190. Structure Determination of New Iridals from *Iris pallida* and *Iris foetidissima*

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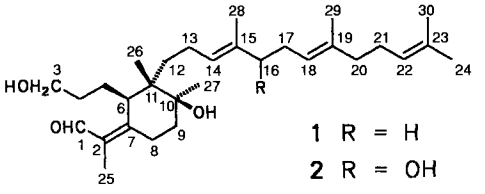
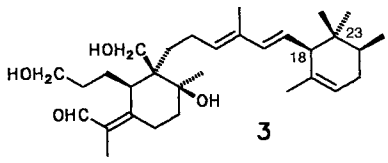
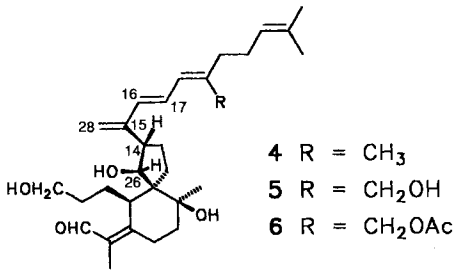
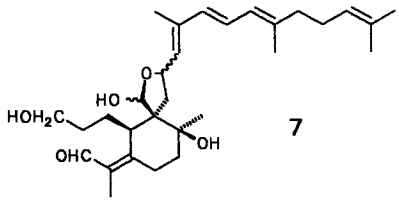
The four novel iridals **8–10** and **18** were isolated from rhizome extracts of *Iris pallida* and *Iris foetidissima*, and their structures were established by spectroscopic methods and oxidative degradation. The compounds **8–10** bearing a conjugated triene moiety are extremely labile and decompose rapidly. Thus, the monocyclic triene **8** was only isolated after its conversion to a *Diels-Alder* adduct with 4-phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione (**14**). The tricyclic iridal **18** is a hitherto unknown precursor of α-irone. The possible biogenesis of these unusual triterpenoids is discussed.

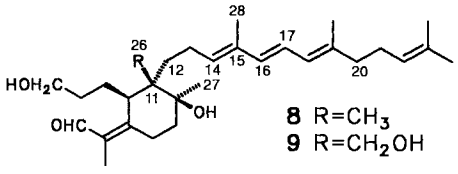
Introduction. – Over the last ten years, we have isolated numerous unusual triterpenoids from rhizomes and roots of various *Iris* species with mono-, bi-, and spirocyclic structures (*e.g.* **1–7**) [1] [2]. All compounds have a seco-ring-A moiety in common and are

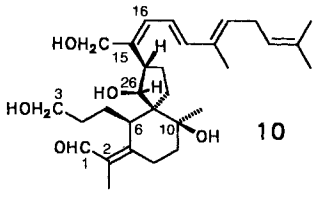












derived from squalene [3], most probably *via* iridal (**1**) which gave this family of triterpenoids its name. Thus, iridal is oxygenated in various positions to give, *e.g.*, the 16-hydroxyiridal **2**. Methylation at C(22) followed by cyclization leads to the cycloiridals (*e.g.* **3**) [3] which serve as precursors of the irones, bringing about the violet-like fragrance of the *Iris* oil. The formation of the spiroiridals **4**–**7** can be explained by oxidation at C(26) to give an aldehyde function and subsequent cyclization by intramolecular *Prins* reaction [4] [5]. The two monocyclic iridals **8** and **9** were postulated as intermediates between iridal and the irone precursors or the spiroiridals **4**–**7** [4]. The conjugated triene moiety, apparently, results from introduction of an additional double bond C(16)=C(17) in the homofarnesyl side chain by dehydrogenation of **1** rather than from dehydration of **2** [4]. In our efforts to investigate the biosynthesis and metabolism of the iridals, the search for these compounds is one of our main aims.

Results. – *I. foetidissima* is a very rich source of iridals with a conjugated triene substructure. These compounds are easily recognized during HPLC analysis by their typical UV spectra with absorption maxima around 280 nm. In an earlier investigation [4], compound **4** was isolated from rhizome extracts of this species accounting for 20% of the iridal fraction. Now we were able to identify in *I. foetidissima* isolates the spiroiridals **5** (2%), **6** (12%), and **7** (35%), previously isolated from *I. pseudacorus* [5], and the iridals **1** (5%) and **2** (7%), which are present in most *Iris* extracts studied to date [1] [2]. One main product (8%), **10**, with a triene chromophore (maximum at 282 nm, shoulders at 272 and 292 nm) remained unidentified. When isolated by repeated reversed-phase chromatography according to [5], compound **10** proved to be very labile, rapidly decomposing in different solvents or in the dry state. It was stable, however, when stored in CH_2Cl_2 at $-20°$.

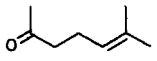
The MS of **10** reveals an M^+ at m/z 486 and fragment ions at m/z 468 and 450, arising from the consecutive loss of two molecules of H_2O. A prominent peak at m/z 69 suggests the presence of a terminal isoprene unit. The molecular composition is $C_{30}H_{46}O_5$ (by HR-MS). Comparison of the NMR data (^{1}H- and ^{13}C-NMR, ^{1}H,^{1}H- and ^{1}H,^{13}C-COSY) with the values recorded for compounds **4**–**6** [4] [5] shows that the spirobicyclic ring system is again present. Differences are seen, however, in the resonances of the side chain. Thus, the *AB* system of the CH_2=C group is missing. Instead, signals of 5 olefinic CH groups are seen: a *t* at 5.1 ppm shows a cross-signal to a CH_2 at 2.85 and allylic coupling to two Me groups at 1.7 and 1.65 ppm. The CH_2 at 2.85 ppm, apparently, is in a bis-allylic position as it couples with another olefinic CH at 5.5 ppm, which in turn shows long-range coupling to a Me group at 1.79 ppm. This olefinic double bond is connected to a diene moiety having three protons, which appear as an *AMX* system at 6.28, 6.35, and 6.18 ppm. The coupling constant (J_{AM} = 15 Hz) indicates the (*E*)-configuration of the CH=CH bond. The last C-atom of this isoprenoid side chain is connected to the spirobicyclic system at C(14) and further substituted by a CH_2OH group, the protons of which form an *AB* system at 3.92 and 4.12 ppm. Since no allylic coupling is observed between this CH_2OH and H–C(16), the (*E*)-configuration is assigned to the C(15)=C(16) bond.

The spectral data established the proposed overall structure for **10**. From biosynthetic considerations and from the identical NMR data of the ring systems, we assigned to **10** the same (6*R*,10*S*,11*S*,14*S*,26*R*)-configuration as found for the spiroiridals **4**–**6** [4] [5]. The formation of **10** may follow the route outlined above for the isomers **4**–**6** [4] [5]: Oxidation at C(26) of the conjugated triene **9** yielding an aldehyde group and its subsequent proton-triggered *Prins* reaction with C(14) gives the spiro system, which is stabilized by loss of a proton from C(20) instead of C(28), thus leading to a shift of the triene moiety along the isoprenoid chain.

The intermediates **8** and **9** in this reaction, however, are not present in the extracts of *I. foetidissima*. We, therefore, decided to reinvestigate the iridal fraction of *I. pallida* LAM.,

which previously was shown to consist mainly of 18,23-cycloiridal **3** [6]. In this first investigation of *I. pallida*, no iridals with conjugated triene substructure were found, since the initial separation of the crude extracts was performed on silica gel leading to decomposition of these labile components. On analysis of this extract by reversed-phase HPLC, however, **3** (49% of the iridals) as well as the 16-hydroxyiridal **2** (9%) and the spiroiridals **4** (3%), **5** (3%), and **6** (3%), together with two unknown trienes, identified as **8** (15%) and **9** (12%), were found.

The more abundant compound **9** is moderately stable and was isolated by repeated reversed-phase chromatography. Its UV spectrum shows the typical triene pattern with a maximum at 278, a smaller maximum at 268, and shoulders at 256 and 290 nm. The MS reveals an M^+ at m/z 472 and a molecular composition of $C_{30}H_{48}O_4$. The NMR data (^{1}H- and ^{13}C-NMR, ^{1}H,^{1}H- and ^{1}H,^{13}C-COSY) show that 3 of the 7 double-bond equivalents are located in the α,β-unsaturated aldehyde and the six-membered ring of the seco-ring-A system. The remaining double bonds are found in the side chain, which upon oxidative degradation with pyridinium chlorochromate [7] yielded 6-methylhept-5-en-2-one (**11**), citral (**12**), and pseudoionone (**13**). Therefore, the skeleton of the long-sought-after monocyclic trienes must be present in **9**, as confirmed by the NMR resonances and appropriate cross-peaks in the 2D spectra. One of the ring Me groups is replaced by a CH_2OH group which appears as an *AB* system at 3.93 and 4.09 ppm and is attributed to C(26) by comparing the spectroscopic data of **9** with the values recorded for the cycloiridal **3** [6]; confirmation is given by the absence of a ^{13}C-NMR signal at 18 ppm (Me(26)) and the presence of the Me(27) signal at 26.4 ppm.



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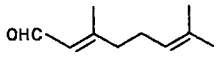

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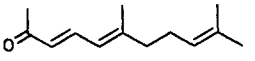

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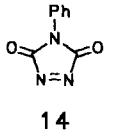
The minor compound **8** has an UV spectrum identical with that of **9**, and in reversed-phase HPLC, **8** shows a retention behaviour similar to iridal (**1**). The MS of a fraction collected during anal. HPLC shows an M^+ at m/z 456 compatible with structure **8**.

These findings suggested the proposed structures **8** and **9**, the latter, at least, with the (6*R*,10*S*,11*S*)-configuration of the iridal ring system, which is identical for all iridals of the *Iris* species studied [8]. It was not possible to isolate compound **8** since decomposition took place in solution, which was accelerated upon evaporation of the solvent. As the conjugated-triene region was inferred to be responsible for this instability, we hoped to stabilize the system by removing the conjugation. A promising reagent seemed to be 4-phenyl-3*H*-1,2,4-triazole-3,5-(4*H*)-dione (**14**) which is known to act as a dienophile in *Diels-Alder* reactions under extremely mild conditions [9–11].



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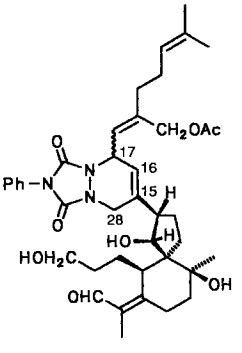
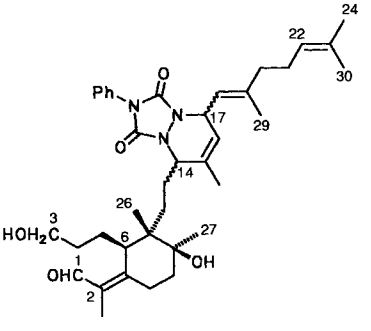
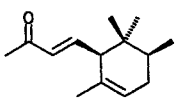


15a/b



16a/b



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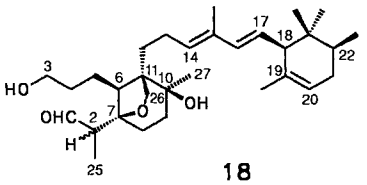

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To study the reaction of **14** with an iridal triene and obtain spectroscopic data of adducts with derivable structures, we first treated the readily available acetate **6** with **14**. A smooth reaction to the two products **15a, b** occurred which eluted prior to the educt **6** from reversed-phase columns and showed UV spectra with overlapping acroleine und phenyl chromophores (λ_{max} 256 nm). No change in product composition or yield was observed when the reaction was carried out at lower temperatures (0°) or in MeOH/H_2O 4:1 solutions[1]). The α,β-unsaturated-aldehyde moiety of **6** reacted much slower than the triene moiety, and an optimal yield of **15a, b** was obtained by gradually adding the dienophile and monitoring the progress of the reaction by HPLC. Separation of the adducts **15a, b** was readily achieved by prep. HPLC. The compounds proved to be stable, and the proposed structures were established by spectral data. The regioselectivity of the reaction may be explained by the sterical hindrance of the diene moiety at C(16)–C(19) of **6**. Molecular models show that the acetate residue at C(29) prevents this diene from adopting an s-*cis*-conformation.

The ^{1}H- and ^{13}C-NMR spectra of **15a** and **15b** indicate that they are two adducts of the C(28)–C(17) diene system epimeric at C(17). Thus, the protons of C(28) now give rise to an *AB* system at 3.93 and 4.23 ppm (epimer, 3.90 and 4.25 ppm), and the corresponding C-atom is found at 45.6 (45.6) ppm. Due to its bis-allylic position and the neighbourhood of an N-atom, the resonance of H–C(17) is shifted to 5.38 (5.14), C(17) appears at 51.8 (52.3) ppm.

The reaction of the unstable new triene **8** from *I. pallida* with **14** under similar conditions was less selective and gave four stable products in the ratio 4:4:1:1. The two main *Diels-Alder* adducts **16a, b** were purified by repeated prep. reversed-phase HPLC.

The UV spectra of **16a, b** again show a maximum at 256 nm, and the CI-MS gives an M^+ at *m/z* 631, the correct value for a reaction product between **8** and **14**. The NMR analyses (^{1}H- and ^{13}C-NMR, ^{1}H,^{1}H-COSY, and DEPT-HMQC) confirm the compounds to be the two possible *Diels-Alder* adducts **16a, b** of **14** to the C(14)–C(17) diene part of **8** with the substituents at C(14) and C(17) in a *cis*-position at the newly formed six-membered ring. The spectra of the two isomers show only small differences and, therefore, only the structure elucidation of **16a** is described (data of **16b**, see *Exper. Part*). The seco-ring-A segment is readily recognized in the ^{1}H-NMR by the aldehyde resonance at 10.16 ppm, the *AB*-system of the 2 H–C(3) at 3.56, H–C(6) at 3.17, Me(26) at 1.06, and Me(27) at 1.12 ppm and by the corresponding ^{13}C-NMR resonances, all in perfect agreement with the data of iridal (**1**) [6] [12]. The terminal isoprene unit of the side chain is identified by long-range coupling of H–C(22) (5.02 ppm) with Me(24) (1.63 ppm) and Me(30) (1.55 ppm). Following the cross-signals in the ^{1}H,^{1}H-COSY, the 2 H–C(21) (2.05 ppm) and 2 H–C(20) (1.97 ppm) can be found. Another sequence starts with H–C(18) (4.92 ppm), showing allylic coupling to Me(29) (1.78 ppm) and vicinal coupling to H–C(17) which exhibits δ(H) and δ(C) values (5.02 and 51.8 ppm, resp.) comparable to that of H–C(17) in **15a, b**. Furthermore, *H*–C(17) couples with the olefinic *H*–C(16) (5.42 ppm). The signals of *H*–C(14) at 4.36 ppm and C(14) at 57.4 ppm indicate that this CH is connected to the other N-atom of the heterocyclic unit. The remaining signals in the NMR spectra can be unambiguously assigned.

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[1]) MeOH/H_2O solutions of **6** were obtained upon purification by reversed-phase MPLC of **6** from a crude extract.

Thus, the unstable triene is identified as the (6*R*,10*S*,11*S*)-16,17-didehydroiridal (**8**). The two by-products of the *Diels-Alder* reaction were not examined, but presumably are the adducts to the C(16)–C(19) diene segment.

All iridals isolated to date have the typical seco-ring-A moiety with an α,β-unsaturated aldehyde giving rise to a chromophore with a dominant absorption at 254 nm, which appears as a shoulder in the UV spectra of the trienes or dienes. Thus, the irone precursors (*e.g.* **3**) are easily detected in the 254-nm trace of an HPLC analysis. It was, therefore, surprising to find *cis*-α-irone (**17**), when a MPLC fraction of the *I. pallida* extract, apparently containing only the spiroiridal **4**, was oxidatively degraded with pyridinium chlorochromate. Reinvestigation of the fraction by HPLC at a detection wavelength of 230 nm, however, indicated the presence of a second peak arising from a compound **18** which overlapped with the elution profile of **4**. The UV spectrum of **18** was typical of a diene with λ_{max} 236.5 nm. Since the triene moiety of **4** reacted much faster with **14** than the diene segment of **18**, it was possible to selectively remove **4** as its *Diels-Alder* adduct and to isolate the new iridal **18** by prep. reversed-phase HPLC.

The MS of **18** displays an M^+ at *m/z* 486 and the loss of one molecule of H_2O. The molecular composition is $C_{31}H_{50}O_4$ (MS) and, thus, is not different from that of the cycloridial **3**, indicating the same number of double-bond equivalents. NMR analyses (^{1}H- and ^{13}C-NMR, ^{1}H,^{1}H- and ^{1}H,^{13}C-COSY) show the presence of only 1 C=O (aldehyde) group, appearing as a *s* at 9.89 ppm (^{13}C: 205.9 ppm) and 3 olefinic double bonds. As seen by the oxidative degradation, the *cis*-α-irone moiety is part of the molecule, and the C(14)–C(17) diene system is responsible for the UV maximum. This is confirmed by the NMR data which are identical with the corresponding values of **3** [6]. Hence, all olefinic double bonds are located within this structural segment, and the further unsaturation has to be found in an additional ring system. One O-atom is part of this ring since after H/D exchange, M^+ is shifted to *m/z* 488, suggesting that only 2 OH groups are present as compared to 3 OH in the irone precursor **3**. Distinct differences are found for most NMR signals of the iridal ring system of **18** compared to the cycloiridal **3**. Only the substitution pattern at C(10) seems unchanged (C(10) at 75.1 and C(27) at 24.4 (δ(H) 1.33) ppm) and the hydroxypropyl side chain at C(6) is definitely present, H–C(3) appearing at 3.62 and C(3) at 63.0 ppm. Me(25) appears as a *d* (δ(H) 0.98) coupled with H–C(2) at 2.79 ppm, which in the 1D ^{1}H-NMR spectrum shows no further couplings. In the ^{1}H,^{1}H-COSY, however, a very small cross-peak to the aldehyde proton is observed. Therefore, C(7) is the quaternary C-atom at 87.5 ppm and is connected with C(11) *via* an O–C(26) bridge. The resonances of 2 H–C(26) are found as an *AB* system at 3.76 and 4.17 and C(26) at 72.5 ppm. The rather-low-field signal of C(11) at 54.7 ppm compares well with the resonance of this C-atom in the spiroiridals and is indicative for the high ring strain in the bicyclic system of **18**. Final confirmation of the structure assignment is obtained by a HMBC (^{1}H-detected multiple-bond ^{13}C-multiple-quantum-coherence [13]) spectrum recorded in the inverse mode at high magnetic field (14 Tesla, 600 MHz, ^{1}H). The cross-peaks in this 2D ^{1}H,^{13}C-NMR spectrum are derived exclusively from H,C coupling *via* two or three bonds. In this correlation spectrum, *inter alia* cross-peaks of *H*–C(2) with C(26), C(7), and C(8) are seen, and *H*–C(26) couples with C(7), thus definitely establishing the ether bridge between C(26) and C(7).

In a previous investigation, the variety of *I. pallida* used in this work was shown to exclusively produce (–)-*cis*-α-irone [14]. The two chiral centers of this moiety of **18**, therefore, have the (18*R*,22*S*)-configuration, and from the arguments mentioned above, (6*S*,10*S*,11*S*)-configuration is assumed (due to the O-substitution at C(7), the configuration at C(6) changes from *R* to *S*). Molecular models show that attack of the OH–C(26) group at C(7) is only possible from 'above'. Thus, the (*R*)-configuration is assigned to C(7), whereas the configuration at C(2) remains undetermined. Accordingly, compound **18** has the structure of a (6*S*,7*R*,10*S*,11*S*,18*R*,22*S*)-22-methyl-26-*O*,7:18,23-dicycloiridal.

Discussion. – The new triterpenoids isolated in the course of this study give insight into the metabolism of these uncommon natural products. The structures of most compounds in this family found to date find an explanation in the (successive) action of

monooxygenases on iridal (**1**). Unusual reactions, however, have to occur during formation of the spiro- and cycloiridals. Undoubtedly, the biogenetic sequence follows the route from **1** *via* triene **8** to hydroxytriene **9**. The cyclization of the homofarnesene side chain to form the irone ring system of the cycloiridals is initiated by transfer of a Me group from *S*-adenosylmethionine to the terminal double bond [3]. C(26) of **9** may be further oxidized to give the aldehyde employed in the formation of the spiroiridals in an acid-catalyzed *Prins* reaction, usually taking place under rather drastic conditions, which almost certainly would lead to decomposition of the triene. Therefore, enzymatic control of this peculiar reaction has to be postulated. The synthesis of the tricyclic irone precursor **18** may be considered to arise from a 1,4-*Michael* addition of OH–C(26) of **3** to the acroleine moiety with intermediate formation of an enol (C(2)=C(1)). Thus, it would be interesting to determine the configuration at C(2) of **18**, since enzymatic control of this reaction should lead to a configurationally homogeneous product, whereas a diastereoisomer mixture is to be expected upon chemical control. The iridals occur in relatively high amounts in all parts of the plants, and their production is strongly season-dependent [15]. Their biological significance is still unknown, but based on their structure and reactivity, one may speculate that they protect the plant against herbivores, peroxidation of membranous lipids, and/or desiccation [15].

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Experimental Part

General. Plant material: Rhizomes of *I. foetidissima* were purchased from *Bornträger & Schlemmer*, D–6521 Offstein, in October 1988; *I. pallida*, obtained several years ago from the garden of the Pharmacological Institute, University of Bonn, was grown in the garden of our institute. GLC: *Shimadzu GC 8A*, cap. column *OV 1* (15 m, 0.25 mm i.d.). Anal. HPLC: *Kontron* model *200*; column, *LiChroCart RP 18* (125 mm, *Merck*); solvent: MeOH/H_2O 7:3 (5 min), lin. gradient to 100% MeOH (15 min), 100% MeOH (20 min), *Hewlett-Packard-1040A* diode-array detector; UV spectra were recorded during HPLC. Prep. HPLC: *Altex* model *420*; column, *Spherisorb 5 ODS* (240 mm, 5 mm i.d., *Chromatographie-Service*). MPLC: *Büchi* model *681*; column, *RP 18* 14–40 μm (240 mm, 20 mm, i.d.). NMR spectra: *Bruker WH-300* (Köln; ^1H: 300 MHz; ^{13}C: 75.4 MHz), *Bruker WM-400* (Karlsruhe; ^1H: 400 MHz; ^{13}C: 100.6 MHz), *Bruker AM-600* (Braunschweig and Frankfurt; ^1H: 600 MHz; ^{13}C: 150.9 MHz), in $CDCl_3$ or CD_2Cl_2 (**10**), chemical shifts δ in ppm rel. to TMS (= 0 ppm), coupling constants J in Hz. MS: *Finnigan-MAT 4510* GC/MS (EI: 70 eV, CI: NH_3), *m/z* (rel. intensity in %).

Isolation. The chopped rhizomes were extracted with $CHCl_3$/MeOH 1:2 (*v/v*). After evaporation, the residue was partitioned between CH_2Cl_2 and H_2O. The org. phase was washed with sat. NaCl soln., dried ($MgSO_4$), and evaporated to give the crude oil (yield: *I. foetidissima*, 2.4%; *I. pallida*, 2.2%). Initial fractionation of the extracts by MPLC and purification of the compounds by prep. HPLC were performed as described before [5]. In this way, **9** (1.25% of the lipid extract), **10** (0.75%), and **18** (0.15%) were isolated as glass-like solids.

Diels-Alder *Reaction with 4-Phenyl-3*H*-1,2,4-triazole-3,5(4*H*)-dione* (**14**). Compound **14** in acetone was added dropwise at 0° under stirring to a soln. of iridal **6** or **8** in MeOH/H_2O, as obtained by the MPLC separation (see above). The soln. may contain up to 20% of H_2O. The course of the reaction was controlled by HPLC to avoid an excess of **14**. The isomeric products **15a**, **b** or **16a**, **b** (0.2% each, rel. to the lipid extract), resp., were isolated by prep. HPLC.

Oxidative Degradation with Pyridinium Chlorochromate. The reaction was carried out as described previously [7]. The degradation products **11**–**13** and **17** were identified by GC/MS and comparison with authentic standards.

*2-{2-{8-[2-(Acetoxymethyl)-6-methylhepta-1,5-dienyl]-2,3-dihydro-1,3-dioxo-2-phenyl-1*H*-[1,2,4]triazolo[1,2-a]pyridazin-6-yl}-1,10-dihydroxy-6-(3-hydroxypropyl)-10-methylspiro[4.5]dec-7-ylidene}propanal* (**15**).

Isomer **15a**. ^{1}H-NMR[2]): 10.18 (*s*, H–C(1)); 7.3–7.5 (*m*, Ph); 5.48 (br., H–C(16)); 5.38 (br., H–C(17)); 5.38 (br., H–C(18)); 5.07 (br., H–C(22)); 4.67, 4.43 (*AB*, J_{AB} = 13.5, 2 H–C(29)); 4.43 (br., H–C(26)); 4.23, 3.93 (*AB*, J_{AB} = 16.1, 2 H–C(28)); 3.64 (br. *d*, *J*(6,7) = 8.5, H–C(6)); 3.6, 3.55 (2*m*, 2 H–C(3)); 3.04 (*m*, H–C(14)); 2.7, 2.5 (2*m*, 2 H–C(8)); 2.18 (*m*, 2 H–C(21)); 2.07 (*s*, CH_3CO); 2.05, 1.8 (2*m*, 2 H–C(13)); 1.81 (*s*, Me(25)); 1.7 (*s*, Me(24)); 1.62 (*s*, Me(30)); 1.6 (*m*, 2 H–C(9)); 1.2 (*s*, Me(27)). ^{13}C-NMR[2]): 191.0 (*d*, C(1)); 170.7 (*s*, CH_3CO); 162.7 (*s*, C(7)); 152.5, 152.2 (2*s*, 2 NCO); 137.1 (*s*, C(1′) of Ph); 133.0 (*s*, C(2)); 133.0 (*s*, C(15)); 133.0 (*s*, C(19)); 130.9 (*s*, C(23)); 129.2 (*d*, C(3′), C(5′) of Ph); 128.3 (*d*, C(4′) of Ph); 125.4 (*d*, C(2′), C(6′) of Ph); 125.4 (*d*, C(22)); 122.5 (*d*, C(16)); 118.2 (*d*, C(18)); 76.8 (*d*, C(26)); 74.3 (*s*, C(10)); 67.9 (*t*, C(29)); 61.6 (*t*, C(3)); 57.7 (*s*, C(11)); 51.8 (*d*, C(17)); 48.7 (*d*, C(14)); 45.6 (*t*, C(28)); 42.0 (*d*, C(6)); 38.2 (*t*, C(9)); 35.1 (*t*, C(12)); 34.4 (*t*, C(20)); 30.9 (*t*, C(4)); 29.1 (*t*, C(5)); 28.1 (*q*, C(27)); 26.7 (*t*, C(21)); 26.2 (*t*, C(13)); 25.7 (*q*, C(24)); 23.9 (*t*, C(8)); 21.0 (*q*, CH_3CO); 17.9 (*q*, C(30)); 11.1 (*q*, C(25)).

Isomer **15b**. ^{1}H-NMR[2]): 10.15 (*s*, H–C(1)); 7.3–7.5 (*m*, Ph); 5.43 (*d*, *J*(16,17) = 4.1, H–C(16)); 5.33 (*d*, *J*(18,17) = 10, H–C(18)); 5.14 (*dd*, *J*(17,16) = 4.1, *J*(17,18) = 10, H–C(17)); 5.05 (*t*, *J*(22,21) = 1.3, H–C(22)); 4.76 (br., H–C(26)); 4.65, 4.58 (*AB*, J_{AB} = 15.1, 2 H–C(29)); 4.25, 3.90 (*AB*, J_{AB} = 16.3, 2 H–C(28)); 3.5 (*m*, H–C(6)); 3.5 (*m*, 2 H–C(3)); 2.86 (*m*, H–C(14)); 2.7, 2.5 (2*m*, 2 H–C(8)); 2.1 (*s*, CH_3CO); 1.81 (*s*, Me(25)); 1.7 (*s*, Me(24)); 1.6 (*s*, Me(30)); 1.19 (*s*, Me(27)). ^{13}C-NMR[2]): 191.0 (*d*, C(1)); 170.5 (*s*, CH_3CO); 162.8 (*s*, C(7)); 152.4, 152.2 (2*s*, 2 NCO); 137.7 (*s*, C(1′) of Ph); 133.1 (*s*, C(15)); 132.8 (*s*, C(2)); 132.8 (*s*, C(19)); 130.8 (*s*, C(23)); 129.2 (*d*, C(3′), C(5′) of Ph); 128.4 (*d*, C(4′) of Ph); 125.6 (*d*, C(2′), C(6′) of Ph); 122.7 (*d*, C(22)); 122.5 (*d*, C(16)); 117.8 (*d*, C(18)); 76.0 (*d*, C(26)); 74.1 (*s*, C(10)); 66.4 (*t*, C(29)); 62.1 (*t*, C(3)); 57.6 (*s*, C(11)); 52.3 (*d*, C(17)); 47.3 (*d*, C(14)); 45.6 (*t*, C(28)); 42.4 (*d*, C(6)); 37.7 (*t*, C(9)); 35.1 (*t*, C(20)); 34.3 (*t*, C(12)); 31.2 (*t*, C(4)); 29.4 (*t*, C(5)); 27.7 (*q*, C(27)); 26.1 (*t*, C(21)); 25.6 (*t*, C(13)); 25.7 (*q*, C(24)); 23.9 (*t*, C(8)); 21.0 (*q*, CH_3CO); 17.8 (*q*, C(30)); 11.0 (*q*, C(25)).

*(6*R*,10*S*,11*S*)-16,17-Didehydroiridal* (= *2-[4-Hydroxy-2-(3-hydroxypropyl)-3,4-dimethyl-3-(4,8,12-trimethyltrideca-3,5,7,11-tetraenyl)cyclohexylidene]propanal*; **8**). EI-MS: 456 (3, M^+), 387 (6), 369 (2), 243 (4), 216 (7), 147 (81), 69 (100).

*2-{3-{2-[8-(2,6-Dimethylhepta-1,5-dienyl)-2,3-dihydro-6-methyl-1,3-dioxo-2-phenyl-1*H*-[1,2,4]triazolo[1,2-a]pyridazin-5-yl]ethyl}-4-hydroxy-2-(3-hydroxypropyl)-3,4-dimethylcyclohexylidene}propanal* (**16**). *Isomer* **16a**. ^{1}H-NMR[2]): 10.16 (*s*, H–C(1)); 7.48–7.32 (*m*, Ph); 5.42 (br. *s*, H–C(16)); 5.02 (*m*, H–C(22)); 5.02 (*m*, H–C(17)); 4.92 (*d*, *J*(18,17) = 8.9, H–C(18)); 4.36 (br. *s*, H–C(14)); 3.56 (*t*, *J*(3,4) = 7.2, 2 H–C(3)); 3.17 (br. *d*, *J*(6.5) = 11.1, H–C(6)); 2.57, 2.54 (2*m*, 2 H–C(8)); 2.45, 1.6 (2*m*, 2 H–C(13)); 2.08, 2.0 (2*m*, 2 H–C(5)); 2.05 (*m*, 2 H–C(21)); 1.97 (*m*, 2 H–C(20)); 1.85, 1.69 (2*m*, 2 H–C(9)); 1.78 (*s*, Me(25)); 1.78 (*s*, Me(29)); 1.63 (*s*, Me(24)); 1.55 (*s*, Me(30)); 1.55 (*s*, Me(28)); 1.35, 1.23 (2*m*, 2 H–C(4)); 1.29, 1.17 (2*m*, 2 H–C(12)); 1.12 (*s*, Me(27)); 1.06 (*s*, Me(26)). ^{13}C-NMR[2]): 189.9 (*d*, C(1)); 162.8 (*s*, C(7)); 151.4, 150.9 (2*s*, 2 NCO); 141.0 (*s*, C(1′) of Ph); 132.9 (*s*, C(2)); 131.8 (*s*, C(19)); 131.3 (*s*, C(23)); 130.0 (*s*, C(15)); 129.0 (*d*, C(3′), C(5′) of Ph); 127.8 (*d*, C(4′) of Ph); 125.3 (*d*, C(2′), C(6′) of Ph); 123.6 (*d*, C(22)); 121.4 (*d*, C(16)); 120.2 (*d*, C(18)); 74.8 (*s*, C(10)); 62.9 (*t*, C(3)); 57.4 (*d*, C(14)); 51.8 (*d*, C(17)); 44.4 (*s*, C(11)); 43.5 (*d*, C(6)); 39.8 (*t*, C(20)); 37.1 (*t*, C(9)); 32.5 (*t*, C(4)); 30.3 (*t*, C(12)); 26.6 (*t*, C(21)); 26.3 (*q*, C(27)); 26.3 (*t*, C(5)); 23.6 (*t*, C(13)); 25.7 (*q*, C(24)); 23.7 (*t*, C(8)); 19.2 (*q*, C(28)); 18.2 (*q*, C(26)); 17.7 (*q*, C(30)); 16.8 (*q*, C(29)); 10.9 (*q*, C(25)). CI-MS: 631 (M^+).

Isomer **16b**. ^{1}H-NMR[2]): 10.13 (*s*, H–C(1)); 7.48–7.32 (*m*, Ph); 5.39 (br. *s*, H–C(16)); 5.05 (*m*, H–C(22)); 5.02 (*m*, H–C(17)); 4.95 (*d*, *J*(18,17) = 9, H–C(18)); 4.25 (br., H–C(14)); 3.55 (*t*, *J*(3,4) = 7, 2 H–C(3)); 3.25 (br. *d*, *J*(6,5) = 12, H–C(6)); 2.56, 2.5 (2*m*, 2 H–C(8)); 2.08 (*m*, 2 H–C(21)); 2.05, 1.68 (2*m*, 2 H–C(13)); 2.01 (*m*, 2 H–C(20)); 2.0, 1.75 (2*m*, 2 H–C(5)); 1.82, 1.65 (2*m*, 2 H–C(9)); 1.78 (*s*, Me(25)); 1.78 (*s*, Me(29)); 1.74 (*s*, Me(28)); 1.65 (*s*, Me(24)); 1.58 (*s*, Me(30)); 1.45, 1.23 (2*m*, 2 H–C(12)); 1.33, 1.22 (2*m*, 2 H–C(4)); 1.1 (*s*, Me(27)); 1.02 (*s*, Me(26)). ^{13}C-NMR[2]): 189.8 (*d*, C(1)); 161.6 (*s*, C(7)); 151.9, 150.9 (2*s*, 2 NCO); 140.6 (*s*, C(1′) of Ph); 133.4 (*s*, C(2)); 131.3 (*s*, C(23)); 131.8 (*s*, C(19)); 131.2 (*s*, C(15)); 129.0 (*d*, C(3′), C(5′) of Ph); 127.8 (*d*, C(4′) of Ph); 125.3 (*d*, C(2′), C(6′) of Ph); 123.6 (*d*, C(22)); 121.2 (*d*, C(16)); 120.5 (*d*, C(18)); 74.9 (*s*, C(10)); 62.9 (*t*, C(3)); 57.0 (*d*, C(14)); 52.7 (*d*, C(17)); 44.2 (*s*, C(11)); 43.4 (*d*, C(6)); 39.8 (*t*, C(20)); 37.0 (*t*, C(9)); 32.6 (*t*, C(4)); 31.7 (*t*, C(12)); 26.6 (*t*, C(21)); 26.4 (*q*, C(27)); 26.2 (*t*, C(5)); 26.0 (*t*, C(13)); 25.7 (*q*, C(24)); 23.7 (*t*, C(8)); 19.9 (*q*, C(28)); 17.8 (*q*, C(26)); 17.7 (*q*, C(30)); 16.8 (*q*, C(29)); 11.1 (*q*, C(25)).

*(6*R*,10*S*,11*S*)-16,17-Didehydro-26-hydroxyiridal* (= *2-[4-Hydroxy-3-(hydroxymethyl)-2-(hydroxypropyl)-4-methyl-3-(4,8,12-trimethyltrideca-3,5,7,11-tetraenyl)cyclohexylidene]propanal*; **9**). ^{1}H-NMR[2]): 10.2 (*s*, H–C(1)); 6.35 (*dd*, *J*(17,16) = 15.2, *J*(17,18) = 10.8, H–C(17)); 6.05 (*d*, *J*(16,17) = 15.2, H–C(16)); 5.86 (*d*, *J*(18,17) = 10.8, H–C(18)); 5.23 (*t*, *J*(14,13) = 7.2, H–C(14)); 5.08 (*t*, *J*(22,21) = 6.5, H–C(22)); 4.09, 3.93 (*AB*, J_{AB} = 10.9, 2 H–C(26)); 3.7, 3.6 (2*m*, 2 H–C(3)); 3.57 (br. *d*, *J*(6,5) = 11.7, H–C(6)); 2.7, 2.55 (2*m*, 2 H–C(8)); 2.2,

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[2]) Squalene numbering, see **1**.

2.05 (2*m*, 2 H–C(5)); 2.1 (*m*, 2 H–C(21)); 1.8, 1.65 (2*m*, 2 H–C(9)); 2.0, 1.27 (2*m*, 2 H–C(13)); 1.84 (*s*, Me(25)); 1.76 (*s*, Me(29)); 1.68 (*s*, Me(28)); 1.67 (*s*, Me(24)); 1.6 (*s*, Me(30)); 1.41, 1.32 (2*m*, 2 H–C(4)); 1.31 (*s*, Me(27)). ^{13}C-NMR[2]): 190.0 (*d*, C(1)); 162.5 (*s*, C(7)); 138.6 (*s*, C(19)); 134.8 (*s*, C(15)); 134.8 (*d*, C(16)); 133.2 (*s*, C(2)); 131.7 (*s*, C(23)); 130.6 (*d*, C(14)); 125.2 (*d*, C(18)); 124.0 (*d*, C(22)); 123.6 (*d*, C(17)); 76.3 (*s*, C(10)); 68.4 (*t*, C(26)); 62.5 (*t*, C(3)); 46.7 (*s*, C(11)); 42.6 (*d*, C(6)); 37.1 (*t*, C(9)); 35.5 (*t*, C(4)); 27.2 (*t*, C(5)); 26.6 (*t*, C(21)); 26.4 (*q*, C(27)); 25.9 (*q*, C(24)); 23.9 (*t*, C(8)); 21.8 (*t*, C(13)); 17.7 (*q*, C(30)); 16.8 (*q*, C(29)); 12.4 (*q*, C(28)); 11.0 (*q*, C(25)). EI-MS: 472 (2, M^+), 454 (2.5), 414 (5), 385 (4), 216 (13), 147 (79), 69 (100). HR-MS: 472.35526 ($C_{30}H_{48}O_4$, calc. 472.3534).

*(6*R*,10*S*,11*S*,14*S*,26*R*)-15,16,17,18,19,20-Hexadehydro-14,15,18,19-tetrahydro-26,28-dihydroxy-26,14-cycloiridal* (= *2-{1,10-Dihydroxy-2-[1-(hydroxymethyl)-5,9-dimethyldeca-1,3,5,8-tetraenyl]-6-(3-hydroxypropyl)-10-methylspiro[4.5]dec-7-ylidene}propanal*; **10**). ^{1}H-NMR[2]): 10.1 (*s*, H–C(1)); 6.35 (*dd*, *J*(17,18) = 15, *J*(17,16) = 10.8, H–C(17)); 6.28 (*d*, *J*(18,17) = 15, H–C(18)); 6.18 (*d*, *J*(16,17) = 10.8, H–C(16)); 5.5 (*t*, *J*(20,21) = 7.5, H–C(20)); 5.1 (*t*, *J*(22,21) = 7.5, H–C(22)); 4.35 (*d*, *J*(26,14) = 5.4, H–C(26)); 4.12, 3.92 (*AB*, J_{AB} = 12, 2 H–C(28)); 3.56, 3.36 (2*m*, 2 H–C(3)); 3.51 (br. *d*, *J*(6,5) = 9, H–C(6)); 3.26 (*m*, H–C(14)); 2.85 (*t*, *J*(21,20) = *J*(21,22) = 7,5, 2 H–C(21)); 2.68, 2.45 (2*m*, 2 H–C(8)); 2.1, 1.7 (2*m*, 2 H–C(5)); 2.1, 1.6 (2*m*, 2 H–C(13)); 1.79 (*s*, Me(29)); 1.77 (*s*, Me(25)); 1.7 (*m*, 2 H–C(9)); 1,7 (*s*, Me(24)); 1.65 (*s*, Me(30)); 1.45, 1.3 (2*m*, 2 H–C(12)); 1.37, 1.25 (2*m*, 2 H–C(4)); 1.32 (*s*, Me(27)). ^{13}C-NMR[2]): 191.5 (*d*, C(1)); 164.4 (*s*, C(7)); 139.6 (*d*, C(18)); 137.3 (*s*, C(19)); 133.9 (*s*, C(15)); 133.4 (*d*, C(20)); 132,7 (*s*, C(2)); 132.4 (*s*, C(23)); 131.2 (*d*, C(16)); 122.1 (*d*, C(22)); 121.9 (*d*, C(17)); 76.3 (*d*, C(26)); 74.3 (*s*, C(10)); 66.0 (*t*, C(28)); 61.4 (*t*, C(3)); 58.9 (*s*, C(11)); 48.7 (*d*, C(14)); 42.9 (*d*, C(6)); 38.1 (*t*, C(9)); 35.1 (*t*, C(12)); 31.2 (*t*, C(4)); 29.9 (*t*, C(5)); 27.8 (*t*, C(21)); 27.7 (*q*, C(27)); 25.8 (*t*, C(13)); 25.7 (*q*, C(24)); 24.4 (*t*, C(8)); 17.8 (*q*, C(30)); 12.5 (*q*, C(29)); 10.9 (*q*, C(25)). EI-MS: 486 (1, M^+), 468 (7.5), 450 (4), 433 (2.5), 381 (3.5), 109 (55), 69 (75), 43 (100). HR-MS: 468.3222 ($C_{30}H_{44}O_4$, $[M - H_2O]^+$, calc. 468.32396).

*(6*S*,7*R*,10*S*,11*S*,18*R*,22*S*)-16,17,19,20-Tetradehydro-2,7,18,19,22,23-hexahydro-22-methyl-3-*O*,7:18,23-dicycloiridal* (= *2-{2-Hydroxy-8-(3-hydroxypropyl)-2-methyl-1-[4-methyl-6-(2,5,6,6-tetramethylcyclohex-2-enyl)-hexa-3,5-dienyl]-6-oxabicyclo[3.2.1]oct-5-yl}propanal*; **18**). ^{1}H-NMR[2]): 9.89 (*s*, H–C(1)); 6.0 (*d*, *J*(16,17) = 15.1, H–C(16)); 5.42 (br., H–C(20)); 5.36 (*d*, *J*(17,16) = 15.1, H–C(17)); 5.31 (*t*, *J*(14,13) = 6.6, H–C(14)); 4.17, 3.76 (*AB*, J_{AB} = 8.8, 2 H–C(26)); 3.62 (*t*, *J*(3,4) = 6, 2 H–C(3)); 2.79 (*q*, *J*(2,25) = 7, H–C(2)); 2.4, 2.1 (2*m*, 2 H–C(13)); 2.38 (br., H–C(18)); 1.85, 1.7 (2*m*, 2 H–C(21)); 1.84, 1.6 (2*m*, 2 H–C(9)); 1.75, 1.68 (2*m*, 2 H–C(12)); 1.75, 1.6 (2*m*, 2 H–C(4)); 1.73 (*s*, Me(28)); 1.62 (*m*, H–C(6)); 1.61, 1.47 (2*m*, 2 H–C(5)); 1.51 (*s*, Me(29)); 1.5, 1.37 (2*m*, 2 H–C(8)); 1.45 (*m*, H–C(22)); 1.33 (*s*, Me(27)); 0.98 (*d*, *J*(25,2) = 7, Me(25)); 0.85 (*d*, *J*(31,22) = 6.8, Me(31)); 0.84 (*s*, Me(30)); 0.64 (*s*, Me(24)). ^{13}C-NMR[2]): 205.9 (*d*, C(1)); 137.5 (*d*, C(16)); 134.7 (*s*, C(19)); 133.7 (*s*, C(15)); 130.8 (*d*, C(14)); 128.2 (*d*, C(17)); 121.7 (*d*, C(20)); 87.5 (*s*, C(7)); 75.1 (*s*, C(10)); 72.5 (*t*, C(26)); 63.0 (*t*, C(3)); 56.4 (*d*, C(18)); 54.7 (*s*, C(11)); 51.1 (*d*, C(2)); 50.9 (*d*, C(6)); 38.3 (*d*, C(22)); 37.1 (*t*, C(9)); 35.7 (*s*, C(23)); 33.1 (*t*, C(4)); 32.1 (*t*, C(8)); 32.0 (*t*, C(21)); 29.4 (*t*, C(12)); 26.6 (*q*, C(30)); 26.4 (*t*, C(13)); 24.4 (*q*, C(27)); 23.2 (*q*, C(29)); 21.9 (*t*, C(5)); 15.7 (*q*, C(31)); 14.8 (*q*, C(24)); 12.8 (*q*, C(28)); 10.0 (*q*, C(25)). EI-MS: 486 (0.5, M^+), 468 (0.5), 428 (1), 416 (1), 398 (3.5), 358 (3), 230 (15), 160 (100), 55 (85), 43 (95). HR-MS: 486.3683 ($C_{31}H_{50}O_4$, calc. 486.37091).

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