45. Identification and Synthesis of New γ-Lactones from Tuberose Absolute *(Polianthes tuberosa)*

by **Bruno Maurer** and **Arnold Hauser**

Firmenich SA, Research Laboratories, CH-1211 Geneva 8

Dedicated to Professor *George Büchi* on the occasion of his 60th birthday

(11.XII.81)

Summary

Six unsaturated γ-lactones, (*Z*)-5-octen-4-olide (**1**), (*Z*)-5-decen-4-olide (**2**), (*Z*)-6-nonen-4-olide (**3**), (*Z*)-6-dodecen-4-olide (**4**), (*Z,Z*)-6,9-dodecadien-4-olide (**5**), and tuberolide (**6**)[1]) have been identified for the first time in tuberose absolute (from *Polianthes tuberosa* L.). All structures were corroborated by synthesis and all, except **3** and **4**, are new.

An improved method for the stereoselective synthesis of (±)-*cis*-bicyclo[4.3.0]-non-3-en-7-one (**23**) by an $AlCl_3$-catalyzed *Diels-Alder* reaction is reported.

1. Introduction. – In the course of analysis of the lactone fraction from tuberose absolute[2]) we identified, in addition to known[3]) γ- and δ-lactones, six new trace constituents (**1–6**). Except for **4** which has been isolated from various natural sources[4]), none of these unsaturated γ-lactones has been reported to occur in nature. This is rather surprising because these lactones are probably degradation products of the ubiquitous linolenic and linoleic acids[5]). The structure of tuberolide (**6**)[1]) is

[1]) The name 'tuberolactone' has been suggested for (*Z,Z*)-2,7-decadien-5-olide [1]. We propose the name 'tuberolide' for the bicyclic lactone **6**. (IUPAC name (1*R**,5*S**,6*R**,*Z*)-6-(2′-pentenyl)-2-oxabicyclo[3.3.0]octan-3-one).

[2]) The absolute of the flowers of the tuberose plant, *Polianthes tuberosa* L. *(Amaryllidaceae)*, is one of the rarest and most valuable perfume materials [2].

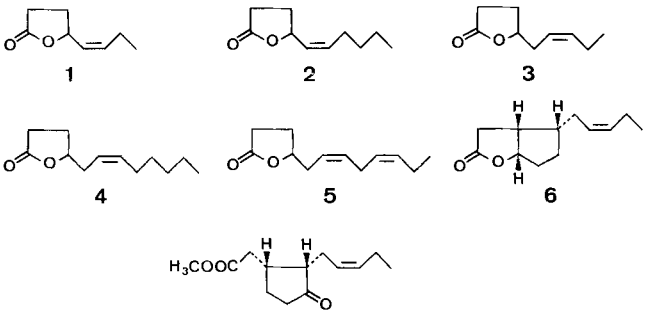
[3]) *Kaiser & Lamparsky* [1] identified (+)-(*R*)-5-decanolide, 2-decen-5-olide (massoia lactone), (+)-(*S,Z*)-7-decen-5-olide (jasmine lactone), (−)-(*R,*7*Z*)-2,7-decadien-5-olide (tuberolactone), 5-undecanolide, 5-dodecanolide, 5-tetradecanolide, 4-octanolide, 4-nonanolide, 4-undecanolide, 4-dodecanolide and coumarin in tuberose absolute.

[4]) (*Z*)-6-Dodecen-4-olide (**4**) has been identified in butter fat [3], the male tarsal scent of black-tailed deer [4], the cultured broth of the microorganism *Sporobolomyces odorus* [5], in lamb flavour from animals fed a lipid-protected dietary supplement [6], and in the pedal gland exudate of the bontebok [7].

[5]) Recently, three closely related unsaturated C_{14}-γ-lactones ((*Z,Z,Z*)-5,8,11-tetradecatrien-4-olide, (*Z,Z*)-5,8-tetradecadien-4-olide and (*Z*)-5-tetradecen-4-olide) were isolated from *Osmanthus* absolute [8].

0018-019X/82/2/0462-15$01.00/0

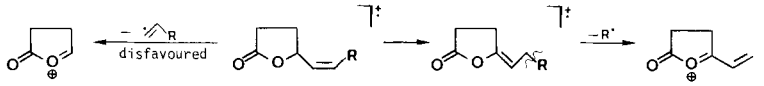
noteworthy because **6** is a cyclic isomer of **5** and at the same time has the C-skeleton of methyl *cis*-(*Z*)-jasmonate.



methyl *cis*-(*Z*)-jasmonate

The structures of the lactones **1**–**6** were indicated by their spectra and corroborated by comparing the chromatographic and spectral data with those of synthetic samples. Sufficient amounts of the lactones **1** and **4**–**6** (*ca.* 0.5–2 mg) could be isolated for recording the IR., ^{1}H-NMR. (360 MHz) and mass spectra, whereas only a mass spectrum (from GC.-MS. coupling) was available for **2** and **3**. None of the samples was large enough to allow the measurement of the optical rotation.

2. Structure elucidations. – *(Z)-5-Octen-4-olide* (**1**). The ^{1}H-NMR. spectrum (12 H) and the mass spectrum (molecular ion at *m/z* 140) indicated the empirical formula $C_8H_{12}O_2$, while the IR. spectrum suggested the presence of a saturated γ-lactone ring (strong absorption at 1780 and 1190 cm^{-1}). The position and geometry of the double bond and the location of the side chain at C(4) were clearly revealed by the 360-MHz-^{1}H-NMR. spectrum (see *Exper. Part*): the coupling constant of 11 Hz between the olefinic protons is typical of a (Z)-double bond and the multiplicities of the signals of H–C(4) and H–C(5) indicated these protons to be adjacent. The 5-position of the double bond was confirmed by the MS. which showed the base peak at *m/z* 111. This ion is typical of 5-alken-4-olides[6]) because α-cleavage (the predominant fragmentation process of simple γ-lactones leading to the characteristic ion (i) at *m/z* 85) is strongly repressed by the presence of a double bond in the 5-position. The formation of a fragment ion at *m/z* 111 may be reasonably explained by assuming the double bond to shift to the 4-position. Loss of R· thus becomes a favourable process and leads to the observed stable ion (ii)[7]).



(i) *m/z* 85

(ii) *m/z* 111 (base peak)

[6]) Except for the lowest member of the series (5-hexen-4-olide) which shows the base peak at *m/z* 112 (molecular ion), all 5-alken-4-olides described in this work have their base peak at *m/z* 111.

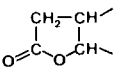
[7]) This view is supported by the fact that 4-nonen-4-olide has the base peak at *m/z* 111.

(Z)-5-Decen-4-olide (**2**). The structure of this lactone was assigned from its MS. which showed the molecular ion at *m/z* 168 and the base peak at *m/z* 111. By analogy with **1**, we assumed the presence of a (*Z*)-double bond in the 5-position.

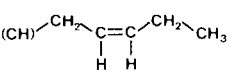
(Z)-6-Nonen-4-olide (**3**). The MS. showed the molecular ion at *m/z* 154 indicating the molecular formula $C_9H_{14}O_2$. The base peak at *m/z* 85 revealed that the double bond was not adjacent to the ring. A (6*Z*)-double bond was thought to be probable for biogenetic reasons.

(Z)-6-Dodecen-4-olide (**4**). The MS. was in agreement with a published spectrum [5] and the 360-MHz-^{1}H-NMR. spectrum fully supported the structure.

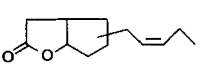
(Z,Z)-6,9-Dodecadien-4-olide (**5**). This structure was deduced from the 360-MHz-^{1}H-NMR. spectrum. Two (*Z*)-double bonds in a 1,4-position, each flanked by two methylene groups, were indicated by the multiplicities of the signals of the olefinic protons and the triplet for C(8) at 2.80 ppm ($J=7$, 2 H). The presence of an ethyl group on a double bond was revealed by the signals at 0.98 (*t*, $J=7.5$, 3 H) and at 2.06 ppm (*qi*, $J=7.5$, 2 H). The MS. showed the base peak at *m/z* 85 and the molecular ion at *m/z* 194 as expected.



A



B



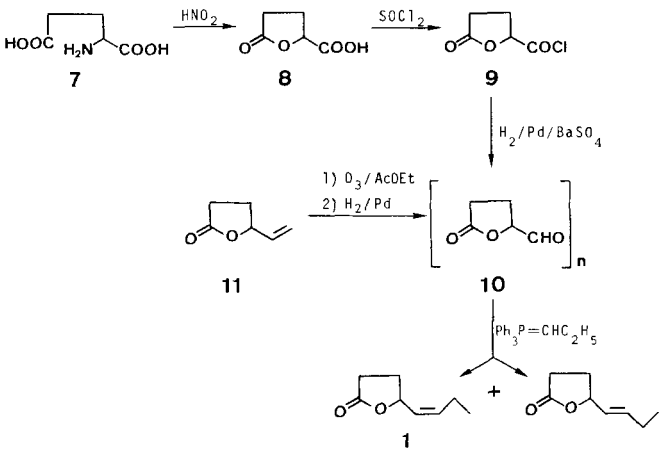
C

(1R,5S*,6R*,Z)-6-(2'-Pentenyl)-2-oxabicyclo[3.3.0]octan-3-one* (tuberolide, **6**). The IR. spectrum (strong absorptions at 1765 and 1195 cm^{-1}) suggested the presence of a saturated γ-lactone ring and the MS. (molecular ion at *m/z* 194) showed the compound to be an isomer of **5**. The 360-MHz-^{1}H-NMR. spectrum revealed the presence of a CO–CH_2–CH–CH–O moiety (verified by decoupling experiments) indicating the presence of a β,γ-disubstituted γ-lactone (**A**). The (*Z*)-2-pentenyl side chain (**B**) attached to a methine C-atom was indicated by signals at 2.12 (*m*, 2 H–C(1')), 5.27 ($t\times t\times d$, $J=7$, 1.5 and 11, H–C(2')), 5.41 ($t\times t\times d$, $J=7$, 1.5 and 11, H–C(3')), 2.04 (*qi*, $J\approx 7.5$, 2 H–C(4')), and 0.97 (*t*, $J=7.5$, 3 H–C(5')). Because the NMR. spectrum shows only one double bond and one methyl group the lactone must be bicyclic with the three remaining C-atoms (not accounted for by the partial structures **A** and **B**) being members of the second ring. This leads to the partial structure **C**. The *cis*-junction of the rings can be safely assumed, because the *trans*-fused lactone is strained and would not form spontaneously during isolation *via* the corresponding hydroxy acid (*cf.* [9], entry 12). The ^{1}H-NMR. spectrum does not reveal with certainty the position and configuration of the side chain. Irradiation at 5.04 (H–C(1)) allowed the assignment of the multiplet at 2.96 to H–C(5) $J(1,5)\approx 6$) and the partly overlapping signal at 1.72 to H_{exo}–C(8) $J(1,8_{exo})\approx 6$). The latter exhibits a large coupling constant ($J(8_{exo}, 8_{endo}) = 15$) typical for geminal H-atoms and thus indicates a methylene group at C(8). The size of the coupling constant $J(5,6)=8$ is in favour of the *endo*-configuration of the substituent at C(6).

3. Syntheses. – *(Z)-5-Alken-4-olides.* (*Z*)-5-Alken-4-olides have not often been described and the only representatives so far isolated from natural sources contain 14 C-atoms[8]). For the synthesis of this class of compounds we explored two methods, both of which allowed the different alkenyl groups to be introduced at a late stage of the synthesis.

In the first approach *(Scheme 1)* the known [10] key step is the *Wittig* reaction of aldehyde **10** with an alkylidenetriphenylphosphorane. The yields of this reaction are low and *ca.* (4:1)-mixtures of (*Z*)- and (*E*)-olefin are obtained even when using lithium salt-free conditions. The lactone-aldehyde **10** has been described only recently as an unstable compound [10] and has never been characterized (see *Exper. Part*). We have prepared the crystalline 2,4-dinitrophenylhydrazone of **10** (n = 1) which showed satisfactory spectral and analytical data. Aldehyde **10** may be prepared in *ca.* 50% overall yield in 3 steps from glutamic acid (**7**) [10] or alternatively, in *ca.* 80% yield, by ozonolysis of 5-hexen-4-olide (**11**)[9]).

Scheme 1



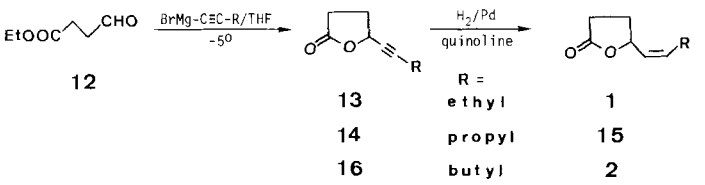
The second approach *(Scheme 2)* involves the reaction of acetylenic *Grignard* reagents with ethyl 4-oxobutanoate (**12**) which is conveniently prepared by ozonolysis of ethyl 4-pentenoate [14]. The reaction of organometallic reagents with oxo-ester **12** is known to produce γ-lactones directly [8] [10a,c] [15] [16] or to give

---

8) (*R,Z*)-5-Tetradecen-4-olide has been identified as a sex attractant for the male Japanese beetle [10a]. The same compound (of unknown absolute configuration) and two closely related lactones have recently been isolated from *Osmanthus* absolute [8], see also *Footnote 5*.

9) Lactone **11** was prepared from (*E*)-1,4-dibromo-2-butene according to [11]. The first attempt to synthesize **11** from 3,4-epoxy-1-butene and diethyl sodiomalonate [12] yielded, instead of the pure lactone **11**, a mixture (inseparable by distillation and GC. on both silicone and *Carbowax* columns) of **11** and the isomeric 3-vinyl-4-butanolide (ratio *ca.* 3:7 by ^{1}H-NMR.). 3,4-Epoxy-1-butene thus reacts with diethyl sodiomalonate preferentially at the secondary allylic position, and not exclusively at the primary position as reported by *Russell et al.* [12]. Our result seems reasonable in view of the fact that the same epoxide reacts with ethyl sodioacetoacetate to give a mixture (*ca.* 1:1) of regioisomeric lactones [13].

Scheme 2

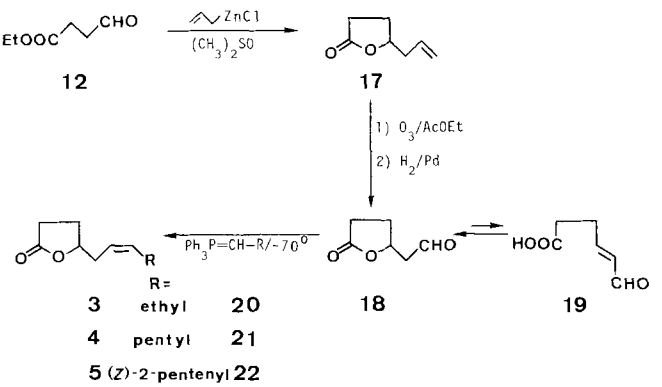


the corresponding ethyl hydroxy-carboxylates [17]. The acetylenic γ-lactones **13**, **14** and **16**, obtained in moderate yields but easily purified *via* the corresponding hydroxy-carboxylates, were hydrogenated over *Lindlar* catalyst to give the corresponding (*Z*)-lactones **1**, **15** and **2** in good yield.

(Z)-6-Alken-4-olides. One member of this series, (*Z*)-6-dodecen-4-olide (**4**, *cf. Footnote 4*), has been synthesized by various methods in its racemic [5] [7] [18–23] and optically active forms [24–26] and (±)-(*Z*)-6-nonen-4-olide (**3**) has been synthesized recently [23]. Of these methods, the *Wittig* reaction of aldehyde **18** [22] *(Scheme 3)* seemed particularly convenient for our series of lactones because the side chains are elaborated in the last step. Furthermore, the *Wittig* reagent **22** required for the synthesis of the diene-lactone **5** is readily synthesized from commercially available (*Z*)-3-hexen-1-ol (leaf alcohol).

Aldehyde **18** was synthesized in two steps from ethyl 4-oxobutanoate (**12**) already used as a starting material in *Scheme 2*. The reaction of **12** with allylzinc chloride in dimethylsulfoxide [27] gave 6-hepten-4-olide (**17**) in 66% yield. The organozinc reagent was superior to allylmagnesium bromide in tetrahydrofuran, reacting selectively with the aldehyde function, whereas the *Grignard* reagent also attacked the ester group. Ozonolysis of **17** followed by catalytic hydrogenation gave aldehyde **18** in good yield. This aldehyde was found to be unstable at room temperature forming an equilibrium mixture containing *ca.* 80% of **18** and *ca.* 20% of the carboxylic acid **19**. At low temperature (−70°), the

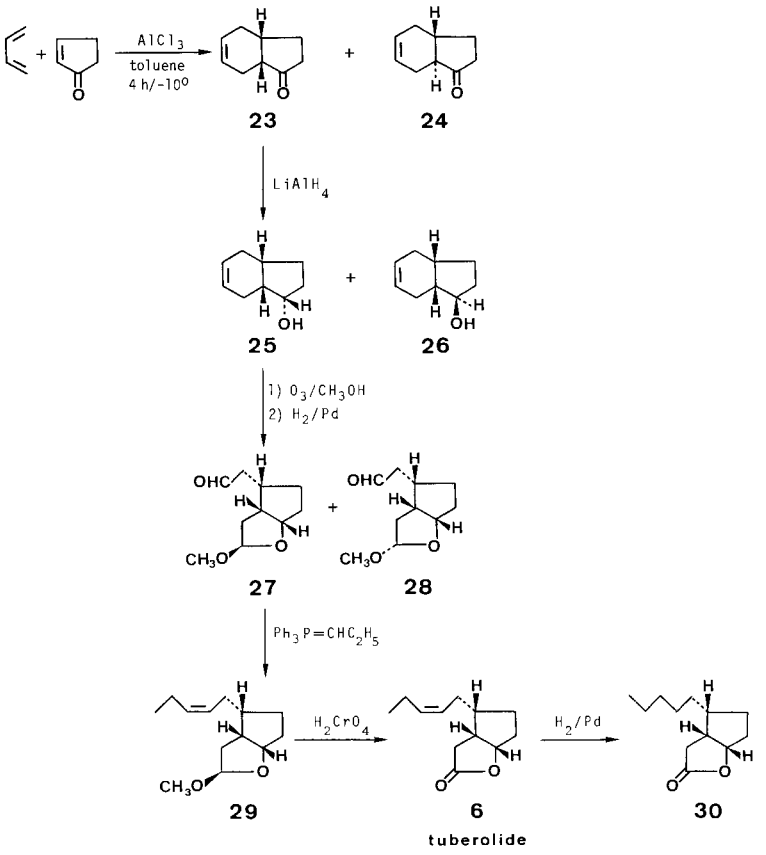
Scheme 3



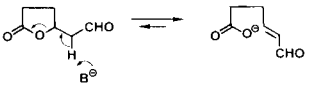
Wittig reaction of **18** afforded the lactones **3**, **4** and **5** in 20–30% yield[10]) with *ca.* 95% (*Z*)-stereoselectivity.

(±)-Tuberolide (**6**). This lactone was synthesized in 4 steps *(Scheme 4)* with high stereoselectivity starting from the *cis*-fused ketone **23** which is easily accessible by the *Diels-Alder* addition of 1,3-butadiene to 2-cyclopentenone using a modified literature procedure [28]. If the $AlCl_3$-catalyzed *Diels-Alder* addition is run under mild conditions (temperature $<20°$), epimerization of **23** to the *trans*-ketone **24**

Scheme 4



[10]) This only moderate yield may be explained by a competing base-catalyzed β-elimination leading to the formation of the carboxylate anion of **19**:



18

hardly occurs[11]). Our method of preparing **23** compares favourably with a recently published two step procedure [29].

Reduction of the *cis*-ketone **23** with lithium aluminium hydride gave a mixture of epimeric alcohols **25** and **26** (ratio 4:1). As expected, hydride addition occurred preferentially from the convex face of **23** to give the desired *endo*-alcohol **25** as the major product. The mixture of **25** and **26** was ozonized at $-70°$ in methanol to give, after catalytic hydrogenation, a mixture of epimeric monoacetals **27** and **28** (ratio 4:1). Chromatography of this mixture on silica gel allowed some impurities[12]) to be removed and **27** and **28** to be partially separated[13]), *cis*-Olefination [30] of pure **27** with triphenylpropylidenephosphorane yielded the (*Z*)-olefin **29** which was converted in 50% yield to (±)-tuberolide (**6**) with chromic acid. To facilitate assignment of the ^{13}C-NMR. signals of **6**, we prepared the dihydro-derivative **30** by catalytic hydrogenation. Dihydrotuberolide (**30**) could not be detected in the lactone fraction of tuberose absolute despite a specific search by GC.-MS.

The title compounds **1–6** may well contribute to the rich, heavy floral odour of tuberose absolute despite their low concentrations (*ca.* 0.001–0.01%). The more volatile lactones **1–3** have a strong smell reminiscent of the corresponding saturated γ-lactones, whereas the C_{12}-lactones **4** and **5** have long-lasting, slightly fatty-aldehydic notes. (±)-Tuberolide (**6**) and its dihydro-derivative **30** display weaker but tenacious lactonic odours.

Experimental Part

(with the valuable collaboration of Miss *M. Krauer* and Mr. *J.-C. Froidevaux*)

1. General remarks. See [31].

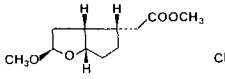
2. Isolation from tuberose absolute. – From concrete of tuberose[14]) (250 g, of Indian origin) an absolute was freshly prepared by stirring with 2.5 l of ethanol for 3 h at 40°. After the addition of 250 g of *Celite* as a filter aid, the suspension was chilled to $-20°$ for 2 h and the insoluble fats were filtered off with suction through a pre-cooled glass filter funnel. The solid was washed with cold ethanol ($-20°$, 500 ml) and the combined filtrates left overnight at $-20°$. A further fraction of insoluble fats was removed by filtration through *Celite* and the filtrate was distilled at 50° (bath)/120 Torr through a packed column in order to remove ethanol. Tuberose absolute (90 g, 36%) was obtained as a yellow, mobile oil.

The absolute (35.0 g) was distilled (bulb-to-bulb) to give 25.4 g of a distillate (boiling range 20–170°/0.1 Torr) which was dissolved in ethanol (100 ml) and 5% aq. Na_2CO_3-solution (250 ml). The mixture was stirred for 2 days at 20° and the bulk of ethanol was removed by distillation at 20 Torr (bath temp. 35°). The alkaline aq. solution was washed by continuous extraction with ether (24 h), then carefully acidified with 30% aq. H_2SO_4-solution, saturated with NH_4Cl and continuously

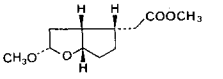
---

[11]) *Wenkert et al.* [28] obtained 85% of a mixture of **23** and **24** (45:55) using the same conditions except for the temperature (16 h at 70°).

[12]) The crude mixture contained *ca.* 20% of four impurities which have been identified by their spectral data (see *Exper. Part*) as the methyl esters **31** and **32** (ratio *ca.* 3:1) and traces of the dimethyl acetals of the aldehydes **27** and **28**.



31



32

[13]) This separation is not necessary as both aldehydes **27** and **28** are converted to the same lactone **6** in the last two steps.

[14]) The petroleum ether extract of the flowers of *Polianthes tuberosa*.

extracted with ether (24 h). This ether extract (2.9 g) containing acids and lactones was distilled (bulb-to-bulb) to give 2.7 g of a fraction which was chromatographed on silica gel (40 g). Petroleum ether b.p. 50–70° (PE)/ether 7:3 eluted 1.62 g of lactones with 5-decanolide and jasmine lactone making up >95% of the mixture. The bulk of the free acids remained absorbed on the silica gel. The lactone fraction, after a short treatment with diazomethane in ether to convert acids to methyl esters, was chromatographed on silica gel (400 g) with PE/ether 7:3→2:8. The following fractions were obtained.

A) 124 mg (eluted with 1 l of PE/ether 7:3), mainly methyl anthranilate; not further investigated.

B) 5 mg (eluted with *ca.* 100 ml of the same solvent) containing (among other compounds) *ca.* 50% of methyl N-acetylanthranilate and 30% of tuberolide (**6**). The latter was obtained pure (*ca.* 1 mg) by prep. GC. (*Carbowax*, 230°). It had the same retention time (t_R) and the same spectral data (IR., ^{1}H-NMR., MS.) as the synthetic material.

C) 17 mg (eluted with *ca.* 300 ml of PE/ether 6:4) containing the main components 4-decanolide (10%), **4** (20%) and **5** (60%). The two latter were obtained in pure form by prep. GC. (*Carbowax*, 230°) and had the same t_R and the same spectral data (IR., ^{1}H-NMR., MS.) as synthetic samples.

D) 26 mg (eluted with *ca.* 500 ml of PE/ether 6:4) containing the main components **5** (*ca.* 40%), 5-decanolide (*ca.* 20%), jasmine lactone (*ca.* 20%), and **1** (*ca.* 10%). The latter was isolated by prep. GC. (*Carbowax*, 150–230°) and showed identical t_R and the same spectral data (IR., ^{1}H-NMR., MS.) as a synthetic sample. Analysis of this fraction by GC.-MS. revealed, in addition, the presence of 4-octanolide, 4-nonanolide, **3**, 4-decanolide, **2**, massoia lactone, tuberolactone, 5-undecanolide, and 5-dodecanolide (in order of t_R on a *UCON* capillary column). These compounds were identified by comparing their t_R and MS. with those of authentic samples.

E) 1.38 g (eluted with 1 l of PE/ether 2:8, 1 l of ether and 1 l of ether/methanol 8:2): mainly jasmine lactone (*ca.* 70%) and 5-decanolide (*ca.* 30%), containing only traces of other lactones.

3. Synthesis of (±)-(*Z*)-5-alken-4-olides. – 3.1. *By* Wittig *reaction of aldehyde* **10** *(Scheme 1).* – 3.1.1. *Preparation of (±)-5-oxo-4-pentanolide* (**10**) *from glutamic acid* (7) [10]. A suspension of Pd on $BaSO_4$ (5%, *Fluka*, 3.0 g) in dry toluene (500 ml) was heated under reflux and *ca.* 100 ml of toluene were slowly distilled to remove traces of water from the reaction flask. After cooling to RT., freshly distilled (±)-4-chloroformyl-4-butanolide (**9**)[15]) (6.60 g, 44.4 mmol) was added. The mixture was heated to 70° with efficient stirring and H_2 was bubbled through the solution. The evolution of HCl was monitored by passing the effluent gasses through water and titrating the hydrochloric acid with 1N NaOH-solution. After 2 days, 43 mmol of HCl had formed. The mixture was cooled, the catalyst removed by filtration through *Celite* and washed with CH_2Cl_2. The filtrate was evaporated and the residue distilled (bulb-to-bulb, 150° (oven)/0.01 Torr) to give a viscous liquid (4.05 g, 80%). Although the product showed a single peak by GC. (silicone, 165°) the spectral data were *not* in agreement with the monomeric structure **10** (n = 1). The ^{1}H-NMR. spectrum (360 MHz) of a freshly collected sample (by GC.) exhibited signals at 9.78 (*d*, $J \approx 1$) and 4.84 (*d*×*d*×*d*, $J \approx 8$, 6 and 1) (monomer of **10**, *ca.* 50%) and at 4.50–4.66 (br.) and 5.06–5.20 (br.) (oligomer of **10**, *ca.* 50%); after a few hours, the signals of the free aldehyde had practically disappeared, but injection of this solution into a GC. (165°) regenerated the monomer of **10**. In order to characterize **10**, we prepared its 2,4-dinitrophenylhydrazone (m.p. 173–176° decomp.) which had satisfactory analytical data.

$C_{11}H_{10}N_4O_6$ (294.22) Calc. C 44.90 H 3.43 N 19.04% Found C 44.56 H 3.32 N 18.87%

^{1}H-NMR. (360 MHz) *of* **10***-2,4-dinitrophenylhydrazone:* 2.44 (*m*, 1H); 2.54–2.70 (br., 3H); 5.24 (*t*×*d*, J = 7 and 5, 1H, H–C(4)); 7.55 (*d*, J = 5, 1H, H–C(5)); 7.93 (*d*, J = 10, 1H, H–C(6′)); 8.37 (*d*×*d*, J = 10 and 2.5, 1H, H–C(5′)); 9.14 (*d*, J = 2.5, 1H, H–C(3′)); 11.18 (br. *s*, 1H, H–N).

3.1.2. *Preparation of (±)-5-oxo-4-pentanolide* (**10**) *from 5-hexen-4-olide* (**11**)[9]). A solution of lactone **11** [11] (1.12 g, 10 mmol) in ethyl acetate (80 ml) was ozonized at –70° until the blue colour persisted. The solution was purged with Ar and was allowed to warm to RT. The catalyst (100 mg of Pd/C 10%, *Fluka*) was added and the solution was stirred in a hydrogen atmosphere until no more hydrogen was absorbed (2 h). After removing the catalyst by filtration, the solvent was evaporated and the product distilled (bulb-to-bulb, 150° (oven)/0.01 Torr) to give 0.95 g (83%) of **10** showing the above-mentioned behaviour and ^{1}H-NMR. spectrum.

---

[15]) Prepared from (±)-glutamic acid (**7**) according to [10b].

3.1.3. *Preparation of (±)-(Z)-5-octen-4-olide* (**1**). To a stirred solution of distilled aldehyde **10** (7.07 g, 62 mmol) in dry THF (50 ml) was added within 30 min at 0° a solution of triphenylpropylidenephosphorane (62 mmol), prepared by the sodium amide method [30] in toluene. The mixture was stirred overnight at RT., poured on ice, extracted with ether and the extract concentrated. The residue was treated with pentane and the insoluble phosphorus compounds were removed by filtration. After evaporation of the solvent the product was distilled (bulb-to-bulb, 85° (oven)/0.01 Torr) to give 2.97 g (34%) of a mixture of the (*Z*)-lactone **1** and its (*E*)-isomer (ratio *ca.* 4:1 by NMR.). The mixture was partially separated by chromatography (twice) on silica gel/$AgNO_3$ (10%) using PE/ether 7:3 as eluent. Analytically pure (*Z*)-lactone **1** (1.3 g, 15%) was obtained as an oil. – IR. (neat): 3025 *S*, 2970*s*, 2945*m*, 2885*m*, 1780*s*, 1665*m*, 1470*m*, 1430*m*, 1335*m*, 1300*m*, 1230*m*, 1190*s*, 1170 *S*, 1135*m*, 1025*m*, 985*m*, 925*m*, 820*m*. – ^{1}H-NMR. (360 MHz): 1.02 (*t*, J=7.5, 3 H, 3 H–C(8)); 1.95 (*m*, 1H, H–C(3)); 2.14 (*m*, 2 H, 2 H–C(7)); 2.38 (*m*, 1H, H–C(3)); 2.56 (*m*, 2 H, 2 H–C(2)); 5.26 (*qa*, $J\approx$8, 1 H, H–C(4)); 5.43 (*t*×*d*×*d*, J= 1, 11 and 8, 1H, H–C(5)); 5.68 (*t*×*d*, J=7.5 and 11, 1H, H–C(6)). – ^{13}C-NMR. (22.63 MHz): 14.2 (*qa*, C(8)); 21.2 (*t*, C(7)); 29.0 (*t*, C(2) or C(3)); 29.4 (*t*, C(3) or C(2)); 76.4 (*d*, C(4)); 126.9 (*d*, C(6)); 137.4 (*d*, C(5)); 177.2 (*s*, C(1)). – MS.: 140 (9, M^+), 111 (100), 85 (24), 83 (16), 81 (20), 67 (10), 57 (11), 56 (31), 55 (30), 41 (24), 39 (16), 29 (27), 27 (22).

3.2. *By* Grignard *reaction of oxo-ester* **12** *(Scheme 2).* – 3.2.1. *Preparation of (±)-5-octyn-4-olide* (**13**). To a solution of ethyl 4-oxobutanoate (**12**) [14] (6.5 g, 50 mmol) in dry THF (50 ml) was added dropwise with stirring at 15–20° (cooling) a solution of 1-butynylmagnesium bromide [32] (*ca.* 60 mmol) in THF (120 ml). Stirring at RT. was continued for 1 h and the mixture was poured onto ice. The mixture was acidified with 2N HCl, saturated with NaCl and extracted with ether (3×200 ml). After evaporation of the solvent, the crude product (6.35 g) was dissolved in ether (50 ml) and the solution was stirred vigorously with 30 ml of 10% of aq. NaOH-solution at RT. for 1 h. The aq. phase was washed with ether, acidified with conc. hydrochloric acid, stirred for 1 h, saturated with NaCl and extracted with ether. The ether extract (2.6 g) was distilled (bulb-to-bulb, 80–110° (oven)/0.1 Torr) to give 1.4 g (20%) of the pure lactone **13**. – IR. (neat): 2280*m*, 1785*s*, 1195*s*, 1160*s*. – ^{1}H-NMR. (60 MHz): 1.12 (*t*, J=7.5, 3 H, 3 H–C(8)); 2.02–2.85 (br., 6 H); 5.12 (*m*, 1H, H–C(4)). – MS.: 138 (2, M^+), 96 (47), 95 (100), 83 (33), 81 (26), 79 (61), 77 (42), 67 (16), 56 (59), 55 (30), 53 (32), 51 (16), 39 (47).

3.2.2. *Preparation of (±)-(Z)-5-octen-4-olide* (**1**). A solution of the acetylenic lactone **13** (1.38 g, 10 mmol) in cyclohexane (40 ml) was stirred in a H_2-atmosphere in the presence of 200 µl of quinoline and 100 mg of *Lindlar* catalyst. After 3 h *ca.* 230 ml of H_2 were absorbed. The catalyst was removed by filtration and the product distilled (bulb-to-bulb, 80–90° (oven)/0.1 Torr) to give 1.20 g (85%) of the (*Z*)-lactone **1**. The product was free of any (*E*)-isomer and was identical with the lactone obtained by the *Wittig* reaction.

3.2.3. *Preparation of (±)-5-nonyn-4-olide* (**14**). To a solution of ethyl 4-oxobutanoate (**12**) [14] (6.5 g, 50 mmol) in dry THF (50 ml) was added dropwise at −5–0° a solution of 1-pentynylmagnesium bromide [32] (*ca.* 70 mmol) in dry ether (120 ml). Stirring was continued for 2 h at RT. and the mixture was treated as described for the homologue **13**. After distillation (bulb-to-bulb, 100° (oven)/0.1 Torr), 5.0 g (65%) of practically pure **14** were obtained as a liquid. – IR. (neat): 2275*m*, 1780*s*, 1195*s*, 1160*s*. – ^{1}H-NMR. (60 MHz): 0.97 (*t*, $J\approx$7, 3 H, 3 H–C(9)); 1.55 (*qa*×*t*, $J\approx$7 and 6.5, 2 H, 2 H–C(8)); *ca.* 2.00–2.85 (br., 6 H); 5.12 (*m*, 1H, H–C(4)). – MS.: 152 (<1, M^+), 124 (36), 109 (46), 97 (42), 95 (100), 79 (50), 77 (61), 56 (81), 55 (39), 41 (38), 39 (47), 29 (38), 27 (47).

3.2.4. *Preparation of (±)-(Z)-5-nonen-4-olide* (**15**). Catalytic hydrogenation of **14** as described in *Section 3.2.2* for the hydrogenation of **13** gave the pure (*Z*)-lactone **15** in 93% yield. – IR. (neat): 1780*s*, 1670*w*, 1190*s*, 1170*s*. – ^{1}H-NMR. (60 MHz): 0.92 (*t*, $J\approx$7, 3 H, 3 H–C(9)); 1.43 (*m*, 2 H, 2 H–C(8)); 1.9–2.73 (br., 6 H); 5.05–5.90 (br., 3 H). – MS.: 154 (4, M^+), 111 (100), 98 (19), 94 (20), 85 (20), 81 (17), 57 (22), 56 (26), 55 (28), 41 (33), 39 (17), 29 (22), 27 (21).

3.2.5. *Preparation of (±)-5-decyn-4-olide* (**16**). As described in *Section 3.2.3* by addition of 1-hexynylmagnesium bromide [32] to the oxo-ester **12** in THF at −5–0°. – IR. (neat): 2270*m*, 1780*s*, 1190*s*, 1155*s*. – ^{1}H-NMR. (60 MHz): 0.90 (distorted *t*, 3 H, 3 H–C(10)); 1.15–1.75 (br., 4 H); 2.0–2.9 (br., 6 H); 5.13 (*m*, 1H, H–C(4)). – MS.: 166 (<1, M^+), 137 (70), 124 (60), 111 (73), 85 (85), 81 (64), 79 (100), 77 (62), 56 (99), 55 (63), 41 (79), 39 (67), 27 (77).

3.2.6. *Preparation of (±)-(Z)-5-decen-4-olide* (**2**). Catalytic partial hydrogenation of **16** as described in *Section 3.2.2* for the reduction of **13** gave the pure (*Z*)-lactone **2** in 90% yield. The product had the same t_R and MS. as the natural compound. – IR. (neat): 3025 *S*, 2975*s*, 2950*s*, 2890*m*, 1780*s*, 1665*m*, 1465*m*, 1430*m*, 1385*w*, 1335*m*, 1300*m*, 1225*m*, 1190*s*, 1170 *S*, 1130*m*, 1020*m*, 990*m*, 920*m*, 820*m*. –

^{1}H-NMR. (60 MHz): 0.90 (distorted *t*, $J \approx 7$, 3 H, 3 H–C(10)); 1.10–1.60 (br., 4 H); 1.70–2.73 (br., 6 H); 5.05–5.90 (br., 3 H). – ^{13}C-NMR. (22.63 MHz): 13.9 (*qa*, C(10)); 22.2 (*t*, C(9)); 27.6 (*t*, C(7)); 29.0 (*t*, C(2) or C(3)); 29.4 (*t*, C(3) or C(2)); 31.6 (*t*, C(8)); 76.4 (*d*, C(4)); 127.4 (*d*, C(6)); 135.7 (*d*, C(5)); 177.0 (*s*, C(1)). – MS.: 168 (9, M^+), 125 (24), 111 (100), 85 (26), 81 (25), 79 (23), 68 (27), 57 (23), 56 (31), 55 (34), 41 (49), 29 (24), 27 (26).

4. Synthesis of (±)-(*Z*)-6-alken-4-olides *(Scheme 3).* – 4.1. *Preparation of (±)-6-hepten-4-olide* (**17**). To a suspension of activated zinc dust [33] (15 g, 0.23 mol) in DMSO (20 ml) was added in small portions with stirring at RT. a solution of allyl chloride (10.8 ml, 0.13 mol) in DMSO (50 ml) at such a rate that the temp. of the reaction mixture did not exceed 40°. The mixture was stirred for 2 h at RT., then the zinc allowed to settle overnight, and the clear solution was decanted into a dropping funnel. This solution of allylzinc chloride (*ca.* 0.13 mol in DMSO) was added within 1 h to a stirred solution of ethyl 4-oxobutanoate (**12**) [14] (13.0 g, 0.10 mol) in 50 ml of dry THF at 0–5°. The mixture was stirred at RT. for 1 h, poured onto ice, acidified with 30% aq. H_2SO_4-solution, saturated with NH_4Cl and extracted with ether (2 × 200 ml) and ethyl acetate (200 ml). The combined extracts were evaporated and the residue (14.8 g) was stirred for 1 h with a mixture of ether (100 ml) and 2N aq. NaOH (100 ml) at RT. The aq. layer was washed with ether, acidified with 30% aq. H_2SO_4-solution, saturated with NH_4Cl and extracted with ethyl acetate. The crude extract (11.0 g) was distilled (bulb-to-bulb, 70–80° (oven)/0.05 Torr) to give 8.3 g (66%) of the pure lactone **17**. – IR. (neat): 3080*m*, 1775*s*, 1640*m*, 1180*s*, 990*m*, 920*m*. – ^{1}H-NMR. (60 MHz): 1.70–2.70 (br., 6 H); 4.57 (*qi*, $J \approx 6.5$, 1 H, H–C(4)); 4.95–5.35 (*m*, 2 H, 2 H–C(7)); 5.82 (*m*, 1 H, H–C(6)). – MS.: 156 (0, M^+), 86 (2), 85 (100), 57 (16), 56 (4), 55 (2), 43 (8), 41 (14), 39 (9), 29 (41), 27 (9).

4.2. *Preparation of (±)-6-oxo-4-hexanolide* (**18**) *and (E)-6-oxo-4-hexenoic acid* (**19**). Ozonized oxygen was passed through a solution of the unsaturated lactone **17** (14.0 g, 0.111 mol) in ethyl acetate (400 ml) at −70° until the blue colour persisted. The solution was allowed to warm to −10° while Ar was bubbled through. The catalyst (1.0 g of 10% Pd/C) was added at −10° and hydrogenation was started. The exothermic reaction was controlled by cooling with an ice-bath (the temp. was not allowed to exceed 20°). After the uptake of 1.74 l of hydrogen (70%), the absorption ceased and the peroxide test was negative. The catalyst was removed by filtration through *Celite* and the filtrate evaporated and distilled (bulb-to-bulb, 120° (oven)/0.02 Torr) to give 11.6 g (81%) of an oil. GC. analysis on both silicone and *Carbowax* columns showed a single broadened peak, but the IR.- and ^{1}H-NMR. spectrum indicated the presence of both **18** and **19** (ratio *ca.* 4:1) in this mixture. – IR. ($CHCl_3$): 3600–2500*w* (br., COOH of **19**), 2740*m* (CHO of **18** and **19**), 1770*s* (C=O of γ-lactone of **18**), 1720*s* (C=O of saturated aldehyde of **18**), 1680*m* (C=O of unsaturated aldehyde of **19**), 1640*w* (C=C of **19**). It was noticed that in a freshly distilled sample the bands assigned to **19** decreased markedly in intensity when the IR. spectrum of the same solution was recorded a second time after 20 h at RT. – ^{1}H-NMR. (90 MHz, recorded 1 day after distillation): 1.71–3.27 (several *m*); 4.96 (*m*, H–C(4) of **18**); 6.15 (*d* × *d*, $J = 15$ and 7, H–C(5) of **19**); 6.88 (*t* × *d*, $J = 5$ and 15, H–C(4) of **19**); 9.50 (*d*, $J = 7$, H–C(6) of **19**); 9.78 (br. *s*, H–C(6) of **18**); *cf.* [22].

4.3. *Preparation of (±)-(Z)-6-nonen-4-olide* (**3**) [23]. To a stirred solution of the (4:1)-mixture of **18** and **19** (2.56 g, 20 mmol) in dry toluene (100 ml), chilled to −70°, was added dropwise (2 h) a salt-free solution of triphenylpropylidenephosphorane (**20**) (20 mmol in 60 ml toluene, prepared by the sodium amide method [30]). The red colour of the ylide disappeared immediately. The solution was allowed to warm to RT. and was stirred for 30 min. The solvent was evaporated *in vacuo* and the residue distilled (bulb-to-bulb, 100–170° (oven)/0.01 Torr). The distillate (1.14 g) was chromatographed on a silica gel column (100 g) with PE/ether 1:1 to give, after distillation, 0.95 g (31%) of the (*Z*)-lactone **3** as an oil (purity 95%, contains *ca.* 5% of the (*E*)-isomer). – IR. (neat): 3020*m*, 2980*s*, 2955*m*, 2900*m*, 1780*s*, 1670*w*, 1475*m*, 1440*w*, 1365*m*, 1305*w*, 1195*s*, 1045*m*, 940*m*, 820*w*. – ^{1}H-NMR. (60 MHz): 0.97 (*t*, $J = 7$, 3 H, 3 H–C(9)); 1.70–2.67 (br., 8 H); 4.47 (*qi*, $J \approx 6.5$, 1 H, H–C(4)); 5.38 (symmetrical *m*, 2 H, H–C(6) and H–C(7)). – ^{13}C-NMR. (90.58 MHz): 14.0 (*qa*, C(9)); 20.8 (*t*, C(8)); 27.2 (*t*, C(3)); 28.7 (*t*, C(2)); 32,8 (*t*, C(5)); 80.2 (*d*, C(4)); 121.7 (*d*, C(6)); 135.7 (*d*, C(7)); 176.9 (*s*, C(1)). – MS.: 154 (2, M^+), 94 (9), 86 (3), 85 (100), 81 (1), 79 (1), 69 (1), 57 (7), 55 (2), 41 (10), 39 (4), 29 (26), 27 (6).

4.4. *Preparation of (±)-(Z)-6-dodecen-4-olide* (**4**). A solution of BuLi (2.3 M in hexane, 13 ml, 30 mmol) was added within 10 min to a stirred suspension of hexyltriphenylphosphonium bromide (12.8 g, 30 mmol) in dry toluene (120 ml) at −70°. After the addition, the solution was allowed to warm to RT., stirred for 1 h, and allowed to settle. The red solution of the ylide **21** was decanted from

insoluble LiBr into a dropping funnel. This solution was added dropwise (1 h) to a stirred solution of the (4:1)-mixture of **18** and **19** (2.56 g, 20 mmol) in dry toluene (100 ml) at −70°. The mixture was stirred for 1 h at RT., the solvent evaporated and the residue distilled (bulb-to-bulb, 100–160° (oven)/0.05 Torr). The distillate (1.2 g) was purified by chromatography on silica gel (PE/ether 1:4) to give, after bulb-to-bulb distillation, 850 mg (21%) of the (*Z*)-lactone **4**, containing less than 5% of the (*E*)-isomer. – IR. (neat): 3025*m*, 2950*m*, 2920*s*, 1780*s*, 1465*m*, 1360*m*, 1185*s*, 1040*m*, 930*m*. – ^{1}H-NMR. (360 MHz): 0.89 (*t*, *J*=7, 3 H, 3 H–C(12)); 1.24–1.41 (br., 6 H, 2 H–C(9), 2 H–C(10) and 2 H–C(11)); 1.90 (*m*, 1 H, H–C(3)); 2.04 (br. *qa*, *J*≈7, 2 H, 2 H–C(8)); 2.30 (*d*×*d*×*d*×*d*, *J*=13, 8, 7 and 6, 1 H, H–C(3)); 2.45 (*m*, partly overlapping, 2 H, 2 H–C(5)); 2.53 (*m*, overlapping, 2 H, 2 H–C(2)); 4.52 (*qi*, *J*≈6.5, 1 H, H–C(4)); 5.36 (*t*×*t*×*d*, *J*=7, ≈1 and 11, 1 H, H–C(6)); 5.58 (*t*×*t*×*d*, *J*=7, ≈1 and 11, 1 H, H–C(7)). – ^{13}C-NMR. (22.63 MHz): 14.0 (*qa*, C(12)); 22.5 (*t*, C(11)); 27.2 (*t*, C(3)); 27.4 (*t*, C(8)); 28.7 (*t*, C(2)); 29.1 (*t*, C(9)); 31.5 (*t*, C(10)); 32.9 (*t*, C(5)); 80.2 (*d*, C(4)); 122.3 (*d*, C(6)); 134.0 (*d*, C(7)); 177.0 (*s*, C(1)). – MS.: 196 (2, M^+), 96 (6), 86 (3), 85 (100), 81 (3), 67 (3), 57 (6), 55 (7), 54 (3), 41 (13), 39 (3), 29 (28), 27 (7); identical with the MS. in [5].

4.5. *Preparation of (±)-(Z,Z)-6,9-dodecadien-4-olide* (**5**). – 4.5.1. *Preparation of (Z)-1-bromo-3-hexene* (*cf.* [34]). A solution of (*Z*)-3-hexenyl *p*-toluenesulfonate [34] (60 g, 0.236 mol) in dry acetone (800 ml) was stirred with dry LiBr (28.8 g, 0.33 mol) under reflux for 5 h. The solids were removed by filtration, the bulk of acetone distilled and replaced by PE (50–70°). The suspension was filtered and the solvent evaporated from the filtrate. The residue was distilled through a *Vigreux* column to give 34.6 g (90%) of (*Z*)-1-bromo-3-hexene, b.p. 55–56°/35 Torr. The stereochemical purity by GC. (silicone oil) was *ca.* 95%.

4.5.2. Wittig *reaction of* **18/19** *with (Z)-3-hexenylidenetriphenylphosphorane* (**22**). In a 100-ml round-bottomed flask (*Z*)-1-bromo-3-hexene (28.6 g, 0.175 mol) and triphenylphosphine (44.5 g, 0.170 mol) were heated to 110° with magnetic stirring. The mixture became homogeneous but soon began to crystallize. Heating at 110° was continued for 5 h. The solid mixture was cooled to RT., powdered, washed several times with ether and dried at 0.1 Torr. The yield of (*Z*)-3-hexenyltriphenylphosphonium bromide was 70.2 g (97%), m.p. 160–162°. The product contained *ca.* 10% of the (*E*)-isomer by ^{1}H-NMR. – ^{1}H-NMR. (360 MHz): 0.84 (*t*, *J*=7.5, 3 H, 3 H–C(6)); 1.80 (*qi*, *J*=7.5, 2 H, 2 H–C(5)); 2.45 (*m*, 2 H, 2 H–C(2)); 3.89 (*m*, 2 H, 2 H–C(1)); 5.37 (*m*, 1 H, H–C(4)); 5.50 (*m*, 1 H, H–C(3)); 7.67–7.89 (several *m*, 15 H, aromat. H). The (*E*)-isomer is easily recognized by the quintuplet for 2 H–C(5) at 1.89 ppm (the other protons have almost the same chemical shifts as the (*Z*)-isomer).

To a stirred suspension of this phosphonium salt (6.36 g, 15 mmol) in toluene (60 ml) was added at −70° a solution of BuLi (2.3 M in hexane, 6.5 ml, 15 mmol). The mixture was allowed to warm to RT., and after 30 min, the red solution of the ylide **22** was decanted from insoluble salts and added, at −70°, to a (4:1)-mixture of **18** and **19** under the conditions described for **4**. The crude lactone **5** (after distillation) was obtained in 77% yield and consisted of *ca.* 80% of **5**, *ca.* 10% of the (6*Z*,9*E*)-isomer and *ca.* 10% of unidentified impurities. Chromatography on silica gel (120 g) with PE/ether 6:4 removed the impurities but did not separate the geometrical isomers. They were separated by repeated chromatography on $AgNO_3$-impregnated (10%) silica gel using PE/ether 8:2→1:9 as eluent. The (*Z*,*Z*)-isomer **5** was eluted after the (*Z*,*E*)-isomer on both silica gel/$AgNO_3$ and GC. (silicone oil) columns and was obtained in pure form (oil) in 19% yield (with respect to **18**+**19**). – IR. (neat): 3025*m*, 2975*s*, 1775*s*, 1650*w*, 1465*m*, 1355*m*, 1220*m*, 1180*s*, 1150*m*, 1030*m*, 925*m*, 805*w*. – ^{1}H-NMR. (360 MHz): 0.98 (*t*, *J*=7.5, 3 H, 3 H–C(12)); 1.91 (*t*×*d*×*d*, *J*=9.5, 13 and ≈7, 1 H, H–C(3)); 2.06 (*qi*, *J*=7.5, 2 H, 2 H–C(11)); 2.30 (*d*×*d*×*d*×*d*, *J*=13, 8, 7 and 6, 1 H, H–C(3)); 2.49 (*m*, partly overlapping, 2 H, 2 H–C(5)); 2.53 (*m*, overlapping, 2 H, 2 H–C(2)); 2.80 (*t*, *J*=7, 2 H, 2 H–C(8)); 4.54 (*qi*, *J*≈6.5, 1 H, H–C(4)); 5.28 (*t*×*t*×*d*, *J*=7, 1 and 11, 1 H, H–C(9)); 5.38 (*m*, overlapping, 1 H, H–C(6)); 5.41 (*m*, overlapping, 1 H, H–C(10)); 5.57 (*t*×*t*×*d*, *J*=7, 1 and 10.5, 1 H, H–C(7)). – ^{13}C-NMR. (90.58 MHz): 14.2 (*qa*, C(12)); 20.6 (*t*, C(11)); 25.7 (*t*, C(8)); 27.2 (*t*, C(3)); 28.7 (*t*, C(2)); 32.9 (*t*, C(5)); 80.1 (*d*, C(4)); 122.6 (*d*, C(6)); 126.3 (*d*, C(9)); 132.3 (*d*, C(7) or C(10)); 132.4 (*d*, C(10) or C(7)); 177.0 (*s*, C(1)). – MS.: 194 (3, M^+), 94 (45), 93 (13), 85 (100), 81 (12), 80 (12), 79 (36), 67 (18), 55 (17), 41 (20), 39 (11), 29 (46), 27 (12).

Spectral data of (±)-(6Z,9E)-6,9-dodecadien-4-olide ((6Z,9E)-isomer of **5**). – IR. (neat): 3025 *S*, 2975*s*, 1775*s*, 1650*w*, 1460*m*, 1355*m*, 1220*w*, 1180*s*, 1150*m*, 1030*m*, 975*m*, 925*m*, 805*w*. – ^{1}H-NMR. (360 MHz): 0.97 (*t*, *J*=7.5, 3 H, 3 H–C(12)); 1.91 (*t*×*d*×*d*, *J*=9.5, 13 and ≈7, 1 H, H–C(3)); 2.01 (*m*, 2 H, 2 H–C(11)); 2.30 (*d*×*d*×*d*×*d*, *J*=13, 8, 7 and 6, 1 H, H–C(3)); 2.47 (*m*, partly overlapping, 2 H, 2 H–C(5)); 2.53 (*m*, overlapping, 2 H, 2 H–C(2)); 2.75 (*t*, *J*≈7, 2 H, 2 H–C(8)); 4.54 (*qi*, *J*≈6.5,

1 H, H–C(4)); 5.30–5.53 (*m*, 3 H, H–C(6), H–C(9) and H–C(10)); 5.61 (*t*×*t*×*d*, *J* = 7, ≈ 1.5 and 11, 1 H, H–C(7)); on simultaneous irradiation at 2.01 and 2.75 ppm the multiplet at 5.30–5.53 was resolved as three signals at 5.37 (*d*, *J* = 15, 1 H, H–C(9)), 5.42 (*t*×*d*, *J* = 6.5 and 11, 1 H, H–C(6)), and 5.49 (*d*, *J* = 15, 1 H, H–C(10)). – MS.: very similar to that of **5**.

5. Synthesis of (±)-tuberolide (6) *(Scheme 4).* – 5.1. *Preparation of* cis-*bicyclo[4.3.0]non-3-en-7-one* (**23**) (*cf.* [28]). A one-necked 1-l pressure vessel (glass) was charged with dry $AlCl_3$ (30 g, 0.225 mol) and dry toluene (100 ml). The mixture was stirred mechanically and heated to 60°. A solution of 2-cyclopentenone (20.5 g, 0.250 mol) in dry toluene (50 ml) was slowly introduced (30 min) through the open neck while maintaining an Ar-atmosphere, and stirring at 60° was continued for 30 min. The red mixture was cooled to RT., the mechanical stirrer replaced by a magnetic stirring bar and the vessel closed with a stainless steel lid equipped with a manometer, a gas-inlet tube (with a stopcock) and a safety-valve. The mixture was cooled to −70° and gaseous 1,3-butadiene (40 g, 0.74 mol, *Fluka AG*) was introduced through the gas inlet (*ca.* 2 h) without stirring. The stopcock was closed, stirring started and the dry ice bath replaced by an ice/salt bath (−10°). Stirring was continued for 4 h at −10° and for 15 h at RT. The mixture was carefully poured onto ice (200 g) (strongly exothermic reaction). The aq. layer was extracted with ether (2×100 ml), the combined organic phases were washed with saturated aq. $NaHCO_3$-solution (2×100 ml) and water (2×100 ml), dried (Na_2SO_4), and evaporated. The crude product (87 g) was chromatographed rapidly through silica gel (400 g) in order to remove the hydrocarbons. PE/ether 9:1 (2 l) eluted a mixture of hydrocarbons (discarded), and ether (2 l) eluted 19.7 g of a liquid which was distilled (bulb-to-bulb, 80° (oven)/0.1 Torr) to give 17.6 g (51.7%) of a mixture of the *cis*-ketone **23** (94%) and the *trans*-ketone **24** (6%). A small sample of the mixture was isomerized with triethylamine to give the equilibrium mixture of *ca.* 52% of **23** and 48% of **24** [35]. From this mixture analytically pure samples of the ketones were isolated by GC. (*Carbowax*, 180°), the *trans*-isomer **24** being eluted first.

Spectral data of **23**. – IR. (neat): in agreement with the literature [35]. – ^{1}H-NMR. (360 MHz): 1.65–1.87 (*m*, 2 H); 2.02 (*m*, 1 H); 2.13–2.28 (br., 4 H); 2.34–2.54 (br., 3 H); 5.64 (*m*, 2 H). – MS.: 136 (100, M^+), 121 (20), 118 (41), 117 (29), 93 (23), 92 (62), 91 (37), 80 (37), 79 (87), 77 (34), 54 (20), 39 (30).

Spectral data of **24**. – IR. (neat): the same as in [35]. – ^{1}H-NMR. (360 MHz): 1.53 (*m*, 1 H); 1.71–2.25 (several *m*, 6 H); 2.34–2.45 (br., 3 H); 5.72 (*m*, 2 H). – MS.: 136 (100, M^+), 121 (16), 118 (25), 117 (23), 107 (18), 93 (21), 92 (72), 91 (28), 80 (45), 79 (92), 77 (31), 39 (27).

5.2. *Reduction of ketone* **23** *with* $LiAlH_4$. In order to avoid epimerization of the *cis*-ketone **23** during purification, the crude ketone was reduced directly. A solution of the crude ketone (200 g, obtained from 0.5 mol of 2-cyclopentenone and excess 1,3-butadiene as above) in dry ether (200 ml) was added to a slurry of $LiAlH_4$ (5 g, 132 mmol) in dry ether (100 ml) at a rate which maintained gentle refluxing (1.5 h). Refluxing was continued for 1 h, the mixture cooled (5°), and water (*ca.* 25 ml) was added dropwise (foaming). The inorganic salts were removed by filtration and the filtrate evaporated. The crude product (200 g) was dissolved in PE (500 ml) and the solution filtered through a short column of silica gel (1 kg). The column was rinsed with PE until no more hydrocarbons were eluted. The wet silica gel was transferred into a beaker and extracted with ether (3×1.5 l). The combined extracts were evaporated and the crude product (48 g) distilled through a *Vigreux* column. A mixture of alcohols **25** and **26** (ratio 4:1), b.p. 111°/13 Torr, 31.6 g (45.7% overall yield with respect to 2-cyclopentenone) was obtained as an oil. Analytically pure samples of each isomer were obtained by prep. GC. *(Carbowax)*, the isomer **25** being eluted first.

*Spectral data of (1*RS,6SR,7RS*)-bicyclo[4.3.0]non-3-en-7-ol* (**25**). – IR. ($CHCl_3$): 3600*m*, 3430 br., 3010*m*, 2960*s*, 2915*s*, 2850*m*, 1665*w*, 1480*w*, 1445*m*, 1105*m*. – ^{1}H-NMR. (360 MHz): 1.51–1.71 (br., 4 H); 1.86 (*m*, 1 H, H_{exo}–C(5)); 1.99–2.17 (br., 5 H); 2.22 (*m*, 1 H, H_{endo}–C(5)); 4.27 (*t*×*d*, *J* = 5 and 8, 1 H, H–C(7)); 5.71 (*m*, 1 H, H–C(3)); 5.78 (*m*, 1 H, H–C(4)). – MS.: 138 (2, M^+), 120 (64), 105 (22), 93 (11), 92 (89), 91 (100), 79 (75), 78 (23), 77 (21), 67 (11), 66 (11), 41 (19), 39 (20).

*Spectral data of (1*RS,6SR,7SR*)-bicyclo[4.3.0]non-3-en-7-ol* (**26**). – IR. ($CHCl_3$): 3600*m*, 3430 br., 3010*m*, 2960 *S*, 2915*s*, 2850*m*, 1665*w*, 1480*w*, 1445*m*, 1075*m*, 1035*w*, 1005*m*, 980*m*, 955*m*, 940*m*, 925*m*. – ^{1}H-NMR. (360 MHz, after shaking with D_2O): 1.38 (*t*×*d*×*d*, *J* = 6, 13 and 9.5, 1 H, H_{endo}–C(9)); 1.52 (*d*×*d*×*d*×*d*, *J* = 14, 10, 6 and 4, 1 H, H_{exo}–C(8)); 1.73–1.95 (br., 4 H); 2.08–2.24 (br., 3 H); 2.30 (*m*, 1 H, H–C(1)); 3.99 (*t*×*d*, *J* = 4 and 7, 1 H, H–C(7)); 5.66 (*m*, $w_{1/2} \approx 4$, 2 H, H–C(3) and H–C(4)). – MS.: 138 (22, M^+), 109 (22), 96 (74), 94 (19), 92 (24), 91 (36), 83 (100), 81 (24), 80 (23), 79 (87), 77 (26), 41 (22), 39 (23).

5.3. *Ozonolysis of the mixture of alcohols* **25** *and* **26**. A solution of a mixture (ratio *ca.* 4:1) of epimeric alcohols **25** and **26** (7.3 g, 52.9 mmol) in dry methanol (150 ml) was ozonized at −78° until the blue colour persisted. Argon was bubbled through the solution which was allowed to reach a temp. of *ca.* −10°. The solution was immediately hydrogenated in the presence of Pd/C (10%, 200 mg) and the temp. was kept between 10 and 15° by cooling (exothermic reaction). After 2 h no more hydrogen was absorbed (820 ml, calculated 1180 ml) and the peroxide test was negative. The catalyst was filtered off, the solvent evaporated and the residue distilled (bulb-to-bulb, 100° (oven)/0.01 Torr) to give 6.3 g (64.7%) of a mixture of aldehydes **27** and **28** (ratio *ca.* 4:1). This mixture contained four major impurities (together *ca.* 20%) which were identified by their 360-MHz-^{1}H-NMR. spectrum and MS. as the dimethyl acetals of **27** and **28** and the methyl esters **31** and **32**. The mixture (6.3 g) was chromatographed in ether on silica gel (330 g). After a fraction containing the impurities (*ca.* 1 g), a mixture of the aldehydes **27** and **28** (ratio *ca.* 3:1, 3.1 g) and a fraction of pure **27** (1.4 g) were eluted. Analytically pure samples of **27** and **28**, the dimethyl acetal of **27**, and the methyl esters **31** and **32** were isolated by prep. GC. (*Carbowax*, 200°).

*Spectral data of (1*RS,*3*SR,*5*SR,*6*RS*)-3-methoxy-2-oxabicyclo[3.3.0]octane-6-acetaldehyde* (**27**). – IR. ($CHCl_3$): 2940*s*, 2830*m*, 2730*m*, 1725*s*, 1450*m*, 1360*w*, 1335*w*, 1295*w*, 1210*m*, 1100*s*, 1045*s*, 1005*m*, 875*m*. – ^{1}H-NMR. (360 MHz): 1.29 (*m*, 1H, H_{endo}–C(7)); 1.55 (*d*×*d*×*d*, J = 12.5, 9 and 4.5, partly overlapping, 1H, H_{endo}–C(4)); 1.57–1.71 (br., 2H, H_{exo}–C(7) and H_{exo}–C(8)); 1.80 (*d*×*d*, $J \approx 13$ and 6, partly overlapping, 1H, H_{endo}–C(8)); 1.81 (*d*×*d*, $J \approx 12.5$ and 8, partly overlapping, 1H, H_{exo}–C(4)); 2.34 (*m*, 1H, H–C(6)); 2.49 (*AB*-part of *ABMX*-system, $\delta_A = 2.48$, $\delta_B = 2.50$, $J_{AB} = 17$, $J_{AM} = 6.5$, $J_{BM} = 7.3$, $J_{AX} \approx J_{BX} \approx 1.2$, 2H, 2H–C(*a*)); 2.97 (br. *qi*, 1H, H–C(5)); 3.30 (*s*, 3H, OCH_3); 4.59 (*t*, J = 6, 1H, H–C(1)); 5.00 (*d*, $J \approx 4.5$, 1H, H–C(3)); 9.78 (*t*, $J \approx 1.2$, 1H, CHO). – MS.: 184 (2, M^+), 153 (45), 109 (32), 95 (100), 82 (42), 81 (86), 80 (65), 79 (44), 71 (74), 67 (51), 55 (35), 41 (70), 39 (34).

*Spectral data of (1*RS,*3*RS,*5*SR,*6*RS*)-3-methoxy-2-oxabicyclo[3.3.0]octane-6-acetaldehyde* (**28**). – IR. ($CHCl_3$): 2950*s*, 2830*m*, 2730*m*, 1720*s*, 1105*m*, 1040*s*. – ^{1}H-NMR. (360 MHz): 1.52–1.68 (br., 3H, 2H–C(7) and H_{exo}–C(8)); 1.70 (*d*×*d*×*d*, J = 13.5, 2.5 and 1.5, partly overlapping, 1H, H_{endo}–C(4)); 1.88 (*m*, 1H, H_{endo}–C(8)); 1.99 (*d*×*d*×*d*, J = 13.5, 10.5 and 5.5, 1H, H_{exo}–C(4)); 2.31 (*m*, 1H, H–C(6)); 2.65 (*AB*-part of *ABMX*-system, $\delta_A = 2.62$, $\delta_B = 2.67$, $J_{AB} = 17$, $J_{AM} = 6$, $J_{BM} = 7.5$, $J_{AX} \approx J_{BX} \approx 1.5$, 2H, 2H–C(*a*)); 2.80 (*d*×*d*×*d*×*d*, J = 10.5, 9.5, 6.5 and 2.5, 1H, H–C(5)); 3.30 (*s*, 3H, OCH_3); 4.68 (*d*×*d*, J = 6.5 and 5, 1H, H–C(1)); 4.90 (*d*×*d*, J = 5.5 and 1.5, 1H, H–C(3)); 9.82 (*t*, $J \approx 1.5$, 1H, CHO). – MS.: 184 (2, M^+), 109 (23), 95 (100), 82 (40), 81 (65), 80 (59), 79 (34), 71 (50), 67 (41), 58 (24), 55 (25), 41 (49), 39 (24).

*Spectral data of (1*RS,*3*SR,*5*SR,*6*RS*)-3-methoxy-6-(2′,2′-dimethoxyethyl)-2-oxabicyclo[3.3.0]octane (dimethyl acetal of* **27**). – IR. (neat): 2980*S*, 2950*s*, 2850*m*, 1450*m*, 1375*m*, 1220*m*, 1140*s*, 1110*s*, 1060*s*, 985*m*, 885*m*. – ^{1}H-NMR. (360 MHz): 1.26 (*m*, 1H, H_{endo}–C(7)); 1.50–1.65 (br., 5H, H_{endo}–C(4), H_{exo}–C(7), H_{exo}–C(8) and 2H–C(1′)); 1.77 (*m*, 1H, H_{endo}–C(8)); 1.83 (*d*×*d*, J = 12.5 and 8.5, 1H, H_{exo}–C(4)); 1.93 (*m*, 1H, H–C(6)); 2.86 (br. *qi*, 1H, H–C(5)); 3.29, 3.31 and 3.32 (3*s*, 9H, 3 OCH_3); 4.40 (*t*, $J \approx 6$, 1H, H–C(2′)); 4.56 (*t*, $J \approx 6$, 1H, H–C(1)); 4.99 (*d*, J = 5, 1H, H–C(3)). – MS.: 230 (0, M^+), 167 (10), 107 (7), 97 (7), 84 (7), 81 (8), 80 (6), 79 (11), 75 (100), 71 (8), 67 (6), 47 (5), 41 (6).

*Spectral data of methyl (1*RS,*3*SR,*5*SR,*6*RS*)-3-methoxy-2-oxabicyclo[3.3.0]octane-6-acetate* (**31**). – IR. ($CHCl_3$): 2960*s*, 1740*s*, 1450*m*, 1110*m*, 1055*s*, 1015*m*. – ^{1}H-NMR. (360 MHz): 1.29 (*m*, 1H, H_{endo}–C(7)); 1.54–1.67 (*m*, overlapping, 2H, H_{exo}–C(7) and H_{exo}–C(8)); 1.56 (*d*×*d*×*d*, J = 12.5, 9 and 4, overlapping, 1H, H_{endo}–C(4)); 1.79 (*m*, partly overlapping, 1H, H_{endo}–C(8)); 1.83 (*d*×*d*, J = 12.5 and 9, partly overlapping, 1H, H_{exo}–C(4)); 2.30 (*m*, partly overlapping, 1H, H–C(6)); 2.35 (*m*, partly overlapping, 2H, 2H–C(*a*)); 2.94 (br. *qi*, 1H, H–C(5)); 3.29 (*s*, 3H, OCH_3); 3.67 (*s*, 3H, $COOCH_3$); 4.58 (*t*, J = 6, 1H, H–C(1)); 5.00 (*d*, $J \approx 4$, 1H, H–C(3)). – MS.: 214 (0, M^+), 213 (1, $M-1$), 183 (42), 151 (68), 123 (31), 122 (49), 95 (38), 94 (84), 81 (98), 80 (65), 79 (64), 71 (100), 41 (67), 39 (32).

*Spectral data of methyl (1*RS,*3*RS,*5*SR,*6*RS*)-3-methoxy-2-oxabicyclo[3.3.0]octane-6-acetate* (**32**). – IR. ($CHCl_3$): same bands as **31**. – ^{1}H-NMR. (360 MHz): 1.55–1.66 (br., 3H, 2H–C(7) and H_{exo}–C(8)); 1.76 (*d*×*d*×*d*, J = 13.5, 2.5 and 1.5, 1H, H_{endo}–C(4)); 1.86 (*m*, 1H, H_{endo}–C(8)); 1.99 (*d*×*d*×*d*, J = 13.5, 10 and 5, 1H, H_{exo}–C(4)); 2.27 (*m*, 1H, H–C(6)); 2.48 (*d*, J = 7.5, 2H, 2H–C(*a*)); 2.78 (*d*×*d*×*d*×*d*, J = 10, 10, 6 and 2.5, 1H, H–C(5)); 3.30 (*s*, 3H, OCH_3); 3.67 (*s*, 3H, $COOCH_3$); 4.66 (*t*, $J \approx 6$, 1H, H–C(1)); 4.90 (*d*×*d*, J = 5.5 and 1.5, 1H, H–C(3)). – MS.: very similar to that of **31**.

5.4. Wittig *reaction of aldehyde* **27** *with triphenylpropylidenephosphorane.* To a solution of aldehyde **27** (1.4 g, 7.6 mmol) in dry toluene (60 ml) was added within 30 min at *ca.* 0° a 'salt-free' solution of triphenylpropylidenephosphorane (*ca.* 8 mmol) in toluene (15 ml, prepared by the sodium amide method [30]). The mixture was stirred at RT. for 1 h, the toluene evaporated and the residue distilled (bulb-to-bulb, 125–150° (oven)/0.01 Torr). The distillate (1.25 g, 78%) contained *ca.* 90% of the (*Z*)-olefin **29** and was used directly for the next step. A pure sample of **29** was isolated by prep. GC. (*Carbowax*, 200°).

*Spectral data of (1*RS,*3*SR,*5*SR,*6*RS,Z*)-3-methoxy-6-(2'-pentenyl)-2-oxabicyclo[3.3.0]octane* (**29**). – IR. (neat): 3010 *S*, 2950*s*, 2880*m*, 2840*m*, 1465*m*, 1450*m*, 1365*w*, 1335*w*, 1305*w*, 1210*s*, 1105*s*, 1050*s*, 1015*m*, 950*m*, 875*m*. – ^{1}H-NMR. (360 MHz): 0.96 (*t*, J=7.5, 3 H, 3 H–C(5')); 1.17–1.29 (*m*, 1 H, H_{endo}–C(7)); 1.49–1.68 (br., 3 H, H_{endo}–C(4), H_{exo}–C(7) and H_{exo}–C(8)); 1.77 (*m*, partly overlapping, 1 H, H_{endo}–C(8)); 1.81 (*d*×*d*, J=13 and 8.5, overlapping, 1 H, H_{exo}–C(4)); *ca.* 1.86 (*m*, overlapping, 1 H, H–C(6)); 1.98–2.14 (*m*, 4 H, 2 H–C(1') and 2 H–C(4')); 2.84 (br. *qi*, 1 H, H–C(5)); 3.30 (*s*, 3 H, OCH_3); 4.57 (*t*, $J \approx 6$, 1 H, H–C(1)); 5.00 (*d*, J=4.5, 1 H, H–C(3)); 5.34 (symmetrical *m*, 2 H, H–C(2') and H–C(3')). – MS.: 210 (1, M^+), 161 (30), 160 (38), 121 (29), 95 (52), 86 (28), 81 (100), 79 (43), 71 (52), 69 (32), 67 (47), 55 (32), 41 (75).

5.5. *Preparation of (1*RS,*5*SR,*6*RS,Z*)-6-(2'-pentenyl)-2-oxabicyclo[3.3.0]octan-3-one (tuberolide,* **6**). To a solution of the acetal **29** (2.45 g, 11.7 mmol) in ether (30 ml) was added dropwise with stirring at 0° 20 ml of a solution of chromic acid (prepared by dissolving 26.7 g of CrO_3 in 23 ml of conc. sulfuric acid and 77 ml of water). The mixture was stirred overnight at RT. and the aq. layer extracted with ether (3 × 20 ml). The combined ether extracts were washed with sat. NaCl-solution, dried (Na_2SO_4), evaporated and the residue (2.1 g) distilled (bulb-to-bulb, 100° (oven)/0.01 Torr). After chromatography of the distillate (1.2 g) on silica gel (160 g) in PE/ether 1:1 and bulb-to-bulb distillation of the homogeneous fractions, analytically pure lactone **6** was obtained as a colourless oil (1.14 g, 50%), identical with natural tuberolide by its spectral and chromatographic data. – IR. ($CHCl_3$): 2970*m*, 2890*m*, 1765*s*, 1660*w*, 1470*w*, 1450*w*, 1425*w*, 1375*m*, 1195*s*, 1080*m*, 1035*m*, 1010*m*. – ^{1}H-NMR. (360 MHz): 0.97 (*t*, J=7.5, 3 H, 3 H–C(5')); 1.24–1.37 (*m*, 1 H, H_{endo}–C(7)); 1.72 (*t*×*d*×*d*, J=6, 15 and 12, partly overlapping, 1 H, H_{exo}–C(8)); 1.78 (*t*×*d*, J=6 and 11, partly overlapping, 1 H, H_{exo}–C(7)); 1.91–*ca.* 2.1 (*m*, overlapping, 2 H, H–C(6) and H_{endo}–C(8)); 2.04 (br. *qi*, $J \approx 7.5$, overlapping, 2 H, 2 H–C(4')); 2.12 (*AB*-part of an *ABMX*-system, δ_A=2.16, J_{AB}=14, $J_{AM} \approx J_{AX} \approx 7$, partly overlapping, 2 H, 2 H–C(1')); 2.48 (*AB*-part of an *ABX*-system with δ_A=2.44, δ_B=2.52, J_{AB}=19, J_{AX}=5, J_{BX}=10, 2 H, 2 H–C(4)); 2.96 (*m*, 1 H, H–C(5)); 5.04 (br. *t*, $J \approx 6$, 1 H, H–C(1)); 5.27 (*t*×*t*×*d*, J=7, 1.5 and 11, 1 H, H–C(2')); 5.41 (*t*×*t*×*d*, J=7, 1.5 and 11, 1 H, H–C(3')). – ^{13}C-NMR. (22.63 MHz): 14.2 (*qa*, C(5')); 20.7 (*t*, C(4')); 28.3 (*t*, C(4) or C(7) or C(8)); 28.9 (2 *t*, C(7) and C(8), or C(4) and C(8), or C(4) and C(7)); 32.9 (*t*, C(1')); 40.4 (*d*, C(6)); 43.0 (*d*, C(5)); 86.0 (*d*, C(1)); 126.7 (*d*, C(2')); 132.7 (*d*, C(3')); 177.7 (*s*, C(3)). – MS.: 194 (7, M^+), 134 (14), 95 (20), 93 (15), 81 (17), 79 (27), 69 (27), 68 (100), 67 (62), 66 (17), 55 (25), 41 (73), 39 (22).

5.6. *Preparation of (1*RS,*5*SR,*6*SR*)-6-pentyl-2-oxabicyclo[3.3.0]octan-3-one (dihydro-tuberolide,* **30**). A solution of synthetic tuberolide **6** (200 mg, 1.03 mmol) in methanol (5 ml) was hydrogenated in the presence of Pd/C (10%, 20 mg) to give a nearly quantitative yield of the pure lactone **30** as an oil. – IR. ($CHCl_3$): 2950*s*, 2930*s*, 2860*m*, 1760*s*, 1475*m*, 1375*m*, 1325*m*, 1195*s*, 1035*m*, 1005*m*. – ^{1}H-NMR. (90 MHz): 0.89 (distorted *t*, 3 H, 3 H–C(5')); 1.07–1.58 (br., 9 H); 1.57–2.17 (br., 4 H); 2.47 (*AB*-part of an *ABX*-system, 2 H, 2 H–C(4)); 2.94 (*m*, 1 H, H–C(5)); 5.02 (*t*, $J \approx 6$, 1 H, H–C(1)). – ^{13}C-NMR. (22.63 MHz): 14.0 (*qa*, C(5')); 22.6 (*t*, C(4')); 28.3 (*t*, C(4) or C(7) or C(8)); 28.7 (*t*, C(7) or C(8) or C(4)); 29.0 (*t*, C(8) or C(4) or C(7)); 30.7 (*t*, C(2')); 32.1 (*t*, C(3')); 33.1 (*t*, C(1')); 40.6 (*d*, C(6)); 42.9 (*d*, C(5)); 86.2 (*d*, C(1)); 177.9 (*s*, C(3)). – MS.: 196 (2, M^+), 97 (28), 83 (29), 82 (48), 81 (49), 69 (41), 68 (39), 67 (46), 57 (30), 55 (97), 43 (53), 41 (100), 39 (30).

REFERENCES

[1] *R. Kaiser & D. Lamparsky*, Tetrahedron Lett. *1976*, 1659.
[2] *S. Arctander*, 'Perfume and Flavor Materials of Natural Origin', p. 630, Elizabeth N.J. (U.S.A.) 1960.
[3] a) *J. Boldingh & R.J. Taylor*, Nature *194*, 909 (1962); b) *A.S.M. van der Zijden, K. de Jong, D. Sloot, J. Clifford & R.J. Taylor*, Rev. Fr. Corps Gras *13*, 731 (1966); Chem. Abstr. *66*, 75049u (1967); c) *W. Stark & G. Urbach*, Chem. and Ind. *1974*, 413.
[4] *R.G. Brownlee, R.M. Silverstein, D. Müller-Schwarze & A.G. Singer*, Nature *221*, 284 (1969).
[5] *S. Tahara, K. Fujiwara & J. Mizutani*, Agric. Biol. Chem. *37*, 2855 (1973).
[6] *R.J. Park, K.E. Murray & G. Stanley*, Chem. and Ind. *1974*, 380.
[7] *B.V. Burger, M. le Roux, C.F. Garbers, H.S.C. Spies, R.C. Bigalke, K.G.R. Pachler, P.L. Wessels, V. Christ & K.H. Maurer*, Z. Naturforsch. C *32*, 49 (1977).
[8] *R. Kaiser & D. Lamparsky*, in 'Essential Oils', Symposium Div. Agric. and Food Chem., 178th Meeting of the ACS, Washington D.C., Sept. 12, 1979, p. 159 (B.D. Mookherjee & C.J. Mussinan, eds.), Allured Publ. Corp., Wheaton Ill. (U.S.A.) 1981; Abstracts of Papers AGFD 052.
[9] *A.I. Meyers, E.D. Mihelich & R.L. Nolen*, J. Org. Chem. *39*, 2783 (1974).
[10] a) *J.H. Tumlinson, M.G. Klein, R.E. Doolittle, T.L. Ladd & A.T. Proveaux*, Science *197*, 789 (1977); b) *J.H. Tumlinson, M.G. Klein, R.E. Doolittle & T.L. Ladd*, US. Pat. 4.179.446 (18.12.1979) = US. Pat. Appl. 932.079 (8.8.1978), Chem. Abstr. *91*, 15182 (1979); c) *R.E. Doolittle, J.H. Tumlinson, A.T. Proveaux & R.R. Heath*, J. Chem. Ecol. *6*, 473 (1980).
[11] *S.F. Birch, R.A. Dean & N.J. Hunter*, J. Org. Chem. *23*, 1390 (1958).
[12] *R.R. Russell & C.A. Vander Werf*, J. Am. Chem. Soc. *69*, 11 (1947).
[13] *R.M. Adams & C.A. Vander Werf*, J. Am. Chem. Soc. *72*, 4368 (1950).
[14] *M. Winter, F. Näf, A. Furrer, W. Pickenhagen, W. Giersch, A. Meister, B. Willhalm, W. Thommen & G. Ohloff*, Helv. Chim. Acta *62*, 135 (1979).
[15] *M. Stoll & P. Bolle*, Helv. Chim. Acta *21*, 1547 (1938).
[16] *F. Bohlmann, P. Herbst & H. Gleinig*, Chem. Ber. *94*, 948 (1961).
[17] *E.R.H. Jones, J.B. Jones, L. Skattebøl & M.C. Whiting*, J. Chem. Soc. *1960*, 3489.
[18] *P. Haverkamp-Begemann, V. Lamberti & W.T. Weller*, Recl. Trav. Chim. Pays-Bas *87*, 1335 (1968).
[19] *S.W. Russell*, Recl. Trav. Chim. Pays-Bas *94*, 43 (1975).
[20] *W. Sucrow & U. Klein*, Chem. Ber. *108*, 3518 (1975) and ref. cited therein.
[21] *M. Benn & K.N. Vohra*, Can. J. Chem. *54*, 136 (1976).
[22] *D. Müller-Schwarze, R.M. Silverstein, C. Müller-Schwarze, A.G. Singer & N.J. Volkman*, J. Chem. Ecol. *2*, 389 (1976).
[23] *A. Alexakis, G. Cahiez & J.F. Normant*, Tetrahedron *36*, 1961 (1980).
[24] a) *U. Ravid & R.M. Silverstein*, Tetrahedron Lett. *1977*, 423; b) *U. Ravid, R.M. Silverstein & L.R. Smith*, Tetrahedron *34*, 1449 (1978).
[25] *W.H. Pirkle & P.E. Adams*, J. Org. Chem. *44*, 2169 (1979).
[26] *M.M. Midland & A. Tramontano*, Tetrahedron Lett. *21*, 3549 (1980).
[27] *L.I. Zakharkin & O. Yu. Ikhlobystin*, Izv. Akad. Nauk SSSR, Ser. Khim. *1963*, 193, engl. 176; Chem. Abstr. *58*, 12589 (1963).
[28] *F. Fringuelli, F. Pizzo, A. Taticchi & E. Wenkert*, Synth. Commun. *9*, 391 (1979).
[29] *S. Knapp, R. Lis & P. Michna*, J. Org. Chem. *46*, 624 (1981).
[30] *M. Schlosser, G. Müller & K.F. Christmann*, Angew. Chem. *78*, 677 (1966); *M. Schlosser & K.F. Christmann*, Justus Liebigs Ann. Chem. *708*, 1 (1967).
[31] *B. Maurer, A. Hauser, W. Thommen, K.H. Schulte-Elte & G. Ohloff*, Helv. Chim. Acta *63*, 293 (1980).
[32] *L. Brandsma*, 'Preparative Acetylenic Chemistry', p. 26 and 28, Elsevier Publ. Comp., Amsterdam, London, New York 1971.
[33] *E. LeGoff*, J. Org. Chem. *29*, 2048 (1964).
[34] *M.C. Mussatto, D. Savoia, C. Trombini & A. Umani-Ronchi*, J. Org. Chem. *45*, 4002 (1980).
[35] *H.O. House & G.H. Rasmusson*, J. Org. Chem. *28*, 31 (1963).