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Stereocontrolled Synthesis of Heteroannular Acetals from Functionalized 1,5-Enynes via Radical Cascades—Construction of Quaternary and 1,2-Diquaternary Centres in Polycyclic Systems

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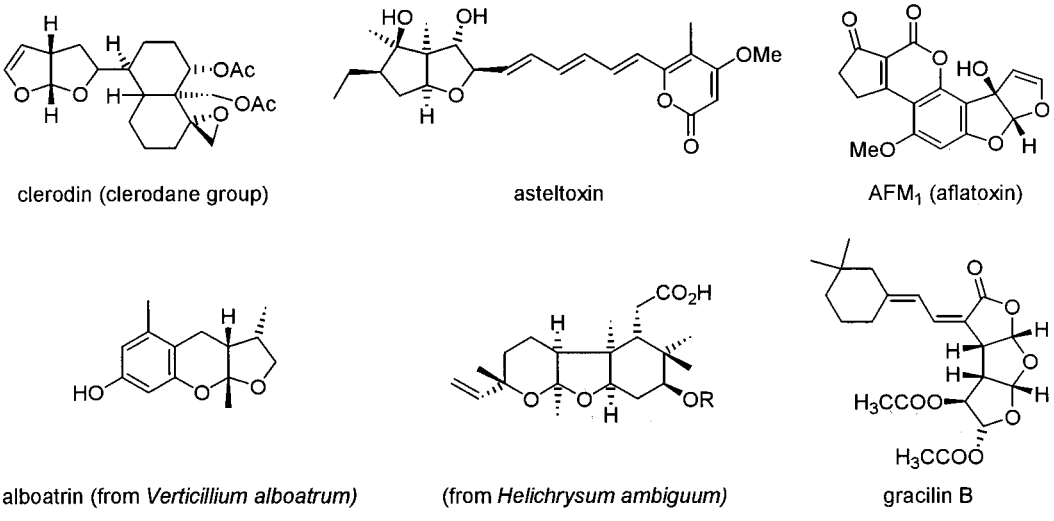
Abstract—Sequential, radical-mediated cyclizations of 1,5-enynes have been evaluated with respect to structure, stereochemistry and reactivity. In series A 5-*exo*-trig, 6-*endo*-dig cascades are favoured. The unusual 6-*endo*-dig cyclization is dictated by ring strain. Diastereomeric series B tolerates leakage into the 5-*exo*-trig, 5-*exo*-dig sequence, especially if a quaternary carbon centre is established during the first five-ring cyclization. The cascade allows construction of four and more chiral centres in a single convergent step. The influence of *E*/*Z* geometry of the olefinic component is also evaluated. © 2000 Published by Elsevier Science Ltd.

Heteroannular acetals containing fused 5·5 and 6·5 ring systems occur in a wide variety of natural products. Because of their biological activity and their intricate structures these oxabicycles have been frequent targets in total synthesis.[1] Selected examples are shown in Scheme 1.

We have recently developed radical mediated cascade cyclizations of 1,5-enynes,[2–4] exemplified by the prototype reactions in Scheme 2. Two characteristic stereochemical series have been encountered. In diastereomeric series *A* cyclization usually proceeds more smoothly and the yield of tricyclic product is often higher than in series *B*. The products of series *A* are favoured thermodynamically, e.g. tricycle ***i*** is more stable than ***ii*** by about 2 kcal/mol. In series *B* diastereomeric tricycle ***ii*** is the major product. In addition, leakage into 5·5 ring system is tolerated, giving a



Scheme 1. Natural products containing heteroannular acetals.

Keywords: stereocontrolled synthesis; heteroannular acetals; 1,5-enynes.

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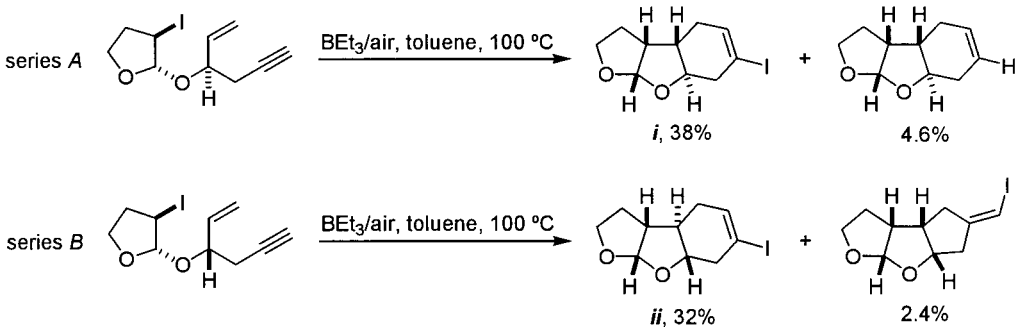
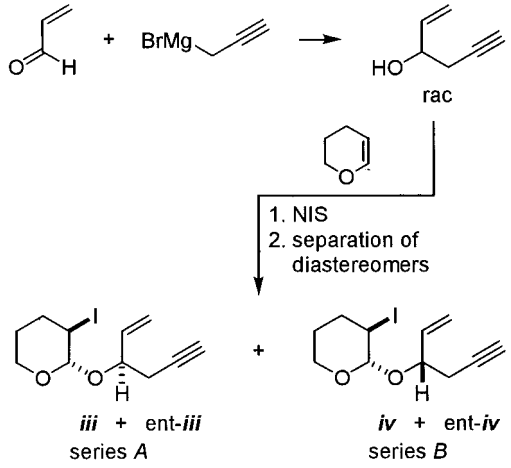


Scheme 2. Tandem radical mediated cyclizations of 1,5-enyne prototypes.



Scheme 3. Generalized approach to diastereomerically pure cyclization precursors.

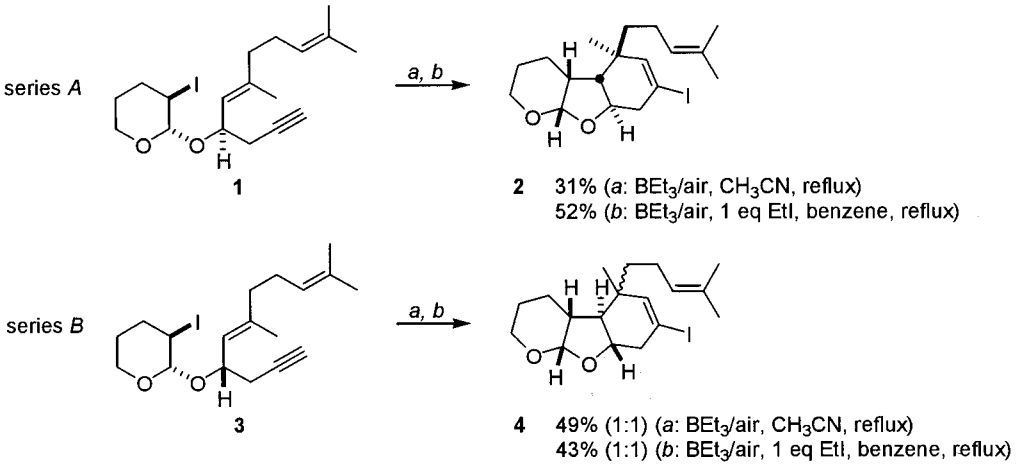
dioxatriquinane as a minor product (ca. 2.4%). In this side product all four hydrogen atoms of the central tetrahydrofuran moiety are placed *cis* to each other. In series *A* the first cyclization to five-membered ring involves a chair-like transition state. In series *B* a nonchair transition state is generally implicated. The unusual 6-*endo* digonal cyclization is dictated by ring strain. Since the 6-membered ring is fused *trans* to the first formed 5-membered ring, a potentially faster 5-*exo*-dig closure is precluded as final step.[2–6]

We now report radical mediated[7] tandem cyclizations of terpenes and related compounds joined to tetrahydropyrans. The reactions complement earlier work on double annulations of glycal conjugates and are of synthetic utility. They also generate chemical diversity and explore and probe stereochemical and mechanistic features as set out in previous work and by the two prototype cyclizations of Scheme 2.

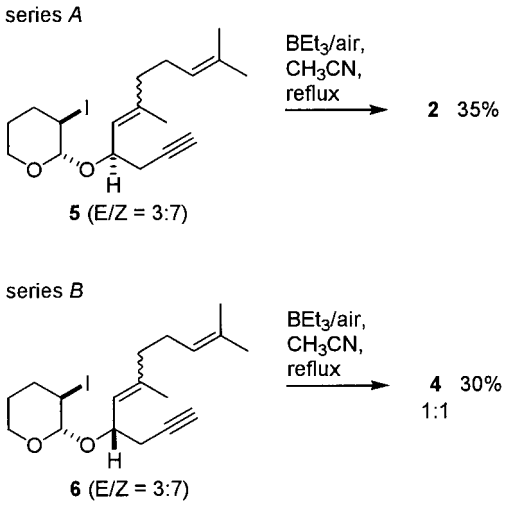
Results

The cyclization precursors were prepared from homologs of hex-5-en-1-yn-4-ols and dihydropyran. An optimized coupling procedure of unsaturated aldehyde with Grignard reagent furnished the desired racemic alcohol in up to 95% yield. *N*-Iodosuccinimide (NIS) promoted alkoxylation was stereospecifically *trans* and gave a diastereomeric mixture of iodo-enynes, which were separated by chromatography and structurally assigned by NMR spectroscopy. The cyclization precursors are pairs of enantiomers, i.e. ***iii***+*ent*-***iii*** (series *A*) and ***iv***+*ent*-***iv*** (series *B*). Each pair is diastereomerically pure. For simplicity and comparison with previous work only one enantiomer is shown below (Scheme 3).

Cyclization of geraniol conjugate **1** was carried out under conventional conditions *a* (BEt_3, air, CH_3CN, reflux) and *b* in the presence of added ethyl iodide (1 equiv.). Addition of



Scheme 4. Geraniol conjugates.



Scheme 5. Nerol conjugates.

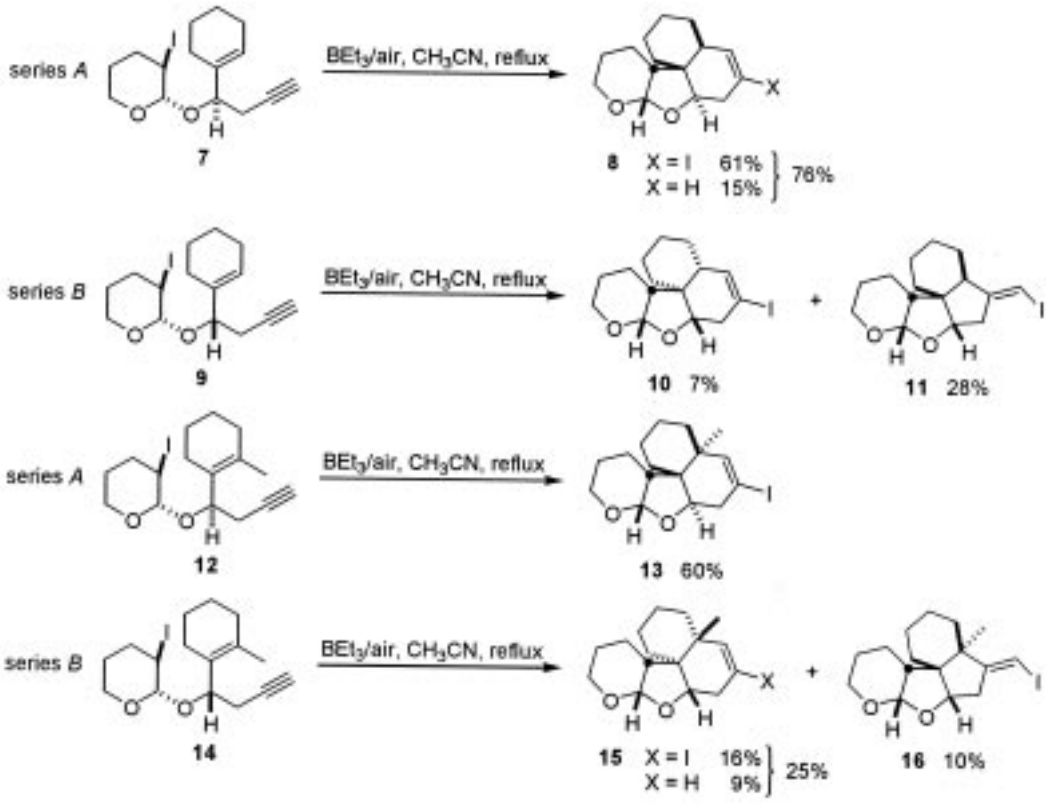
EtI is known to facilitate iodine atom transfer in the radical chain and improved the yield of monoiodinated product **2** (52% vs. 31%). In the absence of EtI the radical chain is also terminated by hydrogen atom transfer from adventitious H-atom donor molecules (cf. Scheme 2, 38+4.6=42.6% yield). The BEt_3/EtI/O_2 protocol is superior to the Bu_3SnH method for polycyclizations involving alkynes and termination by formation of a vinylic iodide.[4b] The quaternary centre[8] in **2** was built up with complete stereocontrol. In contrast to **1**, cyclization of conjugate **3** which belongs to series *B* was stereodivergent, furnishing tricycle **4** as a mixture of diastereomers (1:1). In other words, the internal E-olefin configuration of precursor **3** was partially lost in product **4**.

Nerol-enriched conjugate **5** (*E*/*Z*=3:7) provided just one diastereomeric tricycle **2**, obtained previously from precursor **1**, in a stereoconvergent reaction. Cyclization of conjugate **6**, which belongs to series *B*, gave tricycle **4** (1:1). The diastereomeric ratio (1:1) was the same as that obtained from precursor **3**.

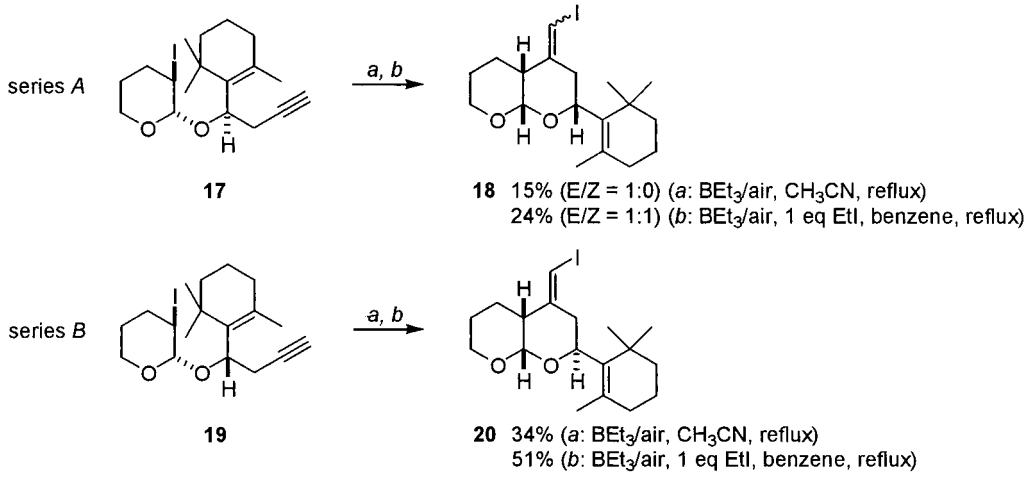
E/*Z*-equilibration, as observed for the reactions in Schemes 4 and 5, is impossible when the olefinic double bond is incorporated into a six-membered ring. Similar to series *A* (Scheme 2) cyclization precursor **7** provided tetracycle **8**, in respectable 61+15=76% yield overall. The quaternary centre of **8** is also a spirocentre. Tetracycle **8** (MMX energy 39.4 kcal/mol) is more stable than diastereomeric tetracycle **10** (MMX energy 41.7 kcal/mol), which was formed as minor product (7%) from series *B* precursor **9**. Formation of mono-oxadiquinane **11** (cf. Scheme 2) was now appreciable (28%).

In series *A* even a second, contiguous quaternary centre was introduced as in tetracycle **13** (60%). Significantly, precursor **14** from series *B* entered into the tandem 5-*exo*-trig, 6-*endo*-dig sequence less readily than **12**. Again, the 5-*exo*-trig, 5-*exo*-dig tetracycle **16** was a byproduct (10%) (Schemes 6 and 7).

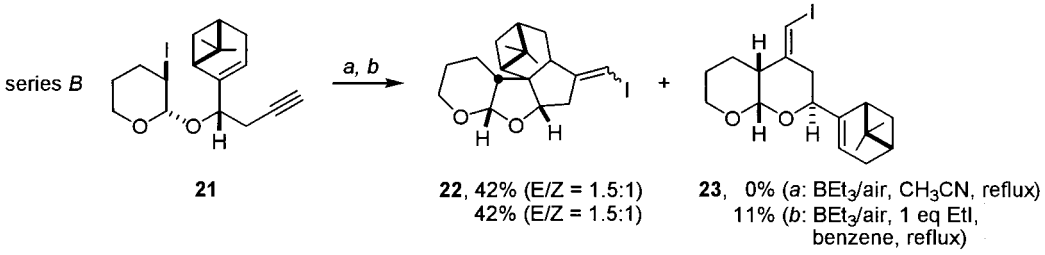
A breakdown of all cyclization cascades was observed for precursors **17** and **19**, which are sterically overloaded, due to the *gem*-dimethyl grouping. The olefinic double bond is



Scheme 6. Stereoselective cyclization of cyclohexenoid 1,5-enynes.



Scheme 7. 1,5-Enynes with overcrowded olefinic double bond.



Scheme 8. Myrtenol conjugate.

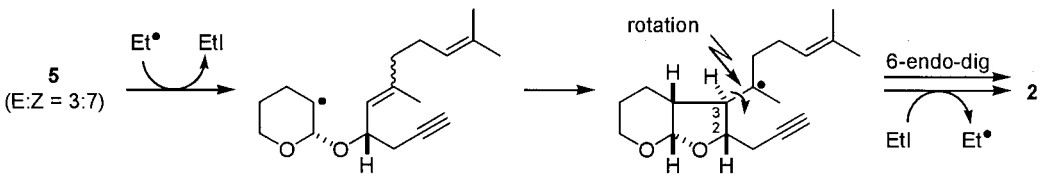
now shielded from radical attack. Instead, 6-*exo*-digonal attack at the triple bond occurs with formation of tricycle **18** and **20**. In product **20**, which was formed in 51% yield under conditions *b*, the bulky trimethyl cyclohexenyl moiety adopts a sterically favourable *exo* position, i.e. *cis* to the two angular hydrogen atoms.

In myrtenol conjugate **21** the olefinic double bond is again crowded, but less so than in **17** and **19**, since the quaternary carbon is now tied back and removed by one more carbon from the olefinic double bond. Precursor **21** belongs to series *B*, which had previously tolerated a 5-*exo*-trig, 5-*exo*-dig cascade. Pentacycle **22** (*E*/*Z*=1.5:1) was formed in 42% yield, although tetracycle **23** with *exo*-oriented norpinene moiety was also obtained in the presence of EtI by breakdown of the radical cascade (Scheme 8).

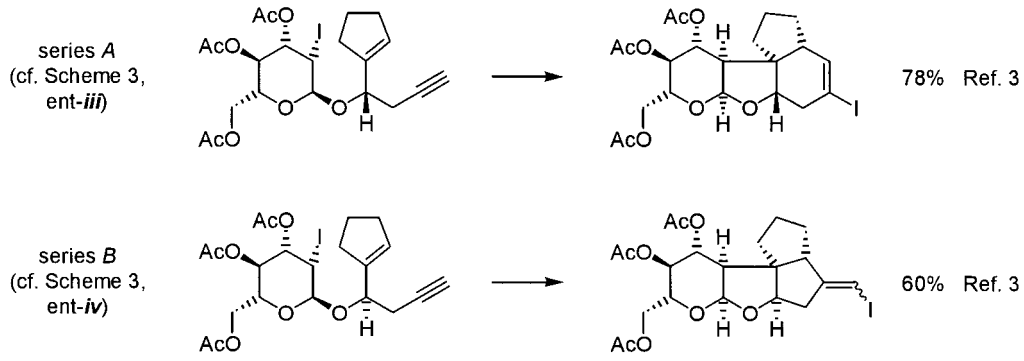
Discussion

MMX calculations suggest that tricycle **2** is the product of thermodynamic control (MMX energy 43 kcal/mol). The homoprenyl chain is *cis* to the neighbouring angular hydrogen. In the diastereomer (cf. **4**) which is less stable (46 kcal/mol) the homoprenyl side chain appears to be pushed into the tricyclic cage. Loss of olefin configuration occurs after the first 5-*exo*-trig cyclization which generates a tertiary radical that is free to rotate about the newly generated exocyclic single bond. Starting from precursor **5** stereoconvergence to tricyclic product **2** (35%) is observed. Leakage into the thermodynamically more stable tricycle is also suggested in two stereo *divergent* reactions, i.e. **3→4** and **6→4**.

When the olefinic double bond is part of a ring (Schemes 6 and 8), the carbon centre arising form the first, 5-*exo*-trig reaction is quaternary rather than tertiary as in Scheme 9. In the absence of two *anti*-oriented neighbouring hydrogen atoms (cf. H2 and H3 in Scheme 9) the tendency to place the two reacting carbon appendages *trans* to each other, is less. Accordingly, consecutive formation of two five-membered rings is feasible in series *B* (cf. **11** and **16**). MMX calculations suggest that tetracycle **10** (41.7 kcal/mol) is less stable than tetracycle **11** (39.4 kcal/mol).



Scheme 9.



Scheme 10. Glycal conjugates.

Replacement of the six-membered ring by a five-membered ring in **9** has been shown to favour the 5-*exo*-trig, 5-*exo*-dig cascade in a related system even more (Scheme 10, series *B*). In series *A* cyclization proceeds with a complete turnaround according to the 5-*exo*-trig, 6-*endo*-dig prototype in Scheme 2. The outcome of these two types of polycyclizations would be puzzling without the comparative work on the various 1,5-enyne systems.

The two tetracyclic products in Scheme 10 contain eight chiral centres each and are enantiomerically pure. The radical approach to 1,2-diquaternary centres complements recent palladium mediated work.[9] Steric effects are minimized in neutral radicals because of the absence of the solvation.[10]

Conclusions

In this and preceding papers we have elucidated synthetic, stereochemical and mechanistic features of tandem cyclizations of 1,5-enynes and also 1,5-diynes.[4b] Starting from the prototypes in Scheme 2 a coherent picture of scope and limitations of the polycyclization has emerged. The classification into series *A* and series *B* reactivity has been useful for the rational design of radical cascades. A variety of complex molecules have been constructed with several stereocentres and with rapid increase in structural complexity. As a rule of thumb a conventional de novo approach to a complex molecule often requires an average of three to four synthetic steps per chiral centre. By comparison, the syntheses described here are brief and convergent. Chemical yields are equally respectable. From the point of view of chemical diversity[11] the various molecules reported are pyranose and furanose models which are fused in glycosidic fashion to propargylated terpenes.

Experimental

General

Melting points: uncorrected, Büchi apparatus. Infrared spectra: Perkin–Elmer 1710 spectrometer. ^{1}H NMR spectra: At 200 MHz, Bruker WP 200 SY spectrometer, solvent $CDCl_3$ unless stated otherwise. ^{13}C NMR spectra: At 50 MHz, Bruker WP 200 SY. APT (*a*ttached *p*roton *t*est): spin echo base selection of multiplicities of ^{13}C signals. Quaternary C and CH_2 carbon atoms give positive signals (+), while CH and CH_3 give negative signals (−). MS: Low and high resolution electron impact mass spectra, Finnigan MAT 312 spectrometer, 70 eV, room temperature, unless otherwise stated. Relative intensities in parentheses. Preparative column chromatography: J. T. Baker silica gel (particle size 30–60 μm). Analytical TLC: Aluminium-backed 0.2 mm silica gel 60 F_{254} plates (E. Merck). Diethyl ether (E) was distilled from sodium benzophenone ketyl prior to use, CH_2Cl_2 (DCM) from CaH_2. PE refers to light petroleum, bp 30–60°C, redistilled prior to use.

General procedure A—preparation of homologs of hex-5-en-1-yn-4-ols

A three-necked flask equipped with reflux condenser, thermometer and septum was charged with Mg turnings (2 equiv.), $HgCl_2$ (0.5 mg/mmol carbonyl compound), iodine (catal.) and E (0.4 ml/mmol carbonyl compound). The reaction was started with a few drops of propargyl bromide. The mixture was allowed to reflux for 2 min and then cooled to −40°C. A pre-cooled solution of carbonyl compound and propargyl bromide (1.7 equiv.) in E (0.7 ml/mmol carbonyl compound was added dropwise. After complete addition (30 min) the mixture was stirred for 16 h at (20°C, then cooled with an ice-bath and treated dropwise with sat. aq. NH_4Cl solution and HCl (1N). The mixture was stirred for 1 h at rt, the aqueous layer separated and extracted with E (3×). The combined organic layer was washed with sat. aq. $NaHCO_3$ solution and brine and then dried (Na_2SO_4). The solvent was removed and the crude product purified by Kugelrohr distillation or chromatography.

General procedure B—*N*-iodosuccinimide-promoted alkoxylation

A flame-dried flask was charged with *N*-iodosuccinimide (1.5 equiv.) and cooled to −30°C under a N_2 atmosphere. DCM (0.5 ml/mmol dihydropyran) was added and the mixture was stirred for 10 min. Then the alcohol (1.2 equiv.) in DCM (0.5 ml/mmol dihydropyran) was added dropwise and the red-coloured mixture was stirred for 5 min. Dihydropyran (1 equiv.) in DCM (0.3 ml/mmol) was added slowly. The reaction mixture was cooled to −70°C and stirred for 16 under exclusion of light (the temperature rises to ca. 10°C). The red-brown mixture was diluted with DCM and extracted with NaOH (1N, 1 ml/

mmol dihydropyran). The organic layer decolorized completely. The aqueous phase was extracted with DCM (3×), the combined organic layer was washed with water (2×), brine and 10% NaS_2O_3. The organic layer was dried (Na_2SO_4), evaporated and purified by chromatography (E/PE).

General procedure C—cyclization with BEt_3

A flame-dried two-necked flask equipped with reflux condenser, $CaCl_2$ drying tube and septum was charged with cyclization precursor in abs. MeCN (0.2 M) under dry air atmosphere. After heating 100°C (preheated oil bath) the triethylborane solution (2 equiv., 1 M in hexane) was added dropwise within 15 min. The mixture was stirrred until TLC showed no starting material. After complete reaction (TLC monitoring) the mixture was cooled to r.t., the solvent removed and the crude product purified by chromatography.

General procedure D—cyclization with BEt_3/EtI

A flame-dried two-necked flask equipped with reflux condenser, $CaCl_2$ drying tube and septum was charged with cyclization precursor and EtI (1 equiv.) in abs. benzene (0.5 M) under dry air atmosphere. This mixture was treated with BEt_3 as described above.

***trans*-6,10-Dimethyl-undeca-5,9-dien-1-yn-4-ol.** *General procedure A.* Carbonyl compound: geranial (31 mmol), purification: distillation (120–130°C), yield: 91%. ^{1}H NMR: δ=5.28 (m, 1H; H-5), 5.20 (m, 1H; H-9), 4.55 (m, 1H; H-4), 2.42 (ddd, *J*=9, 6, 2.5 Hz, 2H; H-3), 2.21–1.85 (m, 8H; CH_2, CH_3, OH), 1.80–1.62 (m, 6H; CH_3).

6,10-Dimethyl-undeca-5,9-dien-1-yn-4-ol. *General procedure A.* Carbonyl compound: citral (78 mmol), purification: distillation (120–130°C), yield: 87%. ^{1}H NMR: δ=5.36 (m, 1H; H-5), 5.09 (m, 1H; H-9), 4.52 (m, 1H; H-4), 2.38 (ddd, *J*=6, 5, 2 Hz, 2H; H-3), 2.22–1.96 (m, 8H; H-7, H-8, CH_3, OH), 1.78–1.55 (m, 6H; CH_3).

1-Cyclohexyl-1-enyl-but-3-yn-1-ol. *General procedure A.* Carbonyl compound: cyclohexen-1-aldehyde (11 mmol), purification: chromatography, yield: 66%. ^{1}H NMR: δ=5.73 (m, 1H; H-6), 4.49 (br. t, *J*=6 Hz, 1H; H-4), 2.49 (ddd, *J*=12, 7, 3 Hz, 1H; H-3a), 2.40–2.32 (m, 5H; H-3b, CH_2), 1.99 (t, *J*=3 Hz, 1H; H-1).

1-(2-Methyl-cyclohex-1-enyl)-but-3-yn-1-ol. *General procedure A.* Carbonyl compound: 2-methyl-cyclohexen-1-aldehyde (8 mmol), purification: chromatography, yield: 73%. ^{1}H NMR: δ=5.82 (m, 1H; H-4), 2.51 (ddd, *J*=16, 8, 2 Hz, 1H; H-3a), 2.32 (ddd, *J*=16, 8, 2 Hz, 1H; H-3b), 2.05 (t, *J*=3 Hz, 1H; H-1), 2.02–1.48 (m, 10H; CH_2, CH_3).

1-(2,6,6-Trimethyl-cyclohex-1-enyl)-but-3-yn-1-ol. *General procedure A.* Carbonyl compound: β-cyclocitral (9 mmol), purification: chromatography, yield: 86%. ^{1}H NMR: δ=4.45 (dd, *J*=10, 3 Hz, 1H; H-4), 3.81 (ddd, *J*=17, 10, 3 Hz, 1H; H-3a), 3.37 (dt, *J*=6, 3 Hz, 1H; H-3b), 2.00 (t, *J*=3 Hz, 1H; H-1), 1.95 (br. t, *J*=6 Hz, 2H; CH_2), 1.83 (s, 3H; CH_3), 1.65–1.35 (m, 4H; CH_2), 1.10 (s, 3H, CH_3), 0.98 (s, 3H; CH_3).

1-(6,6-Dimethyl-bicyclo[3.1.1]hept-2-en-2-yl)-but-3-yn-1-ol. *General procedure A.* Carbonyl compound: (1*R*)-(−)-myrtenal (20 mmol), purification: distillation (125°C), yield: 75%. ^{1}H NMR: δ=5.55 (m, 1H; H-6), 4.18 (br. t, *J*=6 Hz, 1H; H-4), 2.52–1.93 (m, 9H; H-1, H-3, H-7, H-8, H-9a, H-10, OH), 1.30 (s, 3H; CH_3), 1.18 (d, *J*=9 Hz, 1H; H-9b), 0.83 (s, 3H; CH_3).

3-Iodo-2-(3,7-dimethyl-1-prop-2-ynyl-octa-2,6-dienyloxy)-tetrahydropyran (1 and 3). Dihydropyran (10 mmol) and *trans*-6,10-dimethyl-undeca-5,9-dien-1-yn-4-ol were allowed to react according to general procedure B to afford unpolar diastereomer **1** (2.50 g, 62%) and polar diastereomer **3** (1.29 g, 32%). Data for **1**. IR (film): ν=3295 cm^1, 2965, 2926, 2121, 1671, 1440, 1377, 1203, 1121, 1080, 1069, 998; ^{1}H NMR: δ=5.25 (dd, *J*=9, 1 Hz, 1H; H-5), 5.08 (m, 1H; H-13), 4.82 (d, *J*=5 Hz, 1H; H-7), 4.68–4.47 (m, 1H; H-4), 4.19–4.06 (m, 1H; H-8), 4.05–3.89 (m, 1H; H-11a), 3.62–3.47 (m, 1H; H-11b), 2.61–2.28 (m, 3H; H-3, H-9a), 2.18–1.93 (m, 6H; H-1, H-9b, CH_2), 1.81–1.55 (m, 2H; CH_2), 1.72, 1.68, 1.61 (d, *J*=1.8 Hz, 9H; CH_3); ^{13}C NMR (APT): δ=139.76 (+, C-6), 131.50 (+, C-12), 124.10 (−, C-13), 123.89 (−, C-5), 101.17 (−, C-7), 80.76 (+, C-2), 73.05 (−, C-4), 69.77 (+, C-1), 63.31 (+, C-11), 39.57 (+, CH_2), 32.43 (+, C-9), 29.90 (−, C-8), 26.29 (+, CH_2), 25.68 (−, CH_3), 25.36 (+, CH_2), 25.22 (+, CH_2), 17.70 (−, CH_3), 16.81 (−, CH_3); MS (70 eV): *m/z* (%): 402 (0) [M^+], 363 (1), 212 (100), 174 (4), 154 (15), 135 (9), 123 (8), 105 (11), 91 (22), 84 (45), 69 (37). Data for **3**. IR (film): ν=3305 cm^{-1}, 2965, 2927, 2123, 1668, 1436, 1381, 1203, 1123, 1070, 991; ^{1}H NMR: δ=5.18–5.02 (m, 2H; H-5, H-13), 4.68–4.43 (m, 2H; H-7, H-4), 4.17–3.97 (m, 2H; H-8, H-11a), 3.55 (m, 1H; H-11b), 2.58–2.24 (m, 3H; H-3, H-9a), 2.18–1.95 (m, 6H; H-1, H-9b, CH_2), 1.95–1.45 (m, 11H; CH_2, CH_3); ^{13}C NMR (APT): δ=142.45 (+, C-6), 131.68 (+, C-12), 123.74 (−, C-13), 123.06 (−, C-5), 98.28 (−, C-7), 80.96 (+, C-2), 70.30 (−, C-4), 69.45 (+, C-1), 62.94 (+, C-11), 39.59 (+, CH_2), 32.05 (+, C-9), 29.79 (−, C-8), 26.21 (+, CH_2), 25.80 (−, CH_3), 25.72 (+, CH_2), 25.05 (+, CH_2), 17.78 (−, CH_3), 16.65 (−, CH_3); MS (70 eV): *m/z* (%): 402 (0) [M^+], 363 (1), 212 (100), 174 (4), 154 (22), 135 (3), 123 (12), 105 (6), 91 (15), 84 (42), 69 (40).

3-Iodo-2-(3,7-dimethyl-1-prop-2-ynyl-octa-2,6-dienyloxy)-tetrahydropyran (5 and 6). Dihydropyran (10 mmol) and 6,10-dimethyl-undeca-5,9-dien-1-yn-4-ol were allowed to react according to general procedure B to afford unpolar diastereomer **5** (*E*/*Z*=3:7) (2.42 g, 60%) and polar diastereomer **6** (1.33 g, 33%). Data for **5**. IR (film): ν=3295 cm^{-1}, 2965, 2926, 2122, 1669, 1440, 1303, 1282, 1122, 1080, 1070, 992; ^{1}H NMR: δ=5.25 (dd, *J*=9, 1 Hz, 1H; H-5), 5.09 (m, 1H; H-13), 4.82/4.66 (d, *J*=5 Hz, 1H; H-7), 4.61–4.48 (m, 1H; H-4), 4.18–3.89 (m, 2H; H-8, H-11a), 3.53 (m, 1H; H-11b), 2.62–2.28 (m, 3H; H-3, H-9a), 2.25–1.90 (m, 6H; H-1, H-9b, CH_2), 1.85–1.45 (m, 11H; CH_2, CH_3); ^{13}C NMR (50 MHz, APT). δ=142.60/139.74 (+, C-6), 132.00/131.48 (+, C-12), 124.73/124.13 (−, C-13), 123.80/123.66 (−, C-5), 101.16/98.04 (−, C-7), 81.10/80.74 (+, C-2), 73.04/72.65 (−, C-4), 69.78/69.60 (+, C-1), 63.30/62.70 (+, C-11), 39.57

(+, CH_2), 32.41/32.35 (+, C-9), 29.88 (−, C-8), 26.29/25.89 (+, CH_2), 25.68 (−, CH_3), 25.36 (+, CH_2), 25.21 (+, CH_2), 17.70/17.66 (−, CH_3), 16.81 (−, CH_3); MS (70 eV): *m/z* (%): 402 (0) [M^+], 363 (2), 318 (1), 269 (1), 211 (100), 174 (10), 153 (19), 135 (23), 124 (12), 91 (21), 84 (82). Data for **3**. IR (film): ν=3295 cm^{-1}, 2965, 2926, 2122, 1669, 1439, 1303, 1270, 1122, 1079, 992; ^{1}H NMR: δ=5.25/4.82 (dd, *J*=9, 1 Hz, 1H; H-5), 5.10 (m, 1H; H-13), 4.68–4.48 (m, 2H; H-7, H-4), 4.19–3.90 (m, 2H; H-8, H-11a), 3.55 (m, 1H; H-11b), 2.61–2.28 (m, 3H; H-3, H-9a), 2.27–1.88 (m, 6H; H-1, H-9b, CH_2), 1.87–1.43 (m, 11H; CH_2, CH_3); ^{13}C NMR (APT): δ=139.87/139.73 (+, C-6), 131.85/131.65 (+, C-12), 123.95/123.90 (−, C-13), 123.75/123.08 (−, C-5), 101.17/98.27 (−, C-7), 77.72/77.09 (+, C-2), 73.07/72.85 (−, C-4), 69.97/69.46 (+, C-1), 63.44/63.29 (+, C-11), 39.58 (+, CH_2), 32.60/32.04 (+, C-9), 29.82/29.77 (−, C-8), 26.57/26.21 (+, CH_2), 25.80 (−, CH_3), 25.71 (+, CH_2), 25.41 (+, CH_2), 17.78/17.69 (−, CH_3), 16.80/16.64 (−, CH_3); MS (70 eV): *m/z* (%): 402 (0) [M^+], 363 (3), 279 (3), 211 (100), 174 (8), 153 (29), 135 (14), 123 (16), 105 (10), 91 (24), 84 (83).

3-Iodo-2-(1-cyclohex-1-enyl-but-3-ynyloxy)-tetrahydropyran (7 and 9). Dihydropyran (3 mmol) and 1-cyclohexyl-1-enyl-but-3-yn-1-ol were allowed to react according to general procedure B to afford unpolar diastereomer **7** (335 mg, 31%) and polar diastereomer **9** (378 mg, 35%). Data for **7**. IR (film): ν=3294 cm^{-1}, 2927, 2856, 2121, 1668, 1435, 1351, 1270, 1124, 1069, 1009, 990; ^{1}H NMR: δ=5.74 (m, 1H; H-6), 4.77 (d, *J*=5.4 Hz, 1 H; H-7), 4.20–4.03 (m, 2H; H-4, H-8), 4.03–3.88 (m, 1H; H-11a), 3.62–3.47 (m, 1H; H-11b), 2.52 (ddd, *J*=17, 6, 2.5 Hz, 1H; H-3a), 2.41–2.28 (m, 2H; H-3b, H-9a), 2.19–1.85 (m, 5H; H-9b, CH_2), 1.98 (t, *J*=3 Hz, 1H; H-1), 1.85–1.45 (m, 6H; CH_2); ^{13}C NMR (APT): δ=136.16 (+, C-5), 125.70 (−, C-6), 101.37 (−, C-7), 81.39 (−, C-4), 81.05 (+, C-2), 69.93 (+, C-1), 63.70 (+, C-11), 32.75 (+, CH_2), 30.08 (−, C-8), 25.44 (+, CH_2), 25.00 (+, CH_2), 23.38 (+, CH_2), 23.23 (+, CH_2), 22.47 (+, CH_2), 22.41 (+, CH_2); MS (70 eV): *m/z* (%): 360 (0) [M^+], 321 (5), 211 (100), 150 (2), 133 (8), 117 (7), 105 (13), 91 (29), 84 (86), 79 (14). Data for **9**. IR (film): ν=3294 cm^{-1}, 2927, 2856, 2122, 1666, 1435, 1388, 1202, 1124, 1070, 1007, 991; ^{1}H NMR: δ=5.74 (m, 1H; H-6), 4.59 (d, *J*=4.8 Hz, 1H; H-7), 4.17 (br. t, *J*=7 Hz, 1H; H-4), 4.12–3.98 (m, 2H; H-8, H-11a), 3.63–3.47 (m, 1H; H-11b), 2.48 (ddd, *J*=17, 6, 2.5 Hz, 1H; H-3a), 2.42–2.28 (m, 2H; H-3b, H-9a), 2.19–1.43 (m, 12H; H-1, H-9b, CH_2); ^{13}C NMR (APT): δ=134.20 (+, C-5), 128.59 (−, C-6), 98.40 (−, C-7), 81.17 (+, C-2), 78.97 (−, C-4), 69.53 (+, C-1), 63.19 (+, C-11), 32.49 (+, CH_2), 29.59 (−, C-8), 25.33 (+, CH_2), 25.02 (+, CH_2), 23.62 (+, CH_2), 22.52(+, CH_2), 22.41 (CH_2), 22.33 (+, CH_2); MS (70 eV): *m/z* (%): 360 (0) [M^+], 320 (8), 267 (2), 242 (2), 211 (100), 182 (13), 154 (31), 139 (9), 116 (38), 105 (21), 91 (23), 84 (78), 69 (12).

3-Iodo-2-[1-(2-methyl-cyclohex-1-enyl)-but-3-ynyloxy]-tetrahydropyran (12 and 14). Dihydropyran (4 mmol) and 1-(2-methyl-cyclohexyl-1-enyl)-but-3-yn-1-ol were allowed to react according to general procedure B to afford unpolar diastereomer **12** (480 mg, 32%) and polar diastereomer **14** (540 mg, 36%). Data for **12**. IR (film): ν=3295 cm^{-1}, 2927, 2856, 2121, 1668, 1435, 1335, 1236, 1122, 1070, 1011, 944; ^{1}H NMR: δ=4.85 (d, *J*=4.8 Hz, 1H; H-7), 4.77 (br. t, *J*=7 Hz, 1H; H-4), 4.16 (dt, *J*=5 Hz, 1H; H-8), 3.92 (m, 1H; H-11a), 3.53 (m, 1H; H-11b), 2.61 (ddd, *J*=17, 7, 3 Hz, 1H; H-3a), 2.35 (m, 2H; H-3b, H-9a), 2.24–1.39 (m, 14H; H-9b, CH_2, CH_3), 1.95 (t, *J*=3 Hz, 1H; H-1); MS (70 eV): *m/z* (%): 375 (0) [M^+], 335 (9), 211 (100), 148 (11), 131 (12), 125 (58), 105 (12), 91 (16), 84 (90), 79 (9). Data for **14**. IR (film): ν=3307 cm^{-1}, 2927, 2856, 2122, 1667, 1436, 1235, 1133, 1121, 1071, 1020, 990; ^{1}H NMR: δ=4.88 (br. t, *J*=7 Hz, 1H; H-4), 4.47 (d, *J*=5 Hz, 1H; H-7), 4.18–4.01 (m, 2H; H-8, H-11a), 3.63–3.48 (m, 1H; H-11b), 2.64–2.27 (m, 3H; H-3, H-9a), 2. 26–1.40 (m, 14H; H-9b, CH_2, CH_3), 1.93 (t, *J*=3 Hz, 1H; H-1); MS (70 eV): *m/z* (%): 375 (0) [M^+], 335 (1), 211 (11), 147 (6), 125 (55), 105 (8), 91 (11), 85 (100), 67 (22).

3-Iodo-2-[1-(2,6,6-trimethyl-cyclohex-1-enyl)-but-3-ynyloxy]-tetrahydropyran (17 and 19). Dihydropyran (4 mmol) and 1-(2,6,6-trimethyl-cyclohexyl-1-enyl)-but-3-yn-1-ol were allowed to react according to general procedure B to afford unpolar diastereomer **17** (290 mg, 24%) and polar diastereomer **19** (326 mg, 28%). Data for **17**. IR (film): ν=3305 cm^{-1}, 2925, 2856, 2120, 1667, 1438, 1235, 1130, 1120, 1071, 1020, 991; ^{1}H NMR: δ=5.19 (d, *J*=4 Hz, 1H; H-7), 4.44–4.28 (m, 2H; H-4, H-8), 3.86 (m, 1H; H-11a), 3.52 (m, 1H; H-11b), 2.82 (ddd, *J*=17, 10, 2 Hz, 1H; H-3a), 2.39 (dt, *J*=17, 2 Hz, 1H; H-3b), 2.32–2.18 (m, 1H, H-9a), 2.04 (t, *J*=3 Hz, 1H; H-1), 2.02–1.87 (m, 4H; H-9b, CH_2), 1.82 (s, 3H; CH_3), 1.65–1.23 (m, 5H; CH_2), 1.09 (s, 3H; CH_3), 0.98 (s, 3H; CH_3); MS (70 eV): *m/z* (%): 402 (0) [M^+], 363 (4), 211 (100), 174 (2), 153 (48), 133 (3), 119 (7), 105 (9), 91 (13), 84 (77), 69 (11). Data for **19**. IR (film): ν=3307 cm^{-1}, 2927, 2853, 2122, 1665, 1438, 1235, 1133, 1120, 1071, 1020, 995; ^{1}H NMR: δ=4.73 (d, *J*=4 Hz, 1H; H-7), 4.42 (br. dd, *J*=11, 2 Hz, 1H; H-4), 4.29–4.13 (m, 2H; H-8, H-11a), 3.66–3.53 (m, 1H; H-11b), 2.79 (ddd, *J*=17, 10, 2 Hz, 1H; H-3a), 2.48–2.27 (m, 2H; H-3b, H-9a), 2.00 (t, *J*=3 Hz, 1H; H-1), 1.99–1.85 (m, 3H; H-9b, CH_2), 1.78 (s, 3H; CH_3), 1.65–1.33 (m, 6H; CH_2), 1.05 (s, 3H; CH_3), 0.98 (s, 3H; CH_3); MS (70 eV): *m/z* (%): 402 (0.3) [M^+], 363 (4), 211 (100), 175 (3), 159 (4), 154 (57), 119 (8), 106 (9), 91 (14), 84 (84), 69 (12).

3-Iodo-2-[1-(6,6-dimethyl-biyclo[3.3.1]hept-2-en-2-yl)-but-3-ynyloxy]-tetrahydropyran (21). Dihydropyran (4 mmol) and 1-(6,6-dimethyl-bicyclo[3.3.1]hept-2-en-2-yl)-but-3-yn-1-ol were allowed to react according to general procedure B to afford unpolar diastereomer **21** (288 mg, 18%) and polar diastereomer (320 mg, 20%). IR ($CHCl_3$): ν=3308 cm^{-1}, 2948, 2920, 2120, 1652, 1468, 1432, 1332, 1268, 1120, 1068, 1008, 988; ^{1}H NMR: δ=5.57 (m, 1H; H-6), 4.91 (d, *J*=5 Hz, 1H; H-7), 4.26–4.12 (m, 2H; H-4, H-8), 3.96 (m, 1H; H-11a), 3.53 (m, 1H; H-11b), 2.59–2.18 (m, 7H; H-3, CH, CH_2), 2.17–1.75 (m, 3H; H-1, CH, CH_2), 1.71–1.43 (m, 2H; CH_2), 1.29 (s, 3H; CH_3), 1.18 (d, *J*=8 Hz, 1H; CH_2), 0.85 (s, 3H; CH_3); MS (70 eV): *m/z* (%): 400 (0) [M^+], 361 (3), 211 (97), 172 (7), 157 (7), 115 (12), 105 (10), 91 (30), 85 (100), 77 (14).

7-Iodo-5-methyl-5-(4-methyl-pent-3-enyl)-3,4,4a,4b,5,8,8a,9a-octahydro-2*H*-1,9-dioxa-fluorene (2). Reaction of cyclization precursor **1** (0.5 mmol) according to general procedure C (30 min) afforded **2** (62 mg, 31%). Reaction of **1** (1.0 mmol) according general procedure D (3 h) afforded **2** (209 mg, 52%). Reaction of cyclization precursor

5 (1 mmol) according to general procedure C (1 h) afforded **2** (141 mg, 35%), colourless oil. IR (film): ν=2921 cm^{-1}, 1615, 1448, 1408, 1377, 1281, 1249, 1152, 1126, 1099, 1025, 959; ^{1}H NMR: δ=6.05 (d, J=2 Hz, 1H; H-1), 5.34 (d, J=4 Hz, 1H; H-7), 5.05 (m, 1H; H-13), 4.37 (ddd, J=12, 9, 6 Hz, 1H; H-4), 3.83–3.57 (m, 2H; H-11), 3.03 (dd, J=16, 6 Hz, 1H; H-3a), 2.53 (ddd, J=16, 9, 2 Hz, 1H; H-3b), 2.20–1.75 (m, 4H; H-5, H-8, H-14), 1.68 (s, 3H; CH_3), 1.62 (s, 3H; CH_3), 1.61–1.50 (m, 4H; H-10, CH_2), 1.41 (br. t, J=8 Hz, 2H; CH_2), 1.04 (s, 3H; CH_3); NOE: H-7 (5.34 ppm) irradiated: H-8 (7.5%), H-5 (6.4%); H-4 (4.37 ppm) irradiated: H-3a (5.5%), CH_3 (6.4%); H-5/H-8 (2.12 ppm) irradiated: H-7 (9.1%); ^{13}C NMR (APT): δ=147.73 (−, C-1), 131.80 (+, C-12), 124.03 (−, C-13), 101.71 (−, C-7), 90.84 (+, C-2), 72.84 (−, C-4), 60.61 (+, C-11), 48.83 (−, C-5), 47.81 (+, C-3), 43.96 (+, CH_2), 41.71 (+, C-6), 35.95 (−, C-8), 25.71 (−, CH_3), 23.85 (−, CH_3), 23.04 (+, C-10), 22.87 (+, CH_2), 22.19 (+, CH_2), 17.71 (−, CH_3); MS (70 eV): m/z (%): 404 (2) [M^++2], 402 (3) [M^+], 319 (10), 275 (74), 199 (12), 192 (20), 159 (13), 135 (18), 119 (31), 105 (50), 91 (63), 69 (100).

7-Iodo-5-methyl-5-(4-methyl-pent-3-enyl)-3,4,4a,4b,5,8,8a,9a-octahydro-2*H*-1,9-dioxa-fluorene (4). Reaction of cyclization precursor **3** (0.5 mmol) according to general procedure C (5 min) afforded **2** (99 mg, 49%, 1:1 mixture of diastereomers). Reaction of **1** (0.5 mmol) according general procedure D (1 h) afforded **2** (86 mg, 43%, 1:1 mixture of diastereomers). Reaction of cyclization precursor **6** afforded **2** (30%, 1:1 mixture of diastereomers), colourless oil. IR (film): ν=2920 cm^{-1}, 1617, 1445, 1410, 1377, 1280, 1249, 1152, 1126, 1090, 1025, 970; ^{1}H NMR: δ=6.15/6.05 (m, 1H; H-1), 5.05 (m, 1H; H-13), 4.97/4.96 (d, J=3.8 Hz, 1H; H-7), 4.02–3.81 (m, 1H; H-4), 3.56–3.38 (m, 2H; H-11), 3.02/2.94 (dt, J=6, 1 Hz, 1H; H-3a), 3.78–3.60 (m, 1H; H-3b), 2.22–1.78 (m, 4H; H-5, H-8, H-14), 1.70 (br. s, 3H; CH_3), 1.62 (br. s, 3H; CH_3), 1.57–1.31 (m, 6H; CH_2), 1.18/0.98 (s, 3H; CH_3); ^{13}C NMR (APT): δ=147.58/146.99 (−, C-1), 131.87/131.81 (+, C-12), 124.30/123.98 (−, C-13), 101.90 (−, C-7), 90.88/90.64 (+, C-2), 77.83/77.72 (−, C-4), 64.22/63.79 (+, C-11), 47.13/46.82 (+, C-3), 46.87 (−, C-5), 43.99/43.70 (+, CH_2), 42.72/41.48 (+, C-6), 39.22/38.79 (−, C-8), 25.75/25.68 (−, CH_3), 23.21/23.14 (+, H-10), 22.84/21.12 (+, CH_2), 20.45 (+, CH_2), 18.02/17.72 (−, CH_3), 15.37/15.25 (−, CH_3); MS (70 eV): m/z (%):403 (5) [M^++1], 402 (1) [M^+], 319 (11), 275 (83), 197 (13), 192 (15), 157 (23), 134 (11), 119 (12), 105 (58), 91 (43), 69 (100).

6-Iodo-2,3,4,4a,7,7a,8a,11,12,12a-decahydro-1*H*,10*H*-benzo[d]pyrano[2,3-*b*]-benzofuran (8, X=I) and 2,3,4,4a,7,7a,8a,11,12,12a-decahydro-1*H*,10*H*-benzo[*d*]pyrano-[2,3-*b*]-benzofuran (8, X=H). Cyclization precursor (0.5 mmol) **7** was allowed to react according to general procedure C (5 min). Chromatography (DCM) and consecutive crystallization from E/PE yielded **8**(X=I) (110 mg, 61%) as colourless crystals and **8**(X=H) (18 mg, 15%) as light-yellow oil. Data for **8**(X=I), mp 93°C. IR ($CHCl_3$): ν=3000 cm^{-1}, 2940, 2860, 1612, 1444, 1388, 1308, 1252, 1136, 1108, 1088, 1064, 1048, 1028, 940; ^{1}H NMR: δ=6.09 (m, 1H; H-1), 5.47 (d, J=4.6 Hz, 1H; H-7), 4.10 (dd, J=10, 5 Hz, 1H; H-4), 3.63 (m, 2H; H-11), 3.00–2.83 (m, 1H; H-3a), 2.64–2.37 (m, 2H; H-3b, H-6), 2.28–2.12 (m, 1H; H-8), 1.78–1.08 (m, 12H; CH_2); ^{13}C NMR (APT): δ=142.72 (−, C-1), 101.30 (−, C-7), 90.85 (+, C-2), 79.81 (−, C-4), 60.63 (+, C-11), 44.39 (+, C-5), 41.72 (+, C-3), 39.82 (−, C-6), 39.11 (−, C-8), 28.61 (+, CH_2), 24.50 (+, CH_2), 22.37 (+, CH_2), 21.80 (+, CH_2), 21.56 (+, CH_2), 19.43 (+, CH_2); MS (70 eV): m/z (%): 360 (9) [M^+], 259 (6), 233 (15), 193 (6), 159 (5), 145 (10), 117 (7), 106 (35), 91 (100), 81 (17), 71 (49); HRMS calcd for $C_{15}H_{21}O_2I$: 360.0529, found 360.0583. $C_{15}H_{21}O_2I$ (360.22): calcd C 50.01, H 5.88; found C 50.51, H 5.98. Data for **8**(X=H). IR ($CHCl_3$): ν=3000 cm^{-1}, 2940, 2856, 1444, 1364, 1280, 1256, 1132, 1108, 1088, 1064, 1048, 1024, 952; ^{1}H NMR: δ=5.68–5.31 (m, 2H; H-1, H-2) 5.47 (d, J=5 Hz, 1H; H-7), 4.02 (dd, J=10, 5 Hz, 1H; H-4), 3.65 (m, 2H; H-11), 2.61–1.84 (m, 4H; H-3, H-6, H-8), 1.83–1.00 (m, 12H; CH_2); MS (70 eV): m/z (%): 235 (7) [M^++1], 234 (31) [M^+], 217 (9), 159 (11), 147 (35), 133 (78), 119 (27), 105 (41), 91 (100), 79 (50), 67 (41).

6-Iodo-2,3,4,4a,7,7a,8a,11,12,12a-decahydro-1*H*,10*H*-benzo[*d*]pyrano[2,3-*b*]-benzofuran (10) and 5-(iodomethylene)dodecahydro-9*H*-indeno[7a′,1′-4,5]furo[2,3-*b*]pyran (11). Cyclization precursor **9** (0.5 mmol) was allowed to react according to general procedure C (30 min). Twofold chromatography (DCM) afforded **10** (13 mg, 7%) as light-yellow oil and **11** (50 mg, 28%) as colourless crystals, mp 69–72°C. Data for **10**. ^{1}H NMR: δ=5.95 (m, 1H; H-1), 5.01 (d, J=5 Hz, 1H; H-7), 4.02–3.83 (m, 2H; H-11), 3.55 (m, 2H; H-3a, H-4), 3.31 (br. s, 1H; H-3b), 2.64 (m, 1H; H-6), 2.25–1.08 (m, 13H; H-8, CH_2). Data for **11**. ^{1}H NMR: δ=5.83 (dd, J=8, 3 Hz, 1H; H-1), 5.05 (d, J=5 Hz, 1H; H-7), 3.97 (dd, J=5, 2 Hz, 1H; H-4), 3.90 (m, 1H; H-11a), 3.52 (ddd, J=12, 9, 4 Hz, 1H; H-3a), 3.33 (m, 1H; H-11b), 2.64 (m, 2H; H-3b, H-6), 2.18–2.10 (m, 1H; H-8), 2.09–1.11 (m, 12H; CH_2); MS (70 eV): m/z (%): 360 (3) [M^+], 259 (100), 233 (5), 187 (2), 145 (3), 132 (22), 118 (15), 104 (9), 91 (21), 77 (9).

6-Iodo-4a-methyl-2,3,4,4a,7,7a,8a,11,12,12a-decahydro-1*H*,10*H*-benzo[*d*]pyrano[2,3-*b*]-benzofuran (13). Cyclization precursor **12** (0.5 mmol) was allowed to react according to general procedure C (2 h) to afford after chromatography (DCM) tetracycle **13** (113 mg, 60%) as colourless crystals, mp 94–96°C. IR ($CHCl_3$): ν=3000 cm^{-1}, 2924, 2860, 1616, 1444, 1352, 1252, 1140, 1120, 1100, 1052, 940; ^{1}H NMR: δ=5.88 (dd, J=2, 1 Hz, 1H; H-1), 5.30 (d, J=5 Hz, 1H; H-7), 4.52 (dd, J=10, 6 Hz, 1H; H-4), 3.77 (m, 1H; H-11a), 3.58 (m, 1H; H-11b), 2.95 (ddd, J=16, 6, 1 Hz, 1H; H-3a), 2.50 (ddd, J=16, 10, 3 Hz, 1H; H-3b), 2.37 (ddd, J=9, 6, 5 Hz, 1H; H-8), 1.88–1.12 (m, 12H; CH_2), 0.98 (s, 3H; CH_3); ^{13}C NMR (APT): δ=148.76 (−, C-1), 101.67 (−, C-7), 89.48 (+, C-2), 75.99 (−, C-4), 60.00 (+, C-11), 47.45 (+, C-5), 46.11 (+, C-6), 44.77 (−, C-8), 42.99 (+, C-3), 38.23 (+, CH_2), 27.95 (+, CH_2), 27.32 (−, CH_3), 23.26 (+, CH_2), 22.39 (+, CH_2), 22.07 (+, CH_2), 20.92 (+, CH_2); MS (70 eV): m/z (%): 375 (4) [M^+], 328 (1), 248 (5), 207 (6), 178 (6), 142 (65), 133 (5), 125 (10), 113 (23), 107 (69), 91 (12), 79 (91), 77 (100); HRMS calcd for $C_{16}H_{23}O_2I$: 374.0743, found 374.0729. $C_{16}H_{23}O_2I$ (375.25): calcd C 51.35, H 5.93; found C 51.35, H 6.02.

6-Iodo-4a-methyl-2,3,4,4a,7,7a,8a,11,12,12a-decahydro-1*H*,10*H*-benzo[*d*]pyrano[2,3-*b*]-benzofuran (15, X=I), 4a-methyl-2,3,4,4a,7,7a,8a,11,12,12a-decahydro-1*H*,10*H*-benzo[*d*]pyrano[2,3-*b*]-benzofuran (15, X=H) and 5-(iodomethylene)-4a-methyl-dodecahydro-9*H*-indeno-[7a′,1′-4,5]furo[2,3-*b*]pyran (16). Cyclization precursor **14** (1 mmol) was allowed to react according to general procedure C (3 h). Chromatography afford two fractions. The unpolar fraction contained **15**(X=I) and **15**(X=H), which were separated by preparative DC (DCM). The polar fraction contained **16**. Data for **15**(X=I), yield (60 mg, 16%), colourless crystals, mp 101–103°C. ^{1}H NMR: δ=5.88 (dd, *J*=2, 1 Hz, 1H; H-1), 4.98 (d, *J*=5.6 Hz, 1H; H-7), 3.94 (m, 1H; H-11a), 3.82 (dd, *J*=11, 6 Hz, 1H; H-4), 3.53 (m, 1 H; H-11b), 2.86 (ddd, *J*=16, 6, 2 Hz, 1H; H-3a), 2.69 (ddd, *J*=16, 10, 2 Hz, 1H; H-3b), 2.28–1.17 (m, 13H; H-8, CH_2), 0.96 (s, 3H, CH_3); MS (70 eV): *m*/*z* (%): 375 (2) [M^+], 374 (6), 272 (10), 247 (8), 201 (8), 186 (4), 145 (13), 131 (12), 106 (11), 91 (15), 84 (100), 67 (13). Data for **15**(X=H), yield (22 mg, 9%), colourless oil. ^{1}H NMR: δ=5.52 (ddd, *J*=10, 5, 2 Hz, 1H; H-2), 5.18 (ddd, *J*=10, 2, 1 Hz, 1H; H-1), 5.00 (d, *J*=5.5 Hz, 1H; H-7), 3.94 (m, 1H; H-11a), 3.73 (dd, *J*=10, 6 Hz, 1H; H-4), 3.52 (m, 1H; H-11b), 2.43–1.15 (m, 15H; H-3, H-8, CH_2), 0.94 (s, 3H; CH_3); MS (70 eV): *m*/*z* (%): 248 (21) [M^+], 233 (19), 202 (10), 187 (13), 161 (38), 147 (100), 133 (28), 120 (43), 106 (86), 91 (98), 79 (58). Data for **16**, yield (38 mg, 10%), colourless crystals, mp 83°C. IR (film): ν=3000 cm^{-1}, 2936, 2860, 1452, 1380, 1248, 1184, 1148, 1132, 1084, 984; ^{1}H NMR: δ=5.77 (t, *J*=2 Hz, 1H; H-1), 5.48 (d, *J*=3 Hz, 1H; H-7), 4.53 (dd, *J*=9, 4 Hz, 1H; H-4), 3.84–3.55 (m, 2H; H-11), 2.94 (ddd, *J*=18, 9, 2 Hz, 1H; H-3a), 2.53 (ddd, *J*=18, 4, 2 Hz, 1H; H-3b), 1.95–1.10 (m, 16H; H-8, CH_2, CH_3); MS (70 eV): *m*/*z* (%): 375 (4) [M^+], 374 (19), 273 (100), 211 (5), 181 (4), 146 (23), 131 (11), 117 (8), 106 (15), 91 (18), 79 (15).

4-Iodomethylen-2-(2,6,6-trimethylcyclohex-1-enyl)-hexahydro-pyrano[2,3-*b*]pyran (18). Reaction of cyclization precursor **17** (0.5 mmol) according to general procedure C (1 h) afforded **18** (30 mg, 15%, only one isomer). Reaction of **17** (0.5 mmol) according to general procedure D (2.5 h) afforded **18** (48 mg, 24%, *E*/*Z* mixture, 1:1). The isomers could be separated by preparative DC, but were not identified. Data for unpolar isomer, colourless crystals, mp 73–76°C. IR ($CHCl_3$): ν=3000 cm^{-1}, 2932, 2868, 1652, 1468, 1364, 1284, 1172, 1136, 1096, 1052, 996; ^{1}H NMR: δ=5.98 (d, *J*=2 Hz, 1H; H-1), 4.73 (d, *J*=3 Hz, 1H; H-7), 3.93 (m, 2H; H-4, H-11a), 3.73 (m, 1H; H-11b), 2.96–2.82 (m, 1H; H-3a), 2.81–2.60 (m, 1H; H-3b), 2.16 (dd, *J*=16, 2 Hz, 1H; H-8), 2.05–1.15 (m, 10H; CH_2), 1.93 (s, 3H; CH_3), 1.07 (s, 3H; CH_3), 0.94 (s, 3H; CH_3); ^{13}C NMR (APT): δ=149.17 (+, C-2), 135.58 (+, C-5), 132.72 (+, C-6), 97.37 (−, C-7), 75.07 (−, C-1), 74.94 (−, C-4), 61.52 (+, C-11), 45.02 (−, C-8), 39.64 (+, C-3), 38.33 (+, CH_2), 34.59 (+, CH_2), 34.03 (+, C), 28.88 (−, CH_3), 27.77 (−, CH_3), 24.50 (+, CH_2), 22.44 (+, CH_2), 21.27 (−, CH_3), 19.25 (+, CH_2); MS (70 eV): *m*/*z* (%): 402 (1) [M^+], 275 (20), 257 (15), 250 (74), 229 (8), 201 (8), 187 (11), 159 (30), 135 (10), 123 (100), 105 (29), 91 (48), 84 (79). Data for unpolar isomer, colourless oil. IR ($CHCl_3$): ν=3055 cm^{-1}, 2931, 2245, 1716, 1468, 1381, 1366, 1260, 1144, 1113, 1099, 1049, 1000, 930; ^{1}H NMR: δ=6.09 (s, 1H; H-1), 4.73 (d, *J*=3 Hz, 1H; H-7), 4.02–3.83 (m, 2H; H-4, H-11a), 3.69 (m, 1H; H-11b), 2.70–2.42 (m, 3H; H-3, H-8), 2.03–1.18 (m, 10H; CH_2), 1.94 (s, 3H; CH_3), 1.08 (s, 3H; CH_3), 1.03 (s, 3H: CH_3); ^{13}C NMR (APT): δ=150.26 (+, C-2), 135.88 (+, C-5), 132.61 (+, C-6), 97.82 (−, C-7), 75.27 (−, C-1), 74.64 (−, C-4), 61.32 (+, C-11), 47.15 (−, C-8), 39.91 (+, C-3), 37.15 (+, CH_2), 34.79 (+, CH_2), 34.10 (+, C), 28.95 (−, CH_3), 27.78 (−, CH_3), 25.10 (+, CH_2), 24.80 (+, CH_2), 21.16 (−, CH_3), 19.28 (+, CH_2); MS (70 eV): *m*/*z* (%): 403 (1) [M^++1], 275 (13), 257 (17), 250 (100), 229 (10), 187 (13), 159 (35), 123 (78), 105 (18), 95 (33), 84 (76).

4-Iodomethylen-2-(2,6,6-trimethylcyclohex-1-enyl)-hexahydro-pyrano[2,3-*b*]pyran (20). Reaction of cyclization precursor **19** (0.5 mmol) according to general procedure C (1 h) afforded **20** (68 mg, 34%). Reaction of **19** (0.5 mmol) according to general procedure D (1.5 h) afforded **20** (103 mg, 51%), colourless crystals, mp 78–80°C. IR ($CHCl_3$): ν=3000 cm^{-1}, 2932, 2868, 1612, 1456, 1376, 1264, 1156, 1104, 1076, 1024, 984; ^{1}H NMR: δ=6.03 (t, *J*=2 Hz, 1H; H-1), 4.82 (d, *J*=3 Hz, 1H; H-7), 4.53 (dd, *J*=12, 3 Hz, 1H; H-4), 4.05 (br. dd, *J*=11, 4.5 Hz, 1H; H-11a), 3.55 (m, 1H; H-11b), 2.77 (dd, *J*=14, 3 Hz, 1H; H-3a), 2.61–2.38 (m, 1H; H-3b), 2.24 (m, 1H; H-8), 2.02–1.15 (m, 10H; CH_2), 1.85 (s, 3H; CH_3), 1.08 (s, 3H; CH_3), 1.02 (s, 3H; CH_3); ^{13}C NMR (APT): δ=144.92 (+, C-2), 135.88 (+, C-5), 132.93 (+, C-6), 99.10 (−, C-7), 75.06 (−, C-1), 69.70 (−, C-4), 67.55 (+, C-11), 42.54 (−, C-8), 40.96 (+, C-3), 39.88 (+, CH_2), 34.98 (+, CH_2), 34.13 (+, C), 28.70 (−, CH_3), 27.61 (−, CH_3), 24.07 (+, CH_2), 21.10 (−, CH_3), 20.57 (+, CH_2), 19.25 (+, CH_2); MS (70 eV): *m*/*z* (%): 402 (3) [M^+], 275 (15), 257 (11), 250 (100), 205 (6), 173 (12), 159 (26), 133 (12), 123 (94), 105 (20), 95 (41), 84 (74).

5-(Iodomethylene)-dodecahydro-9*H*-methanoindeno-[7a′,1′-4,5]furo[2,3-*b*]pyran (22) and 2-(6,6-diethyl-bicyclo[3.1.1]hept-2-en-2-yl)-4-iodomethylene-hexahydro-pyrano[2,3-*b*]pyran (23). Reaction of cyclization precursor **21** (0.5 mmol) according to general procedure C (5 min) afforded **22** (84 mg, 42%, *E*/*Z* mixture, 1.5:1) as colourless crystals, mp 94–96°C. Reaction of **21** (0.5 mmol) according to general procedure D (5 min) afforded **22** (84 mg, 42%, *E*/*Z* mixture, 1.5:1) and **23** (22 mg, 11%) as colourless oil. Data for **22**. IR ($CHCl_3$): ν=3308 cm^{-1}, 3008, 2944, 2920, 2872, 1612, 1404, 1344, 1268, 1248, 1152, 1080, 1032, 976; ^{1}H NMR: δ=5.97 (dd, *J*=7, 2 Hz, 1H; H-1), 5.28 (d, *J*=4 Hz, 1H; H-7), 4.41 (dd, *J*=8, 4 Hz, 1H; H-4), 3.88–3.57 (m, 2H; H-11), 3.17–2.96 (m, 2H; H-3a, H-6), 2.65–2.13 (m, 3H; H-3b, H-15a, H-16a), 2.03 (t, *J*=6 Hz, 1H; H-12), 1.98–0.81 (m, 7H; CH, CH_2), 1.20 (s, 3H, CH_3), 1.04 (d, *J*=10 Hz, 1H; H-15b), 0.81 (s, 3H; CH_3); ^{13}C NMR (APT): δ=162.91 (+, C-2), 101.08 (−, C-7), 82.09 (−, C-4), 70.46 (−, C-1), 64.06 (+, C-11), 60.74 (+, C-5), 50.25 (−, C-12), 46.75 (+, C-3), 43.21 (−, C-8), 39.87 (−, C-14), 38.38 (+, C-13), 37.70 (−, C-6), 35.00 (+, C-16), 28.81 (+, C-15), 27.46 (−, CH_3), 23.86 (+, C-10), 23.02 (+, C-9), 22.86 (−, CH_3); MS (70 eV): *m*/*z* (%): 400 (4) [M^+], 299 (100), 273 (11), 250 (13), 235 (43), 201 (55), 173 (34), 143 (26), 129 (44), 105 (49), 91 (68), 79 (50); HRMS calcd for $C_{18}H_{25}O_2I$: 400.0899, found 400.0906. Data for **23**. ^{1}H NMR: δ=6.06 (m, 1H; H-1), 5.43 (m, 1H; H-6), 4.79 (d, *J*=3 Hz, 1H; H-7), 4.32 (m, 1H; H-4), 4.10–3.93 (m, 1H;

H-11a), 3.72–3.48 (m, 1H; H-11b), 2.69 (dd, J=14, 4 Hz, 1H; H-3a), 2.58–0.75 (m, 12H; H-3b, CH, CH_2), 1.29 (s, 3H; CH_3), 0.78 (s, 3H; CH_3); ^{13}C NMR (APT): δ=146.63 (+, C-2), 145.67 (+, C-5), 119.22 (−, C-6), 96.70 (−, C-7), 76.12 (−, C-1), 73.40 (−, C-4), 65.46 (+, C-11), 44.01 (−, C-12), 42.79 (−, C-8), 40.95 (−, C-14), 37.96 (+, C-13), 37.12 (+, C-3), 31.66 (+, CH_2), 31.39 (+, CH_2), 26.23 (−, CH_3), 24.34 (+, CH_2), 21.99 (+, CH_2), 21.24 (−, CH_3); MS (70 eV): m/z (%): 400 (3) [M^+], 295 (20), 273 (24), 250 (56), 235 (100), 207 (21), 185 (41), 171 (34), 157 (28), 143 (43), 123 (66), 91 (77), 69 (51).

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