^{13}C$ chemical-shift correlation [30a] shows coupling between the carbonyl C-atom and CH_3(18) and CH_3(19); thus, C(3) of **17** is oxidised.

1,9-Dideoxyforskolin (**22**). No extra carbonyl function is shown by the ^{13}C-NMR data of **26**, the only perturbation being at C(14) and C(15) as compared to **22**. The examination of 2D and 1D spectra of **26** and of the acetate **27** shows that the oxidation of **22** results in a transformation of a vinylic double bond into a CH_2CH_2OH group.

Discussion. – In previous papers [1] [5] [6], we showed that oxidation of various terpenoids and steroids by the '*Gif* system' afforded exclusively ketonic products (with the exception of concomitant side-chain cleavage in cholestane derivatives, but the final products were indeed ketones). We now report the oxidation of 8 other terpenoids and related compounds possessing different types of C skeletons and various functionalities (alcohol, olefin, ketone, and ester groups). It must be pointed out that we focussed our attention only on the major products. In other words, we cannot state for sure that a given compound is strictly absent or present only in trace amounts. When comparison is possible (cedrol (**1**), manoyl oxide (**15**), 1,9-dideoxyforskolin (**22**)), our system presents a regioselectivity different to that displayed by microorganisms, as previously noted for patchouli alcohol [1]. Most of the products formed are the result of the transformation of a CH_2 into a keto group. However, on the basis of our previous work [1–6] on simple and more complex substrates, we could not predict the occurrence of several reactions. If allylic oxidation of the trisubstituted double bond of γ-eudesmol (**7**) to yield carissone (**12**) is reminiscent of the oxidation of cyclohexene (which gives *inter alia* cyclohexenone) and of cholesterol acetate, the cleavage of the exocyclic methylidene group in β-eudesmol (**6**) is a new reaction. Also the conversion of the vinyl group to an α-hydroxy ketone in manoyl oxide (**16**→**19**) and, in particular, the *anti-Markovnikov* hydration of 1,9-dideoxyforskolin (**22**) were not anticipated. Similarly, although σ(C–C) bond cleavage had been observed in the degradation of cholestane derivatives [4] [5] as well as in the oxidation of 3-ethylpentane [33], the multiple C–C bond breakings observed with tetrahydrolinalool (**32**) were not expected in view of the stability of *e.g.* triethylmethanol under '*Gif IV* conditions' [33].

Thus, oxidation can occur at mono- and di-substituted C=C bonds, and C–C bond cleavage becomes a possibility. The diversity of the reactivity shown by the '*Gif* system' when various substrates are used reflects the complexity of the possible reaction pathways and intermediates. In particular the intermediate iron complex which shows such diverse behaviour is under investigation. It is hoped to present an adequate theory in due course.

In the case of fairly rigid saturated hydrocarbons, ketones are always the major products. The regioselectivity can be explained in steric terms using force-field calculations [34].

We thank Dr. *B.J. Willis*, Director of Research, PPF, Ashford, U.K., for the supply of starting materials and for his interest in this field of oxidation chemistry. The 1,9-dideoxyforskolin was a gift from *Hoechst*, Frankfurt, FRG.

Experimental Part

General. HPLC: *Waters Associate* liquid chromatograph equipped with a model *440* absorbance UV detector at 254 mm and a *Jobin Yvon Data* differential refractometer, prep. normal-phase *Ultrasphere-Si* and reverse-phase *Ultrasphere ODS* 5μ, 10 mm × 25 cm columns, *S.D.S. Purex* grade solvents. M.p.: Reichert *Thermovar* hot stage microscope; uncorrected. Optical rotation: *Perkin-Elmer-241* polarimeter; in $CHCl_3$, *c* in g/100 ml. IR spectra: *Perkin-Elmer 297;* in CH_2Cl_2. NMR spectra: *Bruker AM 400* wide bore spectrometer; in $CDCl_3$ with TMS as internal standard. COSY: applied pulse sequence, $(\pi/2)$–(t_1)–$(\pi/4)$–(FID, t_2); spectra width in F_1 and F_2 1000 Hz; number of data points in F_2, 2048; 256 increments were recorded; before applying the *Fourier* transforms, the data were multiplied with unshifted sine bell; zero filling in F_1. ^1H,^{13}C chemical-shift correlation: applied pulse sequence, $(\pi/2, {}^1H)$–$(t_1/2)$, $(\pi, {}^{13}C)$–$(t_1/2)$, (t_1)–$(\pi/2, \tau_2, {}^1H;\ \pi/2, {}^{13}C)$–$(\tau_2)$–BB, (FID, t_2) with $\tau_1 = 0.00357$s, $\tau_2 = 0.00185$s; spectral width in F_1, 1000 Hz, in F_2, 3500 Hz; number of data points in t_2, 4096; 256 increments were recorded; prior to *Fourier* transforms, the data were multiplied with $\pi/10$-shifted sine bell in F_2 and *Lorentz-Gauss*

in F_1; zero filling in F_1. J-Modulation of the spin echo: applied pulse sequence, ($\pi/2$, ^{13}C)–(D_1)–(BB, ^{1}H, π, ^{13}C)–(D_1, BB)–(FID, BB) with D_1 = 0.007s. The ^{13}C- and ^{1}H-NMR are summarized in *Tables 1–12.*

Table 1. *^{13}C-NMR Chemical Shifts of* **7** *and* **12**

C-Atom	**7**	**12**
C(1)	23.43	26.8
C(2)	42.42	42.04
C(3)	26.5	199.0
C(4)	135.0	162.8
C(5)	124.0	128.9
C(6)	33.33	33.88
C(7)	19.29	10.95
C(8)	40.40	37.45
C(9)	19.35	22.5
C(10)	34.6	35.9
C(11)	72.94	72.5
C(12)	27.3	28.8
C(13)	26.9	27.6
C(14)	24.77	22.77
C(15)	50.68	49.7

Table 2. *^{1}H-NMR Chemical Shifts of* **7**

H-Atom	**7**
H_a–C(1)	1.42
H_b–C(1)	1.63
H_a–C(2)	1.20
H_b–C(2)	1.55
H_a–C(3)	1.62
H_b–C(3)	2.63
H_a–C(6)	1.85
H_b–C(6)	1.99
H–C(7)	1.59
H–C(8)	1.27
H–C(8)	1.48
H–C(9)	1.59
H–C(9)	1.59
CH_3(12)	1.20
CH_3(13)	1.20
CH_3(14)	1.02
CH_3(15)	1.23

Table 3. *^{13}C-NMR Chemical Shifts of* **14**, **16**, **17**, **15**, *and* **19**

C-Atom	**14**	**16**	**17**	**15**	**19**
C(1)	39.7	59.39	38.4	39.3	39.01
C(2)	18.5	216.4	34.0	19.0	18.8
C(3)	42.11	55.5	216.8	42.4	42.3
C(4)	33.3	38.7	47.6	33.4	33.3
C(5)	56.2	55.4	55.2	56.6	56.7
C(6)	20.6	20.7	21.5	20.3	20.0
C(7)	43.3	43.7	43.8	43.7	43.0
C(8)	74.8	84.4	74.4	74.9	75.7
C(9)	61.8	60.9	60.7	56.1	56.6
C(10)	39.3	44.3	38.9	37.2	37.1
C(11)	19.1	19.1	19.6	15.75	14.9
C(12)	45.1	44.6	44.8	36.2	33.1
C(13)	73.5	73.7	73.8	73.15	79.3
C(14)	146.4	146.0	145.8	148.8	215.0
C(15)	111.0	111.5	111.5	109.8	64.7
C(16)	26.8	27.0	27.7	29.15	26.1
C(17)	24.2	24.0	24.1	25.8	25.1
C(18)	33.5	33.5	26.5	33.5	33.4
C(19)	21.6	23.1	21.4	21.6	21.5
C(20)	15.5	16.5	14.9	15.7	15.1

Table 4. *^{1}H-NMR Chemical Shifts of* **14**, **16**, *and* **17**

H-Atom	**14**	**16**	**17**
H_a–C(1)	0.91	2.14	1.50
H_b–C(1)	1.6	2.28	1.90
H_a–C(2)	1.29	–	2.35
H_b–C(2)	1.50	–	2.53
H_a–C(3)	1.10	2.11	–
H_b–C(3)	1.34	2.34	–
H–C(5)	0.88	1.54	1.42
H–C(6)	1.25	1.37	1.39
H–C(6)	1.60	1.77	1.57
H–C(7)	1.43	1.53	1.43
H–C(7)	1.81	1.91	1.86
H–C(9)	1.07	1.41	1.17
H–C(11)	1.38	1.31	1.36
H–C(11)	1.60	1.58	1.54
H–C(12)	1.54	1.52	1.56
H–C(12)	1.64	1.67	1.70
H–C(14)	5.9	5.9	5.88
H–C(15)	4.96	5.01	4.99
H–C(15)	5.18	5.19	5.18
CH_3(16)	1.23	1.26	1.25
CH_3(17)	1.13	1.16	1.18
CH_3(18)	0.83	1.05	1.06
CH_3(19)	0.76	0.84	0.98
CH_3(20)	0.76	0.80	0.92

Table 5. *^{13}C-NMR Chemical Shifts of* **6** *and* **11**

C-Atom	**6**	**11**
C(1)	41.3[a])	40.8
C(2)	23.6[b])	22.7
C(3)	37.0	41.3
C(4)	151.0	212.5
C(5)	49.6	57.4
C(6)	25.1	21.5
C(7)	50.0	48.4
C(8)	22.5[b])	21.9
C(9)	42.0[a])	40.3
C(10)	35.9	39.3
C(11)	72.7	72.7
C(12)[c])	27.2	26.7
C(13)[c])	27.2	27.3
C(14)	16.4	17.0
C(15)	105.4	–

[a])–[c]) Assignments may be interchanged.

Table 6. *^{1}H-NMR Chemical Shifts of* **6** *and* **11**

H-Atom	**6**	**11**
H_a–C(1)[a])	1.24	1.32
H_b–C(1)[a])	1.41	1.52
H_a–C(2)[b])	1.57	1.86
H_b–C(2)[b])	1.60	1.90
H_a–C(3)	1.97	2.26
H_b–C(3)	2.27	2.27
H–C(5)	1.75	2.16
H_a–C(6)	1.10	1.19
H_b–C(6)	1.60	1.67
H–C(7)	1.33	1.26
H_a–C(8)[c])	1.06	1.27
H_b–C(8)[c])	1.26	1.60
H_a–C(9)[d])	1.20	1.52
H_b–C(9)[d])	1.50	1.55
CH_3(12)[e])	1.16	1.14
CH_3(13)[e])	1.16	1.13
CH_3(14)	0.67	0.70
H_a–C(15)	4.42	–
H_b–C(15)	4.69	–

[a])–[c]) Assignments may be interchanged.

Table 7. *^{13}C-NMR Chemical Shifts of* **22** *and* **26**

C-Atom	**22**	**26**
C(1)[a])	43.9	43.9
C(2)	18.6	16.9
C(3)[a])	41.5	41.0
C(4)[b])	34.4	34.3
C(5)	55.4	55.4
C(6)	70.1	70.2
C(7)	81.9	80.8
C(8)[c])	78.5	79.1
C(9)	65.8	68.3
C(10)[b])	37.9	37.4
C(11)	204.6	206.0
C(12)	50.3	53.5
C(13)[c])	98.0	81.7
C(14)	146.0	47.2
C(15)	112.0	59.1
C(16)	31.8	29.2
C(17)	24.2	22.7
C(18)[d])	23.9	33.1
C(19)[d])	33.3	23.8
C(20)	17.1	16.8
C(21)	177.0	170.0
C(22)	21.3	21.1

[a])–[d]) Assignments may be interchanged.

Table 8. *^{1}H-NMR Chemical Shifts of* **22** *and* **26**

H-Atom	**22**	**26**
H_a–C(1)[a])	1.14	1.23
H_b–C(1)[a])	1.35	1.44
H_a–C(2)	1.41	1.42
H_b–C(2)	1.73	1.83
H_a–C(3)[b])	0.77	0.90
H_b–C(3)[b])	2.42	2.30
H–C(5)	0.92	1.05
H–C(6)	4.33	4.40
H–C(7)	5.10	5.10
H–C(9)	2.77	2.55
H_a–C(12)	2.54	2.37
H_b–C(12)	2.65	2.70
H–C(14)	5.96	1.81
H_a–C(15)	5.05	3.88
H_b–C(15)	5.27	3.88
CH_3(16)	1.20	1.39
CH_3(17)	1.52	1.66
CH_3(18)[c])	1.18	1.00
CH_3(19)[c])	0.93	1.27
CH_3(20)	1.41	1.55

[a])–[c]) Assignments may be interchanged.

Table 9. *^{13}C-NMR Chemical Shifts of* **28–31**

C-Atom	**28**	**31**	**29**	**30**
C(1)	38.3	38.4	38.7	38.3
C(2)	54.2	50.4	53.1	54.1
C(3)	219.1	208.7	218.5	219.9
C(4)	37.5	37.22	37.6	38.8
C(5)	27.2	27.5	27.2	27.4
C(6)	27.9	41.1	21.8	27.3
C(7)	26.4	191.2	39.0	21.1
C(8)	32.0	44.7	210.0	43.7
C(9)	22.4	17.2	35.9	208.2
C(10)	13.9	13.8	7.8	29.8
C(11)	38.9	38.9	38.7	37.56
C(12)	172.5	171.0	173.0	178.5
C(13)	51.5	51.6	51.7	51.6

Table 10. *^{1}H-NMR Chemical Shifts of* **28–31**

H-Atom	**28**	**31**	**29**	**30**
H–C(1)	2.20	2.31	2.16	2.30
H–C(2)	1.68	2.16	1.73	1.78
H_a–C(4)	2.01	2.27	2.04	2.32
H_b–C(4)	2.20	2.33	2.23	2.61
H_a–C(5)	1.38	1.48	1.40	1.51
H_b–C(5)	2.13	2.20	2.16	2.20
H_a–C(6)	1.45	2.63	1.58	1.51
H_b–C(6)	1.45	2.80	1.80	1.52
H_a–C(7)	1.12	–	2.45	1.46
H_b–C(7)	1.29	–	2.50	1.67
H_a–C(8)	1.14	2.35	–	2.40
H_b–C(8)	1.14	2.35	–	2.40
H_a–C(9)	1.19	1.52	2.31	–
H_b–C(9)	1.19	1.57	2.38	–
H_a–C(11)	2.51	2.36	2.25	2.12
H_b–C(11)	2.51	2.49	2.59	2.32
CH_3(10)	0.76	0.87	0.94	2.09
CH_3(13)	3.58	3.61	3.60	3.67

Table 11. *^{13}C-NMR Chemical Shifts of* **34**, **35**, *and* **36**

C-Atom	**34**	**35**	**36**
C(1)	15.9	*ca.* 155	15.9
C(2)	*ca.* 155	17.0	*ca.* 155
C(3)	39.3	25.6	32.4
C(4)	24.18		10.6
C(5)	38.6	–	–
C(6)	27.8	–	–
C(7)	22.65	–	–
C(8)	22.65	–	–

Table 12. *^{13}C- and ^{1}H-NMR Chemical Shifts of* **1** *and* **3**

C-Atom	**1**	**3**	H-Atom	**1**	**3**
C(1)	54.25	69.26	H–C(2)	1.65	1.95
C(2)	41.6	37.7	H_a–C(3)	1.86	1.80
C(3)	37.15	34.36	H_b–C(3)	1.27	1.40
C(4)	25.5	24.14	H_a–C(4)	1.51	1.74
C(5)	56.7	54.1	H_b–C(4)	1.38	1.65
C(6)	43.54	45.5	H–C(5)	1.77	2.34
C(7)	61.23	59.7	H–C(7)	1.56	1.85
C(8)	75.15	76.62	H_a–C(9)	1.70	2.41
C(9)	35.5	54.3	H_b–C(9)	1.81	2.98
C(10)	31.75	210.7	H_a–C(10)	1.37	–
C(11)	42.13	40.08	H_b–C(10)	1.41	–
C(12)	15.67	16.25	H_a–C(11)	1.35	1.52
C(13)	29.0	29.3[a])	H_b–C(11)	1.64	2.04
C(14)	27.7	28.8[a])	CH_3(12)	0.83	1.09
C(15)	30.3	31.5	CH_3(13)[b])	0.92	1.12
			CH_3(14)[b])	1.30	1.43
			CH_3(15)	1.25	1.32

[a]) Assignments may be interchanged.

[b]) Assignments may be interchanged.

Oxidation: General Procedure. In a typical reaction, substrate (2 mmol), Zn (1.31 g, 10 equiv.), iron cluster [2] $Fe_3O(OAc)_6Pyr_{3.5}$ (5–8 mg), pyridine (28 ml), H_2O (2 ml), and AcOH (2.3 ml) were placed in a 100 ml open-neck conical flask and stirred at r.t. for 6 h (except for (±)-tetrahydrolinalool **32**; 18 h). This was done in several parallel runs. After completion of the reaction (disappearance of Zn), the mixtures were combined, cooled in an ice bath, carefully acidified with 25% H_2SO_4 soln. (until pH *ca.* 2), and extracted continuously with CH_2Cl_2 for 18 h. The extracts were washed successively with 1N H_2SO_4, sat. $NaHCO_3$ soln. and brine, dried (Na_2SO_4), and evaporated to yield the crude oxidation mixture.

In parallel, blank experiments (*i.e.* without iron catalyst) were likewise performed. Only starting material was recovered; no oxidation products could be detected.

Oxidation of 8β-Cedrol (**1**). According to the general procedure (see above) in 4 parallel runs (4 × 444 mg of **1**). The crude mixture was chromatographed on silica gel with hexane/Et_2O (increasing polarity) to give first **1** (1.2 g, 68%). Further elution afforded oxidised products which were subjected to HPLC (normal phase, heptane/i-PrOH 97:3 and heptane/AcOEt/i-PrOH/AcOH 95:5:1:1). The major product thus isolated was 8β-hydroxycedran-10-one (**3**; 23 mg, 1.3%). M.p. 115–117° (MeOH). $[\alpha]_D^{20} = -90°$ ($c = 0.9$). IR (CH_2Cl_2): 1700. MS: 236 ($M^{+\cdot}$). Anal. calc. for $C_{15}H_{24}O_2$: C 76.23, H 10.24; found: C 75.49, H 10.04.

Dehydration of **3**. Ketone **3** (15 mg) was dissolved in $(CF_3CO)_2O$ (1 ml). After 1 h at 20°, TLC indicated that **3** was converted to a less polar compound. A sat. $NaHCO_3$ soln. (3 ml) was then added and the mixture stirred for 10 min. The CH_2Cl_2 extracts were washed with H_2O, dried ($MgSO_4$), and evaporated. The residue (13 mg) was purified by HPLC (normal phase, hexane i-PrOH 93:3) and gave a product identified (anal. HPLC, TLC, NMR, IR) as *8-cedren-10-one* (**5**).

Purification of β- and γ-Eudesmol (**6** and **7**, resp.). A crude plant extract containing α-, β-, and γ-eudesmol (**6–8**) and at least 10 other compounds was prepurified by silica-gel column chromatography. Elution with hexane/Et_2O (increasing polarity) afforded a fraction containing mainly **6–8**. This fraction (11.4 g) in benzene (60 ml) and pyridine (60 ml) was treated with 3,5-dinitrobenzoyl chloride (33.5 g, 0.74 mol) in the presence of traces of 4-(dimethylamino)pyridine. After 72 h at 20°, H_2O (120 ml) was added to the mixture. The Et_2O extracts were washed successively with dil. H_2SO_4 soln., H_2O, sat. $NaHCO_3$ soln., and brine, then dried (Na_2SO_4) and evaporated to yield a crude residue (22.0 g). This residue was subjected to chromatography (*Waters Prepak 500*, silica gel, hexane/AcOEt 97:3; controlled by anal. HPLC *Nucleosil 5μ*, hexane/AcOEt 97:3) and afforded **10** and **9**.

γ-Eudesmyl 3,5-Dinitrobenzoate (**10**): M.p. 101–102°. ([14]: 105–106°). ^{1}H-NMR ($CDCl_3$): 1.15 (*s*, CH_3(14)); 8.9 (3 arom. H).

β-Eudesmyl 3,5-Dinitrobenzoate (**11**): M.p. 135–136° ([14]: 136.7°). ^{1}H-NMR ($CDCl_3$): 0.75 (*s*, CH_3(14)); 4.5 (*d*, CH_2=); 8.9 (3 arom. H).

Alkaline hydrolysis of **10** and **11** according to [14] gave pure **6** and **7**, resp. The purity of these alcohols was controlled by HPLC (normal phase, hexane/AcOEt 9:1). ^{1}H-NMR (**6**; 60 MHz, $CDCl_3$): 0.8 (*s*, CH_3(14)); 1.2 (*s*, CH_3(12), CH_3(13)); 4.55 (=CH_2). ^{1}H-NMR (**7**; 60 MHz, $CDCl_3$): 1.2 (*s*, CH_3(12), CH_3(13), CH_3(14)).

Oxidation of β-Eudesmol (**6**). According to the general procedure (see above) with 444 mg (2 mmol) of **6**. The crude mixture was chromatographed on silica gel and eluted with hexane/Et_2O (increasing polarity) to give first **6** (268 mg, 60%) and then a more polar fraction which was subjected to HPLC (normal phase, hexane/i-PrOH 98.5:1.5). The major product isolated was *11-hydroxyeudesman-4-one* (**11**) (20 mg, 4.5%). M.p. 114–117° (hexane; [36]: 119–120°). IR (CH_2Cl_2): 3490 (OH), 1710. MS: 224 ($M^{+\cdot}$), 206, 166, 151, 95, 81.

Ozonolysis of β-Eudesmol (**6**). A soln. of **6** (222 mg, 1 mmol) in anh. CH_2Cl_2 (3 ml) was cooled to −78°. Through this soln., ozone was bubbled until a persistent blue colour appeared. After 15 min, Me_2S (0.1 ml) was added at −78°, and the reaction mixture was allowed to warm to r.t. After evaporation of the solvent, the residue was chromatographed on silica gel. Elution with hexane/Et_2O (increasing polarity) afforded *spiro[eudesmane-4,3'-1',2',4'-trioxolane]-11-ol* (**13**) (75 mg, 34%). M.p. 115° (hexane). MS: 270 ($M^{+\cdot}$). Anal. calc. for $C_{15}H_{26}O_4$: C 66.64, H 9.69, O 23.67; found: C 66.88, H 9.77, O 23.10.

Further elution gave **11** (75 mg, 34%; m.p. 116–118°), identical with **11** prepared by the '*Gif* oxidation' (TLC, IR, ^{1}H-NMR, mixed m.p.).

Reduction of Ozonide **13** *by Zn/AcOH and by Dimethyl Sulfide.* To a soln. of **13** (12 mg) in CH_2Cl_2 (2 ml) were added AcOH (0.5 ml) and Zn (13 mg). After 1 h at 20°, **13** had disappeared and a new compound formed (same R_f as **11**). H_2O was then added, and the org. layer was successively washed with a sat. $NaHCO_3$ soln., H_2O, and brine, dried (Na_2SO_4), and evaporated: **11** (12 mg, 95%).

When a soln. of **13** (3 mg) in CH_2Cl_2 (1 ml) was treated at 0° with 2 drops of Me_2S, **13** was recovered unchanged after 1 h (TLC).

Oxidation of γ-Eudesmol (**7**). According to the general procedure with 444 mg (2 mmol of **7**). The same purification procedure as for the oxidation of **6** gave **7** (250 mg, 56%) and **12** (12 mg, 2.7%) which was found to be identical (TLC, HPLC; IR (CH_2Cl_2): 1685) to an authentic sample of *carissone* (**9**) [16].

Oxidation of Sclareol (**14**). The crude oxidation mixture, obtained as described above from 5 parallel runs (5 × 2 mmol (3.08 g), reaction time 7 h), was chromatographed on silica gel with hexane/AcOEt 85:15 to give product A (196 mg), product B (100 mg), then **14** (1.91 g, 62%). Further elution with AcOEt yielded mixture of ketones which was subjected to subsequent purifications by HPLC (normal phase, hexane/i-PrOH 9:1). Final purification by HPLC (normal phase, hexane/i-PrOH/AcOH 95:5:1) yielded the 2 major products **16** and **17** isolated as oils.

8α,13-Dihydroxy-14-labden-2-one (**16**): 78 mg (2.5%). $[\alpha]_D^{22} = +9.2°$ ($c = 1.69$). IR (CH_2Cl_2): 3590 (free OH), 1700 (CO). MS: 322 (2, $M^{+\cdot}$), 304 (89), 289 (43), 286 (27), 209 (59), 206 (43), 191 (40), 179 (58), 150 (56), 135 (67), 190 (43), 109 (44), 95 (47), 81 (56), 72 (79), 69 (60), 55 (43), 43 (100). HR-MS: 304.2397 ($C_{20}H_{32}O_2$, $M^{+\cdot} - H_2O$, calc. 304.2402).

8α,13-Dihydroxy-14-labden-3-one (**17**): 22 mg (0.7%). $[\alpha]_D^{22} = -2.5°$ ($c = 0.81$). IR (CH_2Cl_2): 3590 (free OH), 1695 (CO). MS: 322 (2, $M^{+\cdot}$), 304 (36), 289 (17), 286 (15), 209 (37), 121 (46), 109 (61), 107 (46), 95 (60), 93 (40), 83 (49), 81 (94), 71 (100), 69 (62), 68 (56), 67 (46), 55 (63), 43 (100), 41 (67). HR-MS: 304.2404 ($C_{20}H_{32}O_2$, $M^{+\cdot} - H_2O$, calc. 304.2402).

Oxidation of Manoyl Oxide (**15**). The crude oxidation mixture, obtained as described above from 3 parallel runs (3 × 2 mmol (1.74 g), reaction time 5.5 h) was chromatographed on silica gel and eluted with hexane/AcOEt (increasing polarity) to give **15** (985 mg, 57%), followed by a complex mixture of oxidation products which was subjected to further purification by HPLC (normal phase, heptane/AcOEt and heptane/i-PrOH). Two major products, **18** and **19**, were isolated.

8α,13-Epoxy-14-labden-2-one (**18**): 37 mg (21%), identical (m.p., ^{1}H-NMR, IR, MS) with an authentic sample of natural origin. M.p. 76–78° (MeOH) ([21]: 77–78°). IR ($CHCl_3$): 700. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.88 (*dd*, $J = 17, 11$, 1 H); 5.26 (*d*, $J = 17$, 1 H); 4.94 (*d*, $J = 11$, 1 H); 2.31 (2*d*, $J = 12, 15$, 2 H); 2.18 (*d*, $J = 13$, 1 H); 2.02 (*d*, $J = 12$, 1 H); 1.92 (*dt*, $J = 13, 3$, 1 H); 1.80 (*m*, 2 H); 1.30–1.72 (*m*); 1.29 (*s*, 3 H); 1.28 (*s*, 3 H); 1.05 (*s*, 3 H); 0.87 (*s*, 3 H); 0.80 (*s*, 3 H). MS: 304 (1, $M^{+\cdot} - H_2O$), 289 (100), 271 (42), 205 (30).

8α,13-Epoxy-15-hydroxylabdan-14-one (**19**): 12 mg (0.7%). M.p. 113–117° (hexane). $[\alpha]_D^{20} = +61.7°$ ($c = 0.201$). IR ($CHCl_3$): 1715. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.67 (*d*, $J = 20$, 1 H); 4.51 (*d*, $J = 20$, 1 H); 1.37 (*s*, 3 H); 1.30 (*s*, 3 H); 0.88 (*s*, 3 H); 0.80 (*s*, 3 H); 0.78 (*s*, 3 H). ^{13}C-NMR: see *Table 3*; δ of C(1) to C(11), C(18), C(19), and C(20) of **19** are unchanged as compared with **15**, and C(12), C(13), C(16), and C(17) in the vicinity of the side chain are slightly shifted; C(14) is shifted from 148.8 ppm (olef. C-atom in **15**) to 215 (ketone C-atom in **19**); the δ of C(15) at 64.7 ppm is expected for such an α-hydroxy-α'-alkoxy moiety (*e.g.* C(21) of cortisol at 65.8 in DMSO [39]). MS: 307 (2, $M^{+\cdot} - 15$), 289 (20), 263 (37), 245 (100), 137 (35). Anal. calc. for $C_{20}H_{34}O_3$: C 74.49, H 10.24; found: C 74.19, H 10.55.

Oxidation of 1,9-Dideoxyforskolin (**22**). According to the general procedure (see above) with 756 mg (2 mmol) of **22**. The crude oxidation mixture was chromatographed on silica gel with hexane/Et_2O (increasing polarity) gaving first **22** (460 mg, 60%) and then a more polar fraction which was subjected to HPLC (normal phase, hexane/AcOEt 9:1 and hexane/i-PrOH 97:3). The major product thus isolated was *7-acetoxy-8α,13-epoxy-6,15-dihydroxylabdan-11-one* (**26**; 36 mg, 4.5%). MS: 381 ($M^{+\cdot} - 15$), 363 (18, $M^{+\cdot} - 15$), 351, 321, 303; *m** 286 (321→303).

The alcohol **26** (32 mg) was acetylated (pyridine (1 ml), Ac_2O (0.5 ml), 20° overnight) to give *7,15-diacetoxy-8α,13-epoxy-6-hydroxylabdan-11-one* (**27**; 33 mg, 94%). M.p. 172–175° (MeOH). $[\alpha]_D^{20} = -26°$ ($c = 0.74$). MS: 423 ($M^{+\cdot} - 15$), 363.

Oxidation of Methyl trans-*Dihydrojasmonate* (**28**). According to the general procedure (see above) in 5 parallel runs (5 × 452 mg of **28**). The crude mixture was chromatographed on silica gel and eluted with hexane/Et_2O (increasing polarity) to give **28** (1.57 g, 69%) and the oxidised products. The latter were separated by HPLC (normal phase, heptane/i-PrOH 92:8, 88:12, then 84:16) to give, in the order of elution **31**, **29**, and **30**.

Methyl trans-*3-Oxo-2-(2-oxopentyl)cyclopentaneacetate* (**31**): 22 mg (1%). IR (CH_2Cl_2): 1735, 1710. MS: (32, $M^{+\cdot}$), 197 (6.4), 209 (13), 181 (1.6) and 169 (38), 155 (100). HR-MS: 240.1346 ($C_{13}H_{20}O_4$, calc. 240.1361).

Methyl trans-*3-Oxo-2-(3-oxopentyl)cyclopentaneacetate* (**29**): 36 mg (1.7%). IR (CH_2Cl_2): 1735, 1710. MS: 240 ($M^{+\cdot}$). HR-MS: 240.1325 ($C_{13}H_{20}O_4$, calc. 240.1361).

Methyl trans-*3-Oxo-2-(4-oxopentyl)cyclopentaneacetate* (**30**): 31 mg (1.4%). IR (CH_2Cl_2): 1735, 1710. MS: 240 (1.5, $M^{+\cdot}$), 182 (17.6), 167 (49.4), 43 (100). HR-MS: 240.1389 ($C_{13}H_{20}O_4$, calc. 240.1361).

Oxidation of (±)-Tetrahydrolinalool (**32**). In 3 parallel runs, each time **32** (632 mg, 4 mmol), Zn (2.62 g, 20 equiv.), iron-cluster $Fe_3O(OAc)_6Pyr_{3.5}$ [2] (16 mg), pyridine (28 ml), H_2O (2 ml), and AcOH (4.6 ml) in a 100-ml

conical flask connected to an O_2-filled balloon were stirred for 18 h at r.t. The mixtures were combined, acidified with 25% H_2SO_4 soln., and rapidly extracted with Et_2O. To the Et_2O extracts, a soln. of (2,4-dinitrophenyl)hydrazine [37] (83 ml, 8.3 mmol) was added. The org. layer was washed successively with H_2O, sat. $NaHCO_3$ soln., and H_2O, dried (Na_2SO_4), and evaporated. The unreacted volatile **32** was eliminated under high vacuum (20°/1 Torr). The remaining residue was chromatographed on silica gel with hexane/AcOEt (increasing polarity) affording in the order of elution, **34–36**.

6-Methylheptan-2-one (2,4-Dinitrophenyl)hydrazone (**34**): 120 mg (3.2%). M.p. 81–82° (EtOH; [38]: 79°). MS: 308 ($M^{+\cdot}$).

Acetone (2,4-Dinitrophenyl)hydrazone (**35**): 380 mg (13.3%). M.p. 124° (EtOH; [38]: 124°). MS: 238 ($M^{+\cdot}$), 180.

2-Butanone (2,4-Dinitrophenyl)hydrazone (**36**): 47 mg (1.55%). M.p. 116–117° (EtOH; [38]: 115°). MS: 238 ($M^{+\cdot} - 15 + 1$).

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