Design and Synthesis of Violet Odorants with Bicyclo[6.4.0]dodecene and Bicyclo[5.4.0]undecene Skeletons

Philip Kraft

Givaudan Roure Fragrance Research Ltd., CH-8600 Dübendorf, Switzerland

Fax +41(1)8242926; E-mail philip.kraft@roche.com

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Dedicated with best wishes to Professor Werner Tochtermann on the occasion of his 65th birthday

Abstract: The Diels–Alder reaction of 1,2-bis(methylene)cyclooctane (**13**), 4-methylenespiro[2.7]decane (**29**), 4-methylenespiro[2.6]nonane (**40**) and 4-methylenespiro[2.7]dec-8-ene (**46**) with different α,β-unsaturated carbonyl compounds afforded various derivatives **16**, **18**, **20**, **22**, **24**, **26**, **32**, **36**, **38**, **41**, **42** and **47** of a molecular-modeled lead compound **9**. These less flexible β-ionone-mimics with bicyclo[6.4.0]dodecene and bicyclo[5.4.0]undecene skeletons possess interesting fruity-woody-floral odor notes and provide insight into the structure-odor correlation of violet odorants. 5-(2-Methylcycloalk-1-en-1-yl)hex-3-en-2-ones (e.g. **35**) were identified as byproducts of the Rh(I)-catalyzed reactions of the vinylcyclopropanes **29** and **40**.

Key words: cycloadditions, ionones, molecular modeling, vinylcyclopropanes, Wilkinson's catalyst

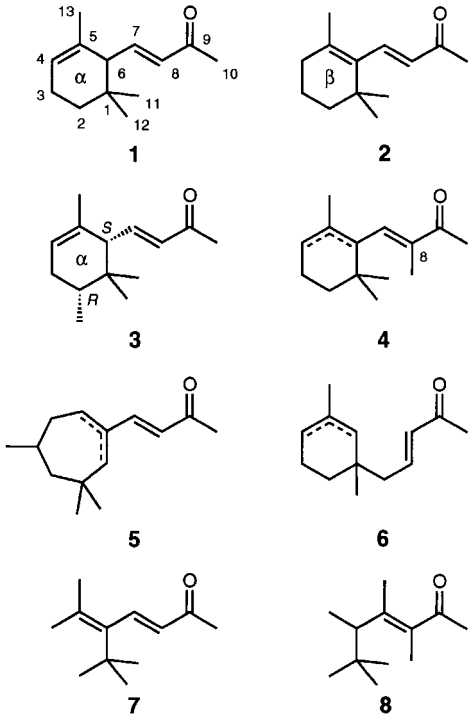


Figure 1. Survey of diverse violet odorants

About hundred years ago, violet flower oil (*Viola odorata* L., fam. Violaceae) was one of the most valuable perfumery materials, and v. Soden[1] estimated the production cost of this highly esteemed essential oil to exceed 80 000 German gold marks per kg. On the assumption that their odor was due to the same natural product, Tiemann and Krüger[2] used the similarly smelling but much cheaper orris root oil (*Iris pallida* Lam., fam. Iridaceae) in their search for the odorous principle of violets. The odor of a mixture of α-ionone (**1**) and β-ionone (**2**) (Figure 1) obtained by acid-catalyzed cyclization of pseudoionone possessed the typical odor of violets in bloom. Thus, in combination with incorrect elemental analyses, Tiemann and Krüger believed the isolated irone to be a double-bond isomer of ionone (**1**/**2**).[2] The correct constitution of the irones was established only 54 years later in 1947,[3–5] and the stereochemistry was elucidated as late as 1971.[6] In terms of odor, (+)-(2*R*,6*S*)-*cis*-α-irone (**3**)[7] with its intense and very fine orris character is the most important irone isomer of orris root oil. However, in 1972 an in-depth analysis of violet flower oil[8] showed a mixture of α- and β-ionone (**1**/**2**) to be indeed responsible for the odor of violets. Although, Tiemann and Krüger had inaccurately analyzed orris root oil in search of the odorous principle of violets, they had actually discovered what they were initially looking for.

β-Ionone (**2**) was not only found in *Viola odorata* L., it also occurs in a great variety of floral scents.[9] In the *Orchidaceae* family, the headspace of *Encyclica adenocarpa* (La Llave et Lex.) Schltr. for example contains 10.0% of **2**, that of *Maxillaria nigrescens* Lindl. 13.6% of **2**, and that of *Oncidium tigrinum* La Llave et Lex. even 14.5% of β-ionone (**2**). In modern perfumery, 8-methylionone (**4**), which is more intense than **1**/**2** and possesses a very fine odor reminiscent of orris and violets with a slightly woody-vetiver tonality, became the most popular violet odorant, and one can find up to 20% of it in some creations.[10]

Interestingly, the constitutional irone-isomer **5** with a seven-membered ring was said to be reminiscent of 8-methylionone (**4**) with a pronounced floral character,[11] while the constitutional ionone-isomer **6** is more reminiscent of irone (**3**) with an additional fruity raspberry note.[12] Two *seco* ionones, 5-*tert*-butyl-6-methylhepta-3,5-dien-2-one (**7**)[13] and (3*E*)-3,4,5,6,6-pentamethylhept-3-en-2-one (**8**, Koavone®)[14] (Figure 1), are known to possess the odor characteristics of ionone (**1**/**2**) and 8-methylionone (**4**), respectively. Yet, no attempts have been made to construct conformationally more rigid violet odorants that

would provide insight into the structural requirements of this highly interesting odor.

For this purpose, we carried out in-depth molecular-modeling calculations,[15] and not surprisingly found the antiperiplanar *s-trans* conformation of the two conjugated double bonds that is depicted in Figure 2 to be the global energy minimum of β-ionone (**2**). This led to the idea of mimicking the steric bulk of the dimethyl substitution by fusing a six-membered ring. The remaining 5-methyl group was then found to be best superimposed by a cyclooctene structure. Combination of these structural features gave the bicyclic ketone **9**, our first molecular target. A local minimum 0.236 kcal/mol above the lowest energy conformer showed the best overlap with β-ionone (**2**). This is illustrated with a stereoplot in Figure 2.

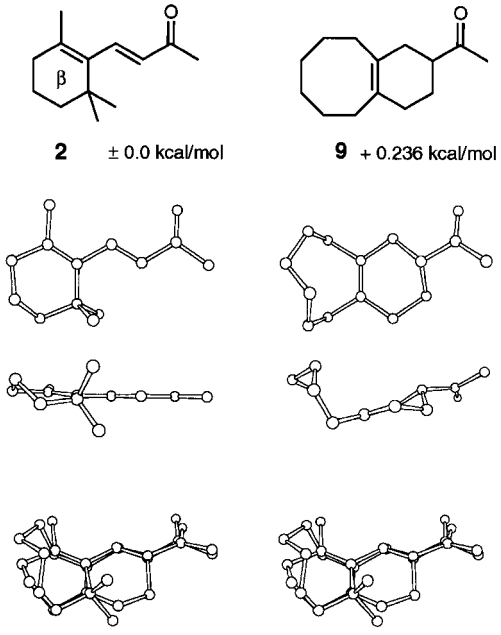
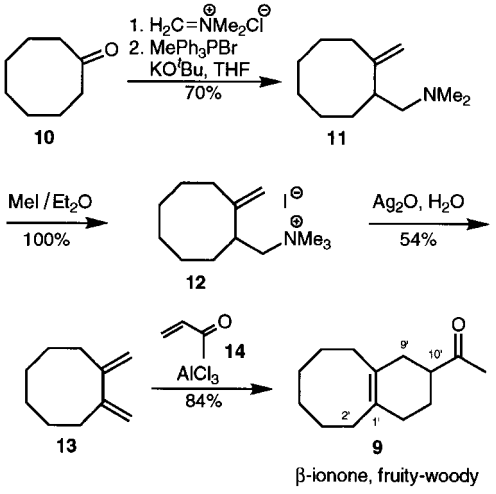


Figure 2. Molecular-modeling calculations

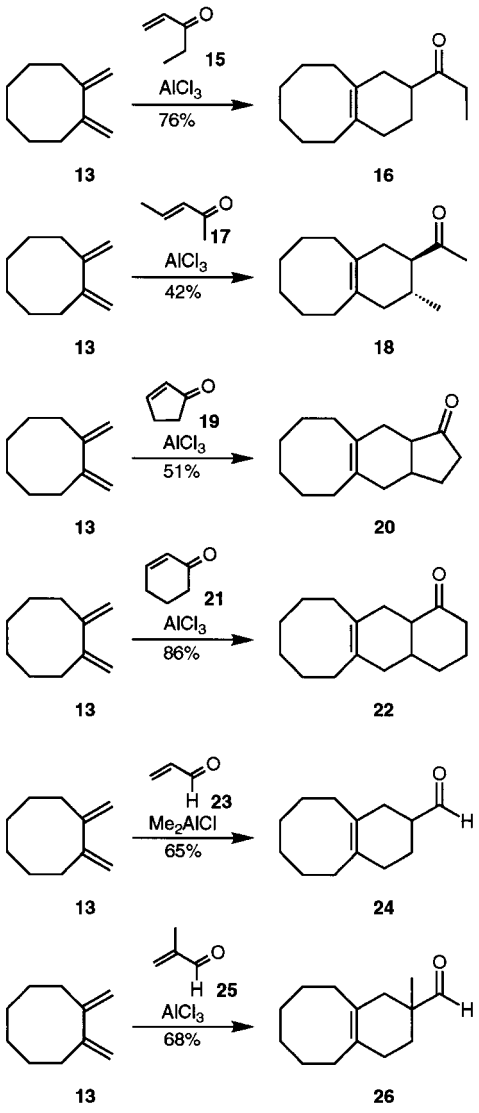
The molecular target **9** is easily accessible by Diels–Alder reaction of but-3-en-2-one (**14**) with bis(methylene)cyclooctane (**13**, Scheme 1). We synthesized the latter diene according to a modified sequence of Bickelhaupt et al.,[16] starting from cyclooctanone (**10**). Mannich reaction employing Eschenmoser salt,[17] followed by a Wittig reaction using potassium *tert*-butoxide[18] provided **11** in 70% isolated overall yield. This was then quaternized quantitatively by the action of methyl iodide to yield **12**. A classical Hofmann degradation[16] of **12** in the next step furnished the diene **13** in 54% yield. This circuitous route to **13** is necessary, because direct Wittig methylenation of 2-methylenecyclooctan-1-one is not possible.[16] The Diels–Alder reaction of **13** with the dienophile **14** in the presence of aluminum trichloride was straightforward, and gave the target molecule **9** in 84% yield. The fruity-woody odor of the tailored molecular target **9** was indeed found to be very close to that of the parent β-ionone (**9**). Consequently, and since methylated ionones are also important odorants (e.g. **4** and **8**), we were aiming at the synthesis of methylated analogs of **9** and the related *cyclo*-derivatives **20** and **22**.



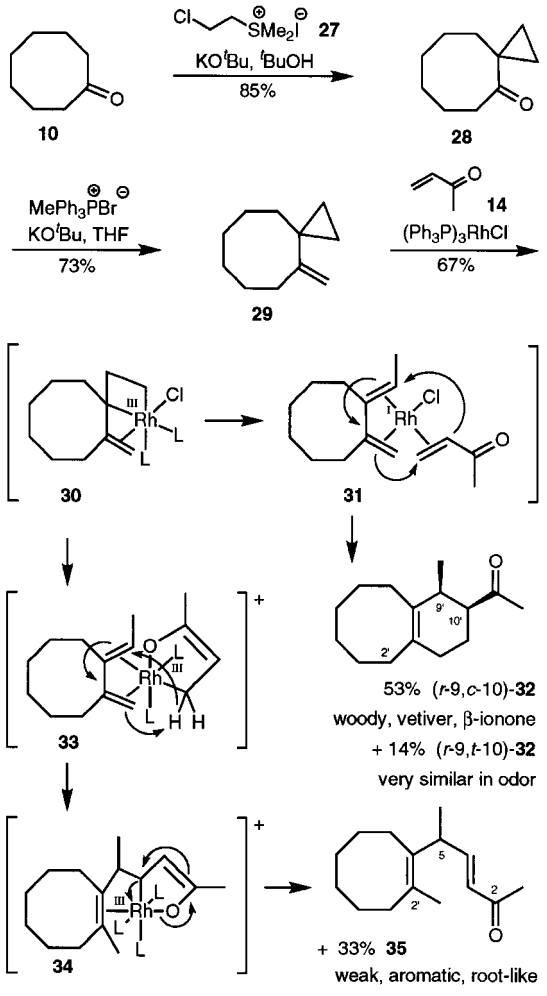
Scheme 1

Compounds **16**, **18**, **20**, **22**, **24** and **26** (Scheme 2) were synthesized in good yield by analogous Diels–Alder reactions of bis(methylene)cyclooctane (**13**) with pent-1-en-3-one (**15**), (3*E*)-pent-3-en-2-one (**17**), cyclopent-2-en-1-one (**19**), cyclohex-2-en-1-one (**21**), acrolein (**23**), and methacrolein (**25**), respectively. While the 10-(1-oxo)propyl substitution of **16** did not change the typical ionone odor, the *trans* 11-methyl group of **18** diminished the intensity and shifted the odor towards a more woody, coffee-like character. The violet note was, however, completely absent in the *cyclo*-derivatives **20** and **22**, as well as in the aldehydes **24** and **26**.

The synthesis of the compounds **32**, **36**, **38**, **41**, **42** and **47**, methylated in α-position to the bridgehead, was carried out in an unexpected way by a novel Rh(I)-mediated [4+2] cycloaddition of the corresponding dienophiles to vinylcyclopropanes (e.g. **29**, **40**) (Scheme 3). These were synthesized from cyclooctanone (**10**), cyclooct-4-en-1-one[19] (**44**) and cycloheptanone (**39**) by spiroannullation[20] with 2-chloroethyl methyl sulfonium iodide (**27**)[21] and subsequent Wittig methylenation.[18] Employing this two-step sequence, 4-methylenespiro[2.7]decane (**29**) was obtained from cyclooctanone (**10**) on a 30 g scale in 62% isolated overall yield. Methylenespiro[2.7]decane (**29**) reacted with but-3-en-2-one (**14**) in the presence of Wilkinson's catalyst not by means of a [5+2] cycloaddition, discovered by Wender et al.[22] and recently applied by Binger, de Meijere et al.;[23] instead, the diastereoisomeric 9-methylated bicyclo[6.4.0]dodecenylethanones **32** (*E*/*Z* = 1:4) were isolated in 45% yield. (3*E*,1'*E*)-5-(2'-Methylcyclooct-1'-en-1'-yl)hex-3-en-2-one (**35**) was the only byproduct isolated, no regioisomers to **32** nor any compounds with seven-membered ring systems were ob-



Scheme 2

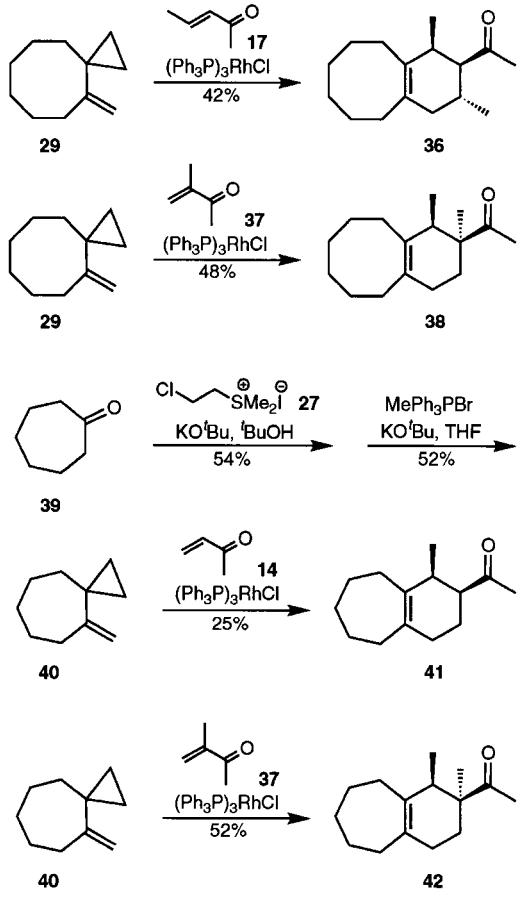


Scheme 3

tained. However, in the presence of one equivalent of silver triflate used by Wender et al.[22] to accelerate the [5+2] cycloaddition by formation of the $[Rh(PPh_3)_3]^+$ ion, (3*E*,1'*E*)-5-(2'-methylcyclooct-1'-en-1'-yl)hex-3-en-2-one (**35**) became the only product and was isolated in 66% yield.

The formal mechanism presented in Scheme 3 might account for the observed reaction products. Though **32** obviously is the Diels–Alder adduct of but-3-en-2-one (**14**) and 1-ethylidene-2-methylenecyclooctane, we were not able to detect this reactive intermediate. This could be due to a fast cycloaddition step or to the formation of rhodium complexes. However, 2-methyl-1-vinylcyclooct-1-ene was found to be present in rather large quantity. The catalysis of [4+2] cycloadditions by low valent rhodium complexes was described by Livinghouse et al.[24] and Wender et al.,[25] but to our best knowledge the rhodium-catalyzed reactions of vinylcyclopropanes in Scheme 3 have not been described before. Compounds **36**, **38**, **41** and **42** were prepared in analogy to the synthesis of **32** employing (3*E*)-pent-3-en-2-one (**17**), 3-methylbut-3-en-2-one (**37**), and but-3-en-2-one (**14**) as dienophiles in the presence of Wilkinson's catalyst (Scheme 4). Corresponding 5-(2-methylcycloalk-1-en-1-yl)hex-3-en-2-ones were again identified as byproducts, and became main products in the presence of silver triflate.

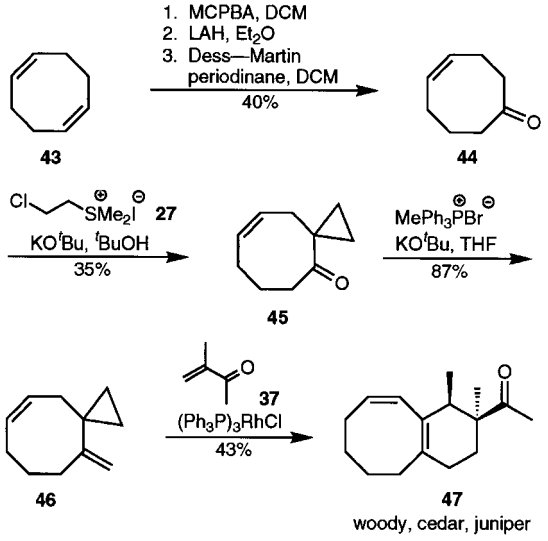
The odor of both diastereoisomeric 9-methylated bicyclo[6.4.0]dodecenylethanones **32** was described as being reminiscent to β-ionone (**2**) with pronounced woody aspects and a *vetiver* tonality. The odor of **32** is however more intense than that of compounds **9** or **16**. As with **18**, the additional methyl group of **36** at C-11 diminishes again both the ionone tonality and odor intensity, resulting in a relatively weak woody-fruity, balsamic note. Transposition of the 11-methyl group of **36** into the 10-position in compound **38** strongly increases the odor intensity, but this goes with a complete loss of the β-ionone (**2**) character. Instead, the interesting woody-ambery, incense-like odor of **38** is close to that of Iso E super.[10] The odors of the ring-contracted compounds **41** and **42**, synthesized from



Scheme 4

4-methylenespiro[2.6]nonane, were quite similar to that of their parent compounds **32** and **38**. However, **41** is more floral, jasmone-like than **32** and less reminiscent of violets, and **42** in contrast to **38** inclines to a sandalwood direction.

Finally, we wanted to see if double-bonds would be tolerated by the reaction conditions of the rhodium-catalyzed vinylcyclopropane addition. Scheme 5 shows the synthesis of 1-{*r*-9,*c*-10-dimethylbicyclo[6.4.0]dodec-1(8),6(7)-diene-10-yl}ethan-1-one (**47**) from cycloocta-1,5-diene (**43**). Cyclooct-4-en-1-one (**44**) was synthesized in 40% overall yield following a sequence of Meier, Mayer and Kolshorn,[19] but using Dess–Martin periodinane[26] in the oxidation step. Spiroannullation of **44** with 2-chloroethyl dimethyl sulfonium iodide[20,21] was regioselective, yet spiro[2.7]dec-8-en-4-one (**45**) was obtained in a moderate to low yield of 35% only. Wittig methylenation[18] in the next step gave 4-methylenespiro[2.7]dec-8-ene (**46**) in 87% yield. This was then reacted in the rhodium(I)-mediated [4+2] cycloaddition with 3-methylbut-3-en-2-one (**37**) to afford **47** in 43% yield, the double bond being shifted into conjugation in the course of the reaction. Connectivity and relative stereochemistry were assigned by two-dimensional NMR experiments. The odor of **47** was much weaker than that of compound **38**, with a pronounced cedarwood tonality and a juniper nuance.



Scheme 5

Reagents and solvents (puriss. or purum) were purchased from Fluka and used without further purification. Flash chromatography (FC): Merck Kieselgel 60 (0.040–0.063 mm). IR: Nicolet 510 FT-IR (neat). NMR: Bruker AVANCE DPX-400 ($CDCl_3$, TMS). MS: Finnigan MAT 95 and MAT 212 (EI: 70 eV). ESI: Finnigan SSQ 710C (H_2O/MeOH, 1:1, + 1% AcOH). Elemental analyses: F. Hoffmann-La Roche AG, Basel, PRPI-S.

2-(Dimethylaminomethyl)-1-methylenecyclooctane (11)

N,*N*-Dimethylmethyleneammonium chloride (75 g, 0.80 mol) was added under N_2 to a solution of cyclooctanone (100 g, 0.79 mmol) in MeCN (250 mL) at 0 °C. The cooling bath was removed, and the mixture was stirred at r.t. for 3 d prior to the addition of 2 N aq NaOH (500 mL). The product was extracted with *t*-BuOMe (3 × 500 mL), and the combined organic extracts were dried (Na_2SO_4) and evaporated to provide 144 g (99%) of 2-(dimethylamino)methylcyclooctan-1-one. With mechanical stirring under N_2, methyl triphenylphosphonium bromide (336 g, 0.941 mol) was added to a solution of *t*-BuOK (100 g, 0.891 mol) in THF (2 L), and the mixture was heated to reflux. At this temperature, 2-(dimethylamino)methylcyclooctan-1-one (144 g, 786 mmol) was added dropwise, and the mixture was stirred for 3 h under reflux and 14 h at r.t. prior to pouring into a mixture of *t*-BuOMe/H_2O (1:1, 2 L). The organic layer was separated, the aqueous layer extracted with *t*-BuOMe (3 × 500 mL), and the combined organic extracts were dried (Na_2SO_4), concentrated in vacuo and purified by silica gel FC (pentane/*t*-BuOMe, 1:1, R_f 0.23) to provide 100 g (71%) of **11** as a colorless liquid.

IR: ν = 2763 (ν N–CH_2), 1457, 1447 (δ H–C–H), 888 (ω $C_2C{=}CH_2$), 1028, 1043 (ν C–N), 1636 (ν C=C), 3066 cm^{-1} (ν C=C–H).

^{1}H NMR: δ = 1.38–1.68 (m, 10 H, 4'-H_2 to 8'-H_2), 2.07–2.18 (m, 2 H, 3'-H_2), 2.20 [s, 6 H, $N(CH_3)_2$], 2.21–2.25 (m, 2 H, 1-H_2), 2.34 (m_c, 1 H, 1'-H), 4.85 (d, *J* = 4.0 Hz, 2 H, $=CH_2$).

^{13}C NMR: δ = 26.0, 26.4, 26.5 (t, C-4', 7', 8'), 28.8, 30.5 (t, C-5', 6'), 33.5 (t, C-3'), 43.4 (d, C-1'), 45.8 [2 q, $N(CH_3)_2$], 66.0 (t, C-1), 111.7 (t, $=CH_2$), 153.2 (s, C-2').

MS: *m*/*z* (%) = 58 ($C_3H_8N^+$, 100), 181 (M^+, 1).

***N,N,N*-Trimethyl 1-(2-methylenecyclooct-1-yl)methyl Ammonium Iodide (12)**

MeI (78.0 mL, 1.25 mol) was added to a stirred solution of **11** (90.7 g, 0.50 mol) in Et_2O (1.5 L) at r.t. under N_2, and the stirring was continued for 4 h. The precipitate was filtered, washed thoroughly with Et_2O (1.5 L), and dried on a vacuum line to provide 164 g (100 %) of **12** as a colorless solid.

IR: ν = 926, 916 (ν C–N), 1481, 1441, 1414 (δ C–H), 1635 cm^{-1} (ν_{as} NR_4^+).

MS: *m/z* (%) = 58 ($C_3H_8N^+$, 100), 127 (I^+, 8), 142 (CH_3I^+, 32).

ESI: *m/z* (%) = 151 ($C_{10}H_{17}N^+$, 3), 196 ($C_{13}H_{26}N^+$, 100).

1,2-Bis(methylene)cyclooctane (13)

Compound **12** (132 g, 0.408 mol) and AgO (185 g, 0.800 mol) were suspended in H_2O (1 L) under N_2. After stirring at r.t. for 1 h, the mixture was concentrated on a rotary evaporator at 60 °C/100 mbar. The resulting residue was pyrolyzed for 3 h at 140 °C/10 mbar with a distillation temperature of 39–40 °C and condensation of the product in a cold trap at –78 °C. The pyrolysis product was added to a mixture of H_2O/*t*-BuOMe (2:1, 600 mL), the organic layer was separated, the aqueous phase extracted with *t*-BuOMe (3 × 200 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo to provide 30.1 g (54%) of **13** as a colorless liquid.

IR: ν = 2921, 2849 (ν C–H), 1467, 1446 (δ H–C–H), 891 (δ C=C–H), 1629 cm^{-1} (ν C=C).

^{1}H NMR: δ = 1.53–1.55 (m, 4 H, 5, 6-H_2), 1.59–1.61 (m, 4 H, 4, 7-H_2), 2.32 (dd, *J* = 6.5, 6.0 Hz, 4 H, 3, 8-H_2), 4.76 (m, 2 H, 9, 10-H_b), 5.08 (d, 2 H, *J* = 2.5 Hz, 9, 10-H_a).

^{13}C NMR: δ = 25.9 (t, C-4, 7), 30.7 (t, C-5, 6), 33.5 (t, C-3, 8), 110.7 (t, C-9, 10), 152.0 (s, C-1, 2).

MS: *m/z* (%) = 67 ($C_5H_7^+$, 80), 79 (100), 93 (100), 107 (58), 121 (38) [$C_nH_{(2n-5)}^+$-series], 136 (M^+, 23).

1-{Bicyclo[6.4.0]dodec-1(8)-en-10-yl}ethan-1-one (9); Typical Procedure

$AlCl_3$ (160 mg, 1.20 mmol) was added to a stirred solution of **13** (2.00 g, 14.7 mmol) and but-3-en-2-one (1.46 mL, 17.8 mmol) in toluene (20 mL) at 0 °C. The mixture was allowed to warm to r.t., stirred for 60 h, and poured into *t*-BuOMe/H_2O (1:1, 400 mL). The organic layer was separated, the aqueous phase extracted with *t*-BuOMe (3 × 200 mL). The combined organic extracts were dried (Na_2SO_4), concentrated in vacuo, and purified by silica gel FC (pentane/*t*-BuOMe, 20:1, R_f 0.58) to provide 2.54 g (84%) of **9** as a colorless liquid.

IR: ν = 1711 cm^{-1} (ν C=O).

^{1}H NMR: δ = 1.35–1.57 (m, 10 H, 3'-H_2 to 6'-H_2, 11'-H_2), 2.18 (s, 3 H, CH_3), 1.93–2.14 (m, 8 H, 2', 7', 9', 12'-H_2), 2.55 (dddd, *J* = 11.5, 10.0, 5.5, 3.0 Hz, 1 H, 10'-H).

^{13}C NMR: δ = 25.3 (t, C-11'), 26.5, 26.5 (t, C-3', 6'), 27.9 (q, C-2), 28.7, 28.8 (t, C-4', 5'), 29.1, 31.1 (t, C-2', 7'), 31.5, 31.7 (t, C-9', 12'), 48.2 (d, C-10'), 128.8 (s, C-1'), 130.3 (s, C-8'), 211.9 (s, C-1).

MS: *m/z* (%) = 43 ($C_2H_3O^+$, 87), 67 ($C_5H_7^+$, 100), 81 ($C_6H_9^+$, 68), 93 (20), 107 (15), 121 (15), 135 (7), 149 (5) [$C_nH_{(2n-5)}^+$-series], 163 ($M^+ - C_2H_3O$, 49), 191 ($M^+ - CH_3$, 4), 206 (M^+, 23).

Anal. $C_{14}H_{22}O$ (206.3): calcd C 81.50, H 10.75; found C 81.49, H 10.57.

1-{Bicyclo[6.4.0]dodec-1(8)-en-10-yl}propan-1-one (16)

Following the procedure described for the preparation of **9**, pent-1-en-3-one (**15**; 7.40 mL, 75.0 mmol) and 1,2-bis(methylene)cyclooctane (**13**; 3.50 g, 25.0 mmol) were reacted together to afford, after FC on silica gel (pentane/*t*-BuOMe, 50:1, R_f 0.41), 4.21 g (76%) of **16** as a colorless liquid.

IR: ν = 1711 cm^{-1}(ν C=O).

^{1}H NMR: δ = 1.06 (t, *J* = 7.0 Hz, 3 H, CH_3), 1.35–1.58 (m, 10 H, 3'-H_2 to 6'-H_2, 11'-H_2), 1.99–2.18 (m, 8 H, 2' ,7', 9', 12'-H_2), 2.48 (dq, *J* = 17.5, 7.5 Hz, 1 H, 2-H_b), 2.54 (dq, *J* = 17.5, 7.5 Hz, 1 H, 2-H_a), 2.57 (dddd, *J* = 11.5, 10.5, 5.0, 3.0 Hz, 1 H, 10'-H).

^{13}C NMR: δ = 7.68 (q, C-3), 25.5 (t, C-11'), 26.5, 26.5 (t, C-3', 6'), 28.7, 28.8 (t, C-4', 5'), 29.1, 31.3 (t, C-2', 7'), 31.5, 31.7 (t, C-9', 12'), 33.7 (t, C-2), 47.2 (d, C-10'), 128.9 (s, C-1'), 130.2 (s, C-8'), 214.3 (s, C-1).

MS: *m/z* (%) = 29 ($C_2H_5^+$, 33), 57 ($C_3H_5O^+$, 40), 67 ($C_5H_7^+$,100), 81 ($C_6H_9^+$, 81), 91 ($C_7H_7^+$, 29), 107 (13), 121 (15), 135 (5) [$C_nH_{(2n-5)}^+$-series], 163 ($M^+ - C_2H_5 - CO$, 49), 191 ($M^+ - C_2H_5$, 16), 220 (M^+, 18).

Anal. $C_{15}H_{24}O$ (220.4): calcd C 81.76, H 10.98; found C 81.80, H 10.90.

(*r*-10, *t*-11)-1-{11-Methylbicyclo[6.4.0]dodec-1(8)-en-10-yl}ethan-1-one (18)

Following the procedure described for the preparation of **9**, (3*E*)-pent-3-en-2-one (**17**; 7.30 mL, 75.0 mmol) and 1,2-bis(methylene)cyclooctane (**13**; 3.50 g, 25.0 mmol) were reacted together to give, after FC on silica gel (pentane/*t*-BuOMe, 20:1, R_f 0.53), 2.32 g (42%) of **18** as a colorless liquid.

IR: ν = 1710 cm^{-1} (ν C=O).

^{1}H NMR: δ = 0.93 (d, *J* = 6.5 Hz, 3 H, 11'-CH_3), 1.35–1.55 (m, 8 H, 3'-H_2 to 6'-H_2), 1.76–2.16 (m, 9 H, 2', 7', 9', 12'-H_2, 11'-H_{ax}), 2.17 (s, 3 H, $COCH_3$), 2.36 [ddd, *J* = 10.5, 10.5, 5.5 Hz, 1 H, 10'-H_{ax}). *J*(10'-H, 11'-H) ≈ *J*(10'-H, 9'-H_{ax}) ≈ 10.5 Hz, i.e. 2 × ax–ax coupling, *J*(10'-H, 9'-H_{eq}) ≈ 5.5 Hz].

^{13}C NMR: δ = 19.5 (q, 11'-CH_3), 26.4, 26.3 (t, C-3', 6'), 28.7, 28.7 (t, C-4', 5'), 29.2 (q, C-2), 30.8 (d, C-11'), 31.3, 31.4, 32.5 (t, C-2', 7', 9'), 37.8 (t, C-12'), 55.2 (d, C-10'), 128.3 (s, C-1'), 130.0 (s, C-8'), 213.0 (s, C-1).

MS: *m/z* (%) = 43 ($C_2H_3O^+$, 61), 67 ($C_5H_7^+$, 100), 95 ($C_7H_{11}^+$, 63), 177 ($M^+ - C_2H_3O$, 52), 205 ($M^+ - CH_3$, 5), 220 (M^+, 19).

Anal. $C_{15}H_{24}O$ (220.4): calcd C 81.76, H 10.98; found C 81.46, H 10.95.

Tricyclo[7.6.0.0^{3,7}]pentadec-1(9)-en-4-one (20)

Following the procedure described for the preparation of **9**, cyclopent-2-en-1-one (**19**; 1.35 mL, 16.7 mmol) and 1,2-bis(methylene)cyclooctane (**13**; 1.70 g, 12.5 mmol) were reacted together to furnish, after FC on silica gel (pentane/*t*-BuOMe, 20:1, R_f 0.33), 1.39 g (51%) of **20** as a colorless product; diastereomeric ratio, 65:35.

IR: ν = 1741 cm^{-1}(ν C=O).

^{1}H NMR: δ = 1.30–1.55 (m, 8 H, 11-H_2 to 14-H_2), 1.66–1.87 (m, 2 H, 7, 8-H_b), 2.00–2.47 (m, 12 H, 7, 8-H_a and 2, 5, 6, 10, 15-H_2).

^{13}C NMR: δ = 25.7, 26.3, 26.4, 26.5, 26.5, 26.6, 27.7, 28.6, 28.8, 28.8, 28.8, 29.1, 30.7, 31.6, 31.9, 31.9, 32.9, 34.2 (t, C-2, 6, 8 and C-10 to C-15), 36.8, 37.6 (t, C-5), 32.0, 39.5 (d, C-7), 47.6, 52.0 (d, C-3), 128.4, 128.8, 129.9, 130.7 (s, C-1, 9), 219.1, 219.7 (s, C-4).

MS: *m/z* (%) = 41 ($C_3H_5^+$, 60), 79 ($C_5H_3O^+$, 55), 91 ($C_7H_7^+$, 93), 105 (46), 133 (29), 147 (17), 161 (19) [$C_nH_{(2n-7)}^+$-series], 174 ($C_{13}H_{18}^+$, 29), 190 ($M^+ - CO$, 15), 200 ($M^+ - H_2O$, 5), 218 (M^+, 100).

Anal. $C_{15}H_{22}O$ (218.3): calcd C 82.52, H 10.16; found C 82.19, H 10.16.

Tricyclo[8.6.0.0^{3,8}]hexadec-1(10)-en-4-one (22)
Following the procedure described for the preparation of **9**, cyclohex-2-en-1-one (**21**; 1.60 mL, 16.6 mmol) and 1,2-bis(methylene)cyclooctane (**13**; 1.70 g, 12.5 mmol) were reacted together to afford, after FC on silica gel (pentane/*t*-BuOMe, 20:1, R_f 0.44), 2.49 g (86%) of **22** as a colorless liquid.

IR: ν = 1711 cm^{-1} (ν C=O).

^{1}H NMR: δ = 1.26–1.71 (m, 11 H, 8-H, 7-H_2 and 12-H_2 to 15-H_2), 1.88–2.10 (m, 8 H, 6, 9, 11, 16-H_2), 2.15–2.26 (m, 3 H, 3-H and 2-H_2), 2.35–2.42 (m, 2 H, 5-H_2).

^{13}C NMR: δ = 26.1, 26.5, 26.6, 28.7, 28.8, 28.8, 31.3, 31.5, 32.4 (t, C-2, 6, 7 and C-11 to C-16), 38.1 (t, C-9), 40.9 (d, C-8), 41.9 (t, C-5), 51.1 (d, C-3), 128.9, 129.4 (s, C-1, 10), 212.6 (s, C-4).

MS: *m/z* (%) = 41 ($C_3H_5^+$, 25), 79 ($C_5H_3O^+$, 26), 91 ($C_7H_7^+$, 63), 105 (29), 147 (38), 161 (17) [$C_nH_{(2n-7)}^+$-series], 173 ($C_{13}H_{17}^+$, 38), 186 ($M^+ - C_2H_6O$, 15), 203 (M^+ – CHO, 18), 214 ($M^+ - H_2O$, 5), 232 (M^+, 100).

Anal. $C_{16}H_{24}O$ (232.4): calcd C 82.70, H 10.41; found C 82.69, H 10.37.

1-{Bicyclo[6.4.0]dodec-1(8)-en-10-yl}methanal (24)
Acrolein (**23**, 13.4 mL, 202 mmol) was added to a stirred solution of **13** (22.9 g, 168 mmol) in toluene (200 mL) under N_2. The mixture was cooled to 0 °C, and a 1.0 M solution of dimethylaluminum chloride in hexanes (14 mL, 14 mmol) was added via a syringe. After stirring for 5 min at this temperature, the cooling bath was removed and stirring was continued at r.t. for 5 d with renewed addition of acrolein (13.4 mL, 202 mmol) and 1.0 M solution of dimethylaluminum chloride in hexanes (14 mL, 14 mmol) after 3 d. The mixture was then poured into H_2O/*t*-BuOMe (1:1, 1 L), and the organic layer was separated. The aqueous layer was extracted with *t*-BuOMe (3 × 250 mL), the combined organic extracts were dried (Na_2SO_4), and the solvent was removed on a rotary evaporator. FC on silica gel (pentane/*t*-BuOMe, 40:1, R_f 0.41) provided 20.9 g (65%) of **24** as a colorless oil.

IR: ν = 1726 cm^{-1} (ν HC=O).

^{1}H NMR: δ = 1.41–1.65 (m, 10 H, 3'-H_2 to 6'-H_2, 11'-H_2), 1.93–2.13 (m, 8 H, 2', 7', 9', 12'-H_2), 2.47 (m_c, 1 H, 10'-H), 9.69 (d, *J* = 1.0 Hz, 1 H, CHO).

^{13}C NMR: δ = 22.8 (t, C-11'), 26.5, 26.5 (t, C-3', 6'), 28.0, 28.5 (t, C-4', 5'), 28.8, 28.8 (t, C-2', 7'), 31.7, 31.8 (t, C-9', 12'), 46.8 (d, C-10'), 128.4 (s, C-1'), 130.8 (s, C-8'), 204.8 (d, C-1).

MS : *m/z* (%) = 29 (CHO, 33), 41 ($C_3H_5^+$, 72), 67 ($C_5H_7^+$, 90), 91 ($C_7H_7^+$, 98), 107 (51), 121 (34), 135 (29), 149 (12) [$C_nH_{(2n-5)}^+$-series], 164 (M^+ – CO, 31), 192 (M^+, 100).

1-{10'-Methylbicyclo[6.4.0]dodec-1'(8')-en-10'-yl}methanal (26)
Following the procedure described for the preparation of **9**, 2-methylprop-2-en-1-al (**25**; 1.45 mL, 17.7 mmol) and 1,2-bis(methylene)cyclooctane (**13**; 2.00 g, 14.7 mmol) were reacted together to afford, after FC on silica gel (pentane/*t*-BuOMe, 50:1, R_f 0.44) 2.06 g (68%) of **26** as a colorless oil.

IR: ν = 1727 cm^{-1} (ν HC=O).

^{1}H NMR: δ = 1.04 (s, 3 H', 10-CH_3), 1.37–1.54 (m, 10 H, 3'-H_2 to 6'-H_2, 11'-H_2), 1.78 (d, *J* = 16.0 Hz, 1 H, 9'-H_b), 2.01–2.12 (m, 6 H, 2', 7'-,12'-H_2), 2.29 (d, *J* = 16.0 Hz, 1 H, 9'-H_a), 9.47 (s, 1 H, CHO).

^{13}C NMR: δ = 20.7 (q, 10'-CH_3), 26.4, 26.5, 26.6 (t, C-3', 6', 11'), 28.8, 28.9 (t, C-4', 5'), 29.1 (t, C-12'), 31.6, 31.9 (t, C-2', 7'), 35.9 (t, C-9'), 45.1 (s, C-10'), 128.2 (s, C-1'), 130.1 (s, C-8'), 206.2 (d, C-1).

MS: *m/z* (%) = 29 (CHO, 36), 41 ($C_3H_5^+$, 78), 67 ($C_5H_7^+$, 65), 81 ($C_6H_9^+$, 100), 95 ($C_7H_{11}^+$, 61), 121 (39), 135 (29), 149 (20), 163 (28) [$C_nH_{(2n-5)}^+$-series], 177 (M^+ – CHO, 70), 191 ($M^+ - CH_3$, 9), 206 (M^+, 31).

2-Chloroethyl Dimethyl Sulfonium Iodide (27)
To a stirred solution of 2-chloroethyl methyl sulfide (25 mL, 0.25 mol) in anhyd MeOH (75 mL) was added MeI (31 mL, 0.50 mol) at r.t. under N_2. Stirring was continued at r.t. for 18 h, then the reaction was quenched by the addition of anhyd Et_2O (250 mL). The resulting precipitate was filtered, washed thoroughly with Et_2O, and dried on a vacuum line to provide 49 g (78%) of **27** as a dark yellow powder. This reagent was sufficiently pure for the following transformations, it should, however, be stored at –18 °C under argon.

IR (KBr): ν = 669 (ν C–S), 869 cm^{-1} (ν C–Cl).

^{1}H NMR (CD_3OD): δ = 3.12 [s, 6 H, $S(CH_3)_2$], 3.94 (t, *J* = 6.5 Hz, 2 H, 1-H_2), 4.13 (t, *J* = 6.5 Hz, 2 H, 2-H_2).

^{13}C NMR (CD_3OD): δ = 26.1 [q, $S(CH_3)_2$], 38.9 (t, C-2), 47.1 (t, C-1).

MS: *m/z* (%) = 61 ($C_2H_5S^+$, 100), 75 ($C_3H_7S^+$, 33), 110 ($C_3H_7ClS^+$, 37), 127 (I^+, 26), 142 (CH_3I^+, 88).

ESI: *m/z* (%) = 63 ($C_2H_4Cl^+$, 2), 97 ($C_2H_6ClS^+$, 6), 125 ($C_4H_{10}ClS^+$, 100).

Spiro[2.7]decan-4-one (28); Typical Procedure
KO*t*-Bu (47.6 g, 0.424 mol) was dissolved in *t*-BuOH (0.5 L) with mechanical stirring at 60 °C under N_2. To this solution was added cyclooctanone (27.0 g, 212 mmol). After 5 min of stirring at r.t., 2-chloroethyl dimethyl sulfonium iodide (**27**; 49.0 g, 0.194 mol) was added in small portions within 15 min, and the stirring was continued at r.t. for 22 h. The mixture was poured into H_2O (0.5 L), and extracted with *t*-BuOMe (3 × 0.5 L). The combined organic extracts were dried (Na_2SO_4), concentrated in vacuo, and purified by FC on silica gel (pentane/*t*-BuOMe, 10:1, R_f 0.69) to provide 24.8 g (85%) of **28** as a colorless liquid.

IR: ν = 1684 (ν C=O), 1113, 1075 cm^{-1} (ν_{as} C–C–C).

^{1}H NMR: δ = 0.67 (dd, *J* = 6.5, 3.6 Hz, 2 H, 1, 2-H_b), 1.22 (dd, *J* = 6.5, 3.2 Hz, 2 H, 1, 2-H_a), 1.45–1.49 (m, 2 H, 9-H_2), 1.54–1.60 (m, 4 H, 7, 8-H_2), 1.71–1.76 (m, 2 H, 10-H_2), 1.91 (m_c, 2 H, 6-H_2), 2.67 (m_c, 2 H, 5-H_2).

^{13}C NMR: δ = 18.1 (2 t, C-1, 2), 25.3, 26.0 (t, C-6, 9), 28.4, 29.5 (t, C-7, 8), 31.3 (s, C-3), 32.1 (t, C-5), 38.9 (t, C-10), 216.3 (s, C-4).

MS: *m/z* (%) = 41 ($C_3H_5^+$, 100), 55 ($C_4H_7^+$, 87), 67 ($C_5H_7^+$, 69), 97 ($C_7H_{13}^+$, 68), 109 ($C_8H_{13}^+$, 63), 124 (M^+ – CO, 44), 137 ($M^+ - CH_3$, 6), 152 (M^+, 7).

4-Methylenespiro[2.7]decane (29); Typical Procedure
Methyl triphenyl phosphonium bromide (124 g, 347 mmol) was added to a mechanically stirred solution of KO*t*-Bu (37.0 g, 0.330 mol) in THF (750 mL) and the mixture was heated to reflux. At this reflux temperature was added dropwise **28** (44.0 g, 289 mmol) with vigorous stirring, and heating was continued for 2 h. After additional 14 h of stirring at r.t., the mixture was poured into H_2O (1 L), and the product extracted with *t*-BuOMe (3 × 1 L). The combined organic extracts were dried (Na_2SO_4), concentrated on a rotary evaporator and purified by FC on silica gel (pentane, R_f 1.00) to provide 31.8 g (73%) of **29** as a colorless liquid.

IR: ν = 2922, 2851, 2997, 3076 (ν C–H), 1444 (δ H–C–H), 879, 1014 (δ C=C–H), 1632 cm^{-1} (ν C=C).

^{1}H NMR: δ = 0.45 (dd, *J* = 6.0, 4.0 Hz, 2 H, 1, 2-H_b), 0.59 (dd, *J* = 6.0, 4.0 Hz, 2 H, 1, 2-H_a), 1.45–1.59 (m, 8 H, 7-H_2 to 10-H_2), 1.67–1.73 (m, 2 H, 6-H_2), 2.25 (ddd, *J* = 14.5, 6.5, 1.0 Hz, 2 H, 5-H_2), 4.71 (dd, *J* = 3.5, 1.0 Hz, 2 H, 11-H_2).

^{13}C NMR: δ = 14.9 (2 t, C-1,-2), 25.0 (s, C-3), 25.2 (t, C-6), 26.4, 26.4 (t, C-7, 8), 29.5 (t, C-9), 34.4 (t, C-5), 37.1 (t, C-10), 108.9 (t, C-11), 155.8 (s, C-4).

MS: *m/z* (%) = 67 ($C_5H_7^+$, 85), 79 (100), 93 (61), 107 (29), 121 (21), 135 (13) [$C_nH_{(2n-5)}^+$-series], 150 (M^+, 3).

1-{9-Methylbicyclo[6.4.0]dodec-1(8)-en-10-yl}ethan-1-one (32) and (3*E*,1'*E*)-5-(2'-Methylcyclooct-1'-en-1'-yl)hex-3-en-2-one (35)

Chlorotris(triphenylphosphine)rhodium(I) (1.10 g, 1.19 mmol) was added to a stirred solution of **29** (2.21 g, 14.7 mmol) and but-3-en-2-one (1.45 mL, 17.8 mmol) in toluene (20 mL) under N_2. The mixture was refluxed for 20 h, filtered through a pad of silica gel, and poured into *t*- BuOMe/H_2O (1:1, 400 mL). The organic layer was separated, the aqueous layer extracted with *t*-BuOMe (3 × 200 mL). The combined organic extracts were dried (Na_2SO_4), concentrated in vacuo, and purified by FC on silica gel (pentane/*t*-BuOMe, 20:1) to provide 288 mg (9%) of (*r*-9,*t*-10)-**32** (R_f 0.46), 1.15 g (36%) of (*r*-9,*c*-10)-**32** (R_f 0.38), and 714 mg (22%) of **35** (R_f 0.22) as colorless liquids.

(*r*-9,*t*-10)-**32**:

IR: ν = 1710 cm^{-1} (ν C=O).

^{1}H NMR: δ = 1.03 (*J* = 7.0 Hz, 3 H, 9'-CH_3), 1.34–1.57 (m, 9 H, 3'-H_2 to 6'-H_2, 11'-H_b), 1.75 (m_c, 1 H, 11'-H_a), 1.87–2.00 (m, 4 H, 2'-H_2, 7', 12'-H_b), 2.17 (s, 3 H, $COCH_3$), 2.21–2.26 (m, 2 H, 7', 12'-H_a), 2.38 (m_c, 1 H, 10'-H), 2.52 (m_c, 1 H, 9'-H). No NOE between 10'-H and 9'-H.

^{13}C NMR: δ = 19.5 (q, 9'-CH_3), 22.9 (t, C-11'), 26.3, 26.5 (t, C-3', 6'), 28.1, 28.6 (t, C-4', 5'), 28.2 (q, C-2), 28.8, 29.5 (t, C-2', 7'), 32.1 (t, C-12'), 33.1 (d, C-9'), 55.1 (d, C-10'), 130.3, 133.3 (s, C-1', 8'), 211.4 (s, C-1).

MS: *m/z* (%) = 43 ($C_2H_3O^+$, 32), 81 ($C_6H_9^+$, 100), 95 ($C_7H_{11}^+$, 41), 121 ($M^+ - C_2H_3O - C_4H_8$, 17), 177 ($M^+ - C_2H_3O$, 37), 205 ($M^+ - CH_3$, 1), 220 (M^+, 6).

(*r*-9,*c*-10)-**32**:

IR: ν = 1709 cm^{-1} (ν C=O).

^{1}H NMR: δ = 0.84 (*J* = 7.0 Hz, 3 H, 9'-CH_3), 1.39–1.61 (m, 8 H, 3'-H_2 to 6'-H_2),1.72 (m_c, 2 H, 11'-H_2), 1.93–2.08 (m, 4 H, 2'-H_2, 7', 12'-H_b), 2.16 (s, 3 H, $COCH_3$), 2.19–2.31 (m, 2 H, 7'-,12'-H_a), 2.52 (m_c, 1 H, 10'-H), 2.56 (m_c, 1 H, 9'-H).

^{13}C NMR: δ = 14.7 (q, 9'-CH_3), 18.1 (t, C-11'), 26.4, 26.9 (t, C-3', 6'), 28.4 (q, C-2), 28.5, 29.2 (t, C-4', 5'), 30.2, 30.8 (t, C-2', 7'), 31.4 (t, C-12'), 34.5 (d, C-9'), 52.6 (d, C-10'), 130.5, 134.4 (s, C-1', 8'), 211.5 (s, C-1).

MS: *m/z* (%) = 43 ($C_2H_3O^+$, 65), 81 ($C_6H_9^+$, 100), 95 ($C_7H_{11}^+$, 50), 177 ($M^+ - C_2H_3O$, 38), 205 ($M^+ - CH_3$, 3), 220 (M^+, 14).

Anal. $C_{15}H_{24}O$ (220.4): calcd C 81.76, H 10.98; found C 81.60, H 10.87.

35:

IR: ν = 982 cm^{-1} (δ C=C, *trans*), 1254 (δ $COCH_3$), 1359 (δ CH_3), 1620 (ν C=CCO),1676 (ν C=O), 1697 (ν C=C).

^{1}H NMR: δ = 1.17 (d, *J* = 7.0 Hz, 3 H, 5-CH_3), 1.41–1.54 (m, 8 H, 4'-H_2 to 7'-H_2), 1.71 (s, 3 H, 2'-CH_3), 2.03–2.23 (m, 4 H, 3', 8'-H_2), 2.25 (s, 3 H, $COCH_3$), 3.59 (qdd, *J* = 7.0, 6.0, 1.5 Hz, 1 H, 5-H), 6.02 (dd, *J* = 16.5, 1.5 Hz, 1 H, 3-H), 6.80 (dd, *J* = 16.5, 6.0 Hz, 1 H, 4-H).

^{13}C NMR: δ = 17.1 (q, C-6), 18.3 (q, 2'-CH_3), 26.1 (t, C-4'), 26.6 (q, C-1), 26.7 (t, C-7'), 27.2, 27.7 (t, C-5', 6'), 31.4 (t, C-8'), 33.0 (t, C-3'), 39.1 (d, C-5), 129.1 (d, C-3), 131.1 (s, C-2'), 132.8 (s, C-1'), 152.2 (d, C-4), 198.8 (s, C-2).

MS: *m/z* (%) = 43 ($C_2H_3O^+$, 100), 81 ($C_6H_9^+$, 38), 95 ($C_7H_{11}^+$, 39), 177 ($M^+ - C_2H_3O$, 26), 205 ($M^+ - CH_3$, 4), 220 (M^+, 5).

(3*E*,1'*E*)-5-(2'-Methylcyclooct-1'-en-1'-yl)hex-3-en-2-one (35)

Chlorotris(triphenylphosphine)rhodium(I) (1.66 g, 1.79 mmol) was added to a stirred solution of **29** (5.00 g, 33.3 mmol) and but-3-en-2-one (3.30 mL, 40 mmol) in toluene (50 mL) under N_2. AgOTf (462 mg, 1.80 mmol) was added and the mixture was refluxed for 23 h, filtered through a pad of silica gel, and poured into *t*-BuOMe/H_2O (1:1, 900 mL). The organic layer was separated, the aqueous layer extracted with *t*-BuOMe (3 × 500 mL). The combined organic extracts were dried (Na_2SO_4), concentrated in vacuo, and purified by FC on silica gel (pentane/*t*-BuOMe, 20:1) to provide 4.87 g (66%) of **35** (R_f 0.22) as a colorless liquid. For spectroscopic data, see above.

(*r*-9, *c*-10, *t*-11)-1-{9,11-Dimethylbicyclo[6.4.0]dodec-1(8)-en-10-yl}ethan-1-one (36)

Following the procedure described for the preparation of **32**, (3*E*)-pent-3en-2-one (**17;** 3.00 mL, 30.8 mmol) and 4-methylenespiro[2.7]decane (**29**, 3.75 g, 25.0 mmol) were reacted together to afford, after FC on silica gel (pentane/*t*-BuOMe, 20:1), 2.32 g (42%) of **36** as a colorless liquid.

IR: ν = 1710 cm^{-1} (ν C=O).

^{1}H NMR: δ = 0.84 (d, *J* = 7.0 Hz, 3 H, 11'-CH_3), 0.91 (d, *J* = 6.0 Hz, 3 H, 9'-CH_3), 1.42–1.55 (m, 8 H, 3'-H_2 to 6'-H_2), 1.67 (dd, *J* = 17.0, 10.5 Hz, 1 H, 12-H_b), 1.89–2.27 (m, 5 H, 2'-H_2, 7'-H_2, 12'-H_a), 2.09 (m_c,1 H, 11'-H_{ax}), 2.15 (s, 3 H, $COCH_3$), 2.37 (qd, *J* = 6.0, 5.0 Hz, 1 H, 9'-H_{eq}), 2.45 (dd, *J* = 11.0, 5.0 Hz, 1 H, 10'-H_{ax}). *J* (9'-H_{eq}, 10'-H_{ax}) = 5.0 Hz (ax–eq), *J* (10'-H_{ax},11'-H_{ax}) = 11.0 Hz (ax–ax).

^{13}C NMR: δ = 15.3 (q, 9'-CH_3), 19.9 (q, 11'-CH_3), 23.9 (d, C-11'), 26.4, 26.9 (t, C-3', 6'), 28.4 (t, C-5'), 30.1 (t, C-4'), 30.5 (q, C-2), 30.7 (t, C-7'), 31.2 (t, C-2'), 35.3 (d, C-9'), 38.5 (t, C-12'), 59.1 (d, C-10'), 129.9 (s, C-1'), 134.1 (s, C-8'), 211.1 (s, C-1)

MS: *m/z* (%) = 43 ($C_2H_3O^+$, 68), 95 ($C_7H_{11}^+$, 100), 109 ($C_8H_{13}^+$, 45), 191.1797 ($M^+ - C_2H_3O$, 38), 219 ($M^+ - CH_3$, 5), 234.1971 (11). [M^+]; calcd for $C_{16}H_{26}O$: 234.1983.

(*r*-9, *c*-10)-1-{9,10-Dimethylbicyclo[6.4.0]dodec-1(8)-en-10-yl}ethan-1-one (38); Typical Procedure

3-Methylbut-3-en-2-one (**37**; 60 mL, 600 mmol) and chlorotris(triphenylphosphine)rhodium(I) (10.0 g, 10.8 mmol) were added in turn to a stirred solution of **17** (31.8 g, 212 mmol) in toluene (0.5 L). The mixture was refluxed for 3 d, filtered through a pad of silica gel, washed with H_2O (200 mL), dried (Na_2SO_4) and concentrated on a rotary evaporator. The residue was purified by FC on silica gel (pentane/*t*-BuOMe, 40:1, R_f 0.41) to give **38** (23.9 g, 48%) as a colorless waxy solid; mp 56.3 °C.

IR: ν = 1704 cm^{-1} (ν C=O).

^{1}H NMR: δ = 0.83 (d, *J* = 7.0 Hz, 3 H, 9'-CH_3),1.10 (s, 3 H, 10'-CH_3), 1.42–2.06 (m, 15 H, 2', 7'-H_b, 3'-H_2 to 6'-H_2, 9'-H, 11', 12'-H_2), 2.14 (s, 3 H, $COCH_3$), 2.23–2.40 (m, 2 H, 2', 7'-H_a).

^{13}C NMR: δ = 17.1 (q, 9'-CH_3), 21.0 (q, 10'-CH_3), 22.7 (t, C-11'), 25.4 (q, C-2), 26.6, 26.7 (t, C-3', 6'), 27.0 (t, C-4'), 28.8 (t, C-5'), 29.7 (t, C-12'), 30.8 (t, C-7'), 31.7 (t, C-2'), 40.7 (d, C-9'), 49.9 (s, C-10'), 128.9 (s, C-1'), 133.1 (s, C-8'), 214.2 (s, C-1).

MS: *m/z* (%) = 95 ($C_7H_{11}^+$, 31), 191.1800 ($M^+ - C_2H_3O$, 100), 219 ($M^+ - CH_3$, 3), 234.2020 (M^+, 12).

Anal. $C_{16}H_{26}O$ (234.4): calcd C 81.99, H 11.18, O 6.83; found C 81.68, H 11.15, O 6.89.

4-Methylenespiro[2.6]nonane (40)

First spiro[2.6]nonan-4-one was prepared from **39** (20.0 g, 0.792 mol), following the procedure for the preparation of the homolog **28** and purified by FC on silica-gel (pentane/*t*-BuOMe, 10:1, R_f 0.58); yield: 5.86 g (54%). Spiro[2.6]nonan-4-one (2.95 g, 42.0 mmol) was then transformed to **40** according to the procedure described for the preparation of **29** and purified by FC on silica gel (pentane, R_f 1.00).

IR: ν = 872, 1015 (δ C=C–H), 1628 cm^{-1} (ν C=C), 2852, 2924, 2997 (ν C–H), 3076.

^{1}H NMR: δ = 0.52 (dd, *J* = 6.0, 4.0 Hz, 2 H, 1, 2-H_b), 0.66 (dd, *J* = 6.0, 4.0 Hz, 2 H, 1, 2-H_a), 1.46–1.49 (m, 2 H, 9-H_2), 1.55–1.59 (m, 4 H, 7, 8-H_2), 1.61–1.66 (m, 2 H, 6-H_2), 2.35 (m_c, 2 H, 5-H_2), 4.44 (d, *J* = 1.5 Hz, 1 H, 10-H_b), 4.58 (d, *J* = 1.5 Hz, 1 H, 10-H_a).

^{13}C NMR: δ = 17.2, 17.2 (t, C-1, 2), 24.7 (s, C-3), 28.0, 29.3, 29.7 (t, C-6, 7, 8), 36.9 (t, C-5), 38.7 (t, C-9), 106.3 (t, C-10), 156.3 (s, C-4).

MS: *m/z* (%) = 67 ($C_5H_7^+$, 68), 79 (100), 93 (57), 107 (22), 121 (18) [$C_nH_{(2n-5)}^+$-series], 136 (M^+, 3).

(*r*-8, *c*-9)-1-{8-Methylbicyclo[5.4.0]undec-1(7)-en-9-yl}ethan-1-one (41)

Following the procedure described for the preparation of **38**, but-3-en-2-one (**14**; 1.0 mL, 12 mmol) and **40** (1.36 g, 10.0 mmol) were reacted together to give, after FC on silica gel (pentane/*t*-BuOMe, 20:1, R_f 0.43), 519 mg (25%) of **41** as a colorless liquid.

IR: ν = 1709 (ν C=O), 1353, 1376 cm^{-1} (δ CH_3).

^{1}H NMR: δ = 0.80 (d, *J* = 7.0 Hz, 3 H, 8'-CH_3), 1.34–1.76 (m, 8 H, 3'-H_2 to 5'-H_2,10'-H_2), 1.99–2.15 (m, 6 H, 2', 6', 11'-H_2), 2.16 (s, 3 H, $COCH_3$), 2.45 (qd, *J* = 6.0, 6.0 Hz, 1 H, 8'-H), 2.58 (ddd, *J* = 12.0, 6.0, 3.0 Hz, 1 H, 9'-H). *J*(9'-H, 8'-H) ≈ *J*(8'-H, 8'-CH_3) ≈ 6.0 Hz.

^{13}C NMR: δ = 14.1 (q, 8'-CH_3), 18.3 (t, C-10'), 26.2, 27.3 (t, C-3',,5'), 28.4 (q, C-2), 31.6, 32.7 (t, C-2', 6'), 34.1, 34.7 (t, C-4', 11'), 36.8 (d, C-8'), 52.3 (d, C-9'), 134.0, 137.3 (s, C-1', 7'), 211.5 (s, C-1).

MS: *m/z* (%) = 28 (CO^+, 38), 43 ($C_2H_3O^+$, 68), 81 ($C_6H_9^+$, 100), 91 ($C_7H_7^+$, 34), 105 ($C_7H_7O^+$, 24),121 ($C_9H_{13}^+$, 13), 163 ($M^+ - C_2H_3O$, 38), 191 ($M^+ - CH_3$, 2), 206 (M^+, 7).

(*r*-8, *c*-9)-1-{8,9-Dimethylbicyclo[5.4.0]undec-1(7)-en-9-yl}ethan-1-one (42)

Following the procedure described for the preparation of **38**, 3-methylbut-3-en-2-one (**37**, 1.2 mL, 12 mmol) and **40** (1.36 g, 10.0 mmol) were reacted together to give, after FC on silica gel (pentane/*t*-BuOMe, 20:1, R_f 0.39), 1.14 g (52%) of **42** as a colorless liquid.

IR: ν = 1703 cm^{-1} (ν C=O).

^{1}H NMR: δ = 0.77 (d, *J* = 7.0 Hz, 3 H, 8'-CH_3), 1.06 (s, 3 H, 9'-CH_3), 1.34–1.44 (m, 5 H, 4'-H_2, 8'-H, 10'-H_2), 1.68–1.75 (m, 4 H, 3', 5'-H_2), 1.93–2-08 (m, 6 H, 2', 6', 11'-H_2), 2.11 (s, 3 H, $COCH_3$).

^{13}C NMR: δ = 16.3 (q, 8'-CH_3), 20.6 (q, 9'-CH_3), 23.0 (t, C-10'), 25.4 (q, C-2), 26.3, 26.8 (t, C-3', 5'), 28.8 (t, C-4'), 32.8 (t, C-11'), 34.4, 34.6 (t, C-2', 6'), 43.3 (d, C-8'), 49.5 (s, C-9'), 132.1 (s, C-1'), 135.5 (s, C-7'), 214.1 (s, C-1).

MS: *m/z* (%) = 43 ($C_2H_3O^+$, 52), 95 ($C_7H_{11}^+$, 100), 107 (40), 121 (32), 149 (4) [$C_nH_{(2n-5)}^+$-series], 177 ($M^+ - C_2H_3O$, 81), 220 (M^+, 7).

Cyclooct-4-en-1-one (44)

Prepared according to the procedure of Meier, Mayer and Kolshorn[19] by epoxidation of cycloocta-1,5-diene (**43;** 86.6 g, 0.800 mol) with 3-chloroperoxybenzoic acid (207 g, 0.840 mol; yield: 60.0 g, 60%, FC on silica gel: pentane/*t*-BuOMe, 10:1, R_f 0.63), $LiAlH_4$ reduction (scale: 0.48 mol; crude yield: 60.5 g, ca 100%), and a standard Dess–Martin oxidation[26] (scale: 0.48 mol) afforded after FC on silica gel (pentane/*t*-BuOMe, 10:1, R_f 0.46) 39.4 g (66%) of **44** as a colorless liquid.

IR: ν = 1705 cm^{-1} (ν C=O).

^{1}H NMR: δ = 1.61 (m_c, 2 H, 7-H_2), 2.19 (m_c, 2 H, 6-H_2), 2.43–2.52 (m, 6 H, 2, 3, 8-H_2), 5.70, 5.73 (m_c, 2 H, 4, 5-H).

^{13}C NMR: δ = 21.7, 23.8 (t, C-3, 7), 26.2 (t, C-6), 40.1, 47.1 (t, C-2, 8), 130.1, 130.6 (d, C-4, 5), 214.5 (s, C-1).

MS: *m/z* (%) = 27 ($C_2H_4^+$, 30), 39 ($C_3H_3^+$, 65), 54 ($C_4H_6^+$, 84), 67 ($C_5H_7^+$, 100), 96 ($M^+ - C_2H_4$, 84), 109 ($M^+ - CH_3$, 33), 124 (M^+, 18).

Spiro[2.7]dec-8-en-4-one (45)

Following the procedure described for the preparation of **28**, cyclooct-4-en-1-one (**44**; 20.0 g, 0.161 mol) and 2-chloroethyl dimethyl sulfonium iodide (**27**; 34.5 g, 0.136 mol) were reacted together to give, after FC on silica gel (pentane/*t*-BuOMe, 50:1, R_f 0.27), 7.15 g (35%) of **45** as a colorless liquid.

IR: ν = 1687 (ν C=O), 1098 cm^{-1} (ν_{as} C–C–C).

^{1}H NMR: δ = 0.69 (dd, *J* = 6.5, 4.0 Hz, 2 H, 1, 2-H_b), 1.17 (dd, *J* = 6.5, 4.0 Hz, 2 H, 1, 2-H_a), 1.72 (m_c, 2 H, 6-H_2), 2.30 (m_c, 2 H, 7-H_2), 2.41 (d, *J* 5.5 Hz, 2 H, 10-H_2), 2.70 (m_c, 2 H, 5-H_2), 5.73 (m_c, 2 H, 8, 9-H).

^{13}C NMR: δ = 16.3, 16.3 (t, C-1, 2), 26.0, 26.8 (t, C-6, 7), 33.0 (s, C-3), 33.9 (t, C-5), 40.7 (t, C-10), 129.3, 130.1 (d, C-8, 9), 214.2 (s, C-4).

MS: *m/z* (%) = 39 ($C_3H_3^+$, 54), 67 ($C_5H_7^+$, 31), 79 (100), 107 (23), 121 (39), 135 (37) [$C_nH_{(2n-5)}^+$-series], 150 (M^+, 7).

4-Methylenespiro[2.7]dec-8-ene (46)

Following the procedure described for the preparation of **29**, spiro[2.7]dec-8-en-4-one (**45**; 4.30 g, 28.6 mmol) and methyltriphenylphosphonium bromide (12.3 g, 34.4 mmol) were reacted together to afford, after FC on silica gel (pentane, R_f 0.91), 3.71 g (87%) of **46** as a colorless liquid.

IR: ν = 899, 1015 (δ C=C–H), 1461 (δ H–C–H), 1636 cm^{-1} (ν C=C), 2853, 2926, 3016, 3075 (ν C–H).

^{1}H NMR: δ = 0.44 (dd, *J* = 6.0, 4.0 Hz, 2 H, 1, 2-H_b), 0.59 (dd, *J* = 6.0, 4.0 Hz, 2 H, 1, 2-H_a), 1.60 (m_c, 2 H, 6-H_2), 2.07 (d, *J* = 7.5 Hz, 2 H, 10-H_2), 2.14–2.22 (m, 4 H, 5, 7-H_2), 4.74 (d, *J* = 2.0 Hz, 11-H_b), 4.81 (d, 1 H, *J* = 2.0 Hz, 11-H_a), 5.68 (m_c, 2 H, 8, 9-H).

^{13}C NMR: δ = 12.4 (2 t, C-1, 2), 25.5 (t, C-6), 28.7 (s, C-3), 30.0 (t, C-7), 33.3 (t, C-5), 35.6 (t, C-10), 111.2 (t), 129.2, 130.4 (d, C-8, 9), 154.2 (s, C-4).

MS: *m/z* (%) = 39 ($C_3H_3^+$, 35), 79 ($C_6H_7^+$, 80), 91 ($C_7H_7^+$, 100), 105 ($M^+ - C_3H_7$, 54), 119 ($M^+ - C_2H_5$, 23), 133 ($M^+ - CH_3$, 19), 148 (M^+, 1).

Anal. $C_{11}H_{16}$ (148.24): calcd C 89.12, H 10.88; found C 88.93, H 10.84.

(*r*-9, c-10)-1-{9,10-Dimethylbicyclo[6.4.0]dodec-1(8),6(7)-dien-10-yl}ethan-1-one (47)

Following the procedure described for the preparation of **32**, 4-methylenespiro[2.7]dec-8-ene (**46**; 3.20 g, 21.6 mmol) and 3-methylbut-3-en-2-one (**37**; 6.5 mL, 29.1 mmol) were reacted together to afford, after FC on silica gel (pentane/*t*-BuOMe, 100:1, R_f 0.18), 2.17 g (43%) of **47** as a colorless liquid.

IR: ν = 1704 cm^{-1} (ν C=O).

^{1}H NMR: δ = 0.79 (d, *J* = 7.0 Hz, 3 H, 9'-CH_3-ax), 1.14 (s, 3 H, 10'-CH_3-ax), 1.23–1.30 (m, 2 H, 3', 11'-H_b), 1.48–1.67 (m, 3 H, 3', 11'-H_a and 4'-H_b), 1.78–2.18 (m, 7 H, 4'-H_a and 2', 5', 12'-H_2), 2.09 (q, *J* = 7.0 Hz, 1 H, 9'-H_{eq}), 2.15 (s, 3 H, $COCH_3$), 5.59–5.73 (m, 2 H,

6', 7'-H). NOEs from 9'-H_{eq} to 9'-CH_3-ax, 7-H, 10'-CH_3-ax, 10'-Ac_{eq} and 12-H_{ax}.

^{13}C NMR: δ = 17.0 (q, 9'-CH_3), 20.7 (q, 10'-CH_3), 23.1 (t, C-4'), 23.3 (t, C-3'), 23.9 (t, C-11'), 25.3 (q, C-2), 27.0 (t, C-12'), 28.9 (t, C-5'), 32.6 (t, C-2'), 40.2 (d, C-9'), 49.2 (s, C-10'), 129.4 (d, C-7'), 131.0, 130.6 (s, C-1', 8'), 131.6 (d, C-6'), 213.7 (s, C-1).

MS: *m/z* (%) = 43 ($C_2H_3O^+$, 50), 91 (57), 105 (43), 119 (52), 133 (39) [$C_nH_{(2n-7)}^+$-series], 189 ($M^+ - C_2H_3O$, 100), 217 ($M^+ - CH_3$, 9), 232 (M^+, 28).

Anal. $C_{16}H_{24}O$ (232.37): calcd C 82.70, H 10.41; found C 82.68, H 10.30.

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