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The Intramolecular Enyne Diels-Alder Reaction. Stereoselective Construction of Tricyclic Dioxadienones and Mechanistic Outline

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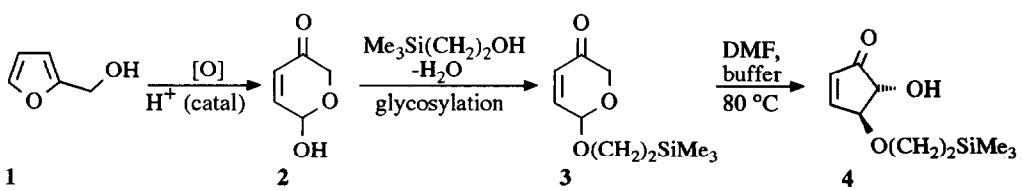
Abstract. 4-Methylpent-4-en-2-yn-1-ols and 6-hydroxy-2,3-dihydro-6*H*-pyran-3-ones are condensed in different ways to a series of tricyclic dioxadienones which contain the basic framework of the cadlinolides. A mechanism of the intramolecular enyne-ene cycloisomerization and the origin of the resulting type I and type II dienes is proposed.

Introduction. Furfurol **1** is a simple carbohydrate-related heterocycle, which is currently available from various suppliers at less than $ 1 per kg. It is therefore important and a longterm challenge to develop useful chemistry from this interesting, naturally derived, low molecular weight raw material. Oxidative rearrangement of **1** with m-CPBA affords 6-hydroxy-2,3-dihydro-6*H*-pyran-3-one[1] (**2**) in high yield (>80%), using an improved work up procedure (see Experimental). Hemiacetal **2** may be regarded as a simplified sugar which is not overfunctionalized and nonetheless offers several sites for further transformations.

Previously we have shown that the derived acetal of type **3** (a 2,3-dideoxy-DL-pent-2-enopyranos-4-ulose) can be rearranged to give a wide variety of functionalized cyclopentenones **4** (Scheme 1) via a tandem reaction consisting of three steps: 1. Enolization, 2. Electrocyclic opening to the substituted 2,4-pentadienal, 3. Nazarov cyclization.[2] This rearrangement has also been applied to the synthesis of racemic and optically pure terrein, a naturally occurring cyclopentenone derivative with antibacterial properties.[3]

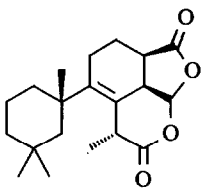


1 2 3 4

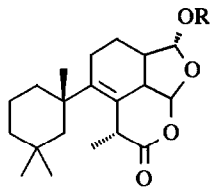
Scheme 1. A Useful Reaction Sequence Starting with Furfurol.

We now describe a further and hitherto unknown reaction of unsaturated hemiacetal **2**, namely the double annulation of the dihydropyranone skeleton with 4-methylpent-4-en-2-yn-1-ols. The reaction affords a

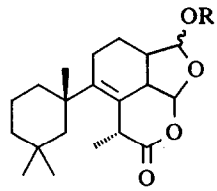
simple access to the tricyclic skeleton of the cadlinolides, marine natural products from the dorid nudibranch *Cadlina luteomarginata*.[4]



cadlinolide A



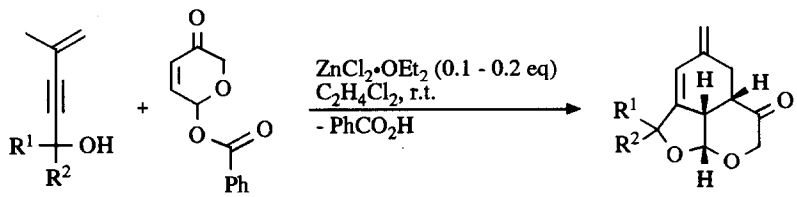
R = Ac:
tetrahydroaplysulphurin-1



R = H (OH group is α and β):
cadlinolide B

Results. The cycloisomerization was carried out in several ways. Benzoate **6A** which is easily available in crystalline form from hemiacetal **2**, was treated with a variety of 4-methylpent-4-en-2-yn-1-ols **5** in the presence of $ZnCl_2$•monoetherate (0.1 - 0.2 eq).[5a] The tricyclic conjugated dienes **7** were obtained. Of the solvents tried 1,2-dichloroethane gave higher yields than dichloromethane (Table 1). The tricyclization proceeded under homogenous conditions.

Table 1. Single Flask Condensation of 6-Benzoyloxy-2,3-dihydro-6*H*-pyran-3-one (**6A**) with 4-Methylpent-4-en-2-yn-1-ols (**5**).



5 **6A** **7**

5	R^1	R^2	**7**	Yield [%]
a	H	H	**a**	42[a]
b	H	Me	**b**[b,c]	16
c	Me	Me	**c**	40
d	Et	Et	**d**	18
e		$-(CH_2)_4-$	**e**	8
f		$-(CH_2)_5-$	**f**	40

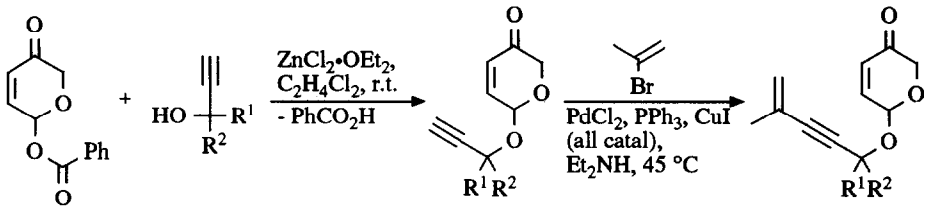
[a]Anhydrous $ZnCl_2$ used as Lewis acid, yield not optimized. [b]Glycoside formed also (25%); cf. **10b** , Table 3. [c]Separable diastereomeric mixture.

An obvious intermediate *en route* to the tricycles is the corresponding 4-penten-2-yn-1-yl glycoside **10**. Indeed, in the course of preparing tricycle **7b**, we isolated glycoside **10b** as a major product (Table 1, footnote b). We decided to prepare various glycosidic intermediates and to subject them to the cyclization conditions.

Glycoside formation is, of course, a key reaction in carbohydrate chemistry. In our case the preparation of various enynyl glycosides proved more difficult than expected.[5b] A practical route to acetals **10** started from the benzoate **6A** and various propargylic alcohols **8** which were first allowed to combine to propargyl acetals **9** in the presence of $ZnCl_2$•monoetherate (high quality $ZnCl_2$•OEt_2 is desirable for this reaction). Sub-

sequently, the 1-methylethenyl group was attached to the acetylenic terminus by palladium catalyzed sp^2-sp cross-coupling (Table 2).

Table 2. Two-Step Synthesis of Glycosides **10** from Benzoate **6A**



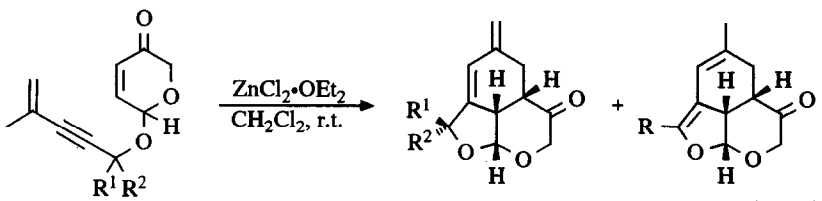
6A **8** **9** **10**

8	R^1	R^2	**9**	Yield [%]	**10**	Yield [%]
a	H	H	**a**	78	**a**	40[a]
b	Me	H	**b**	88[b]	**b**	49[a]
c	Me	Me	**c**	84	**c**	41[a]
e	-$(CH_2)_4$-		**e**	68	**e**	70[c]

[a]Yields after chromatography are moderate, because tricyclization appears to proceed on acidic silica gel. [b]Diastereomers are separable. [c]GC-yield.

In general, the resulting glycosides **10** were unstable and were not stored, but used immediately for the double cyclization (Table 3, footnote *a*). The experimental conditions were similar to those in the single flask procedure (Table 1) and we were pleased to find that the yield of tricycles **7** was, in fact, increased. As a further product, the isomeric dienes **11a,b** were isolated. The geminal-dimethylated precursor **10c** gave the highest yield of tricyclic diene (**7c**, 80%, see also Table 1). Formation of an isomeric diene analogous to **11a** and **11b** is, of course, impossible in this case.

Table 3. Cyclization of Enynyl Glycosides **10**

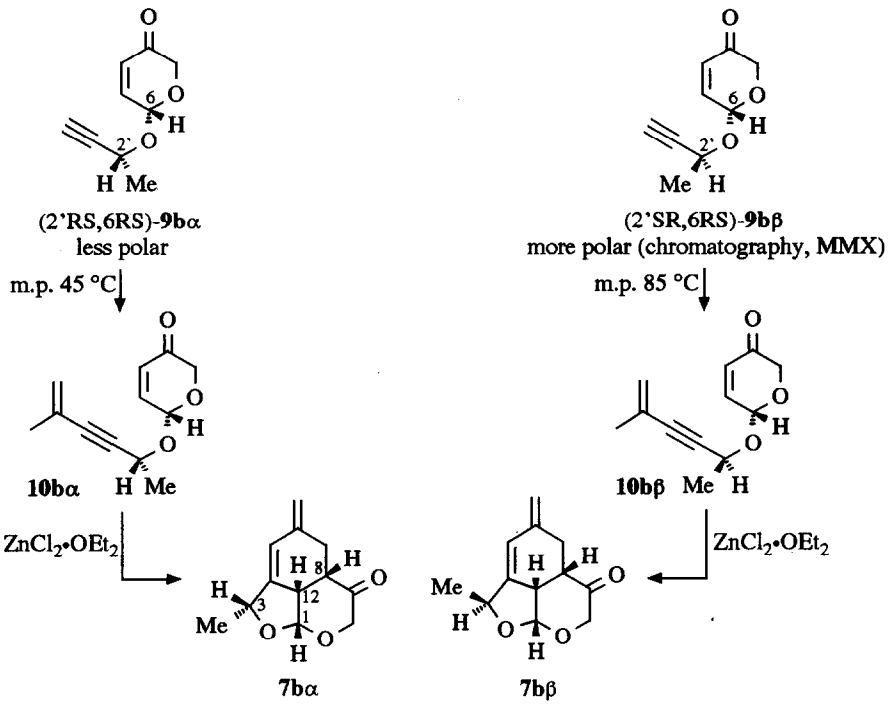


10 **7**[a] **11**,[a] R = R^1 or R^2

10	R^1	R^2	**7**	Yield [%]	**11**	Yield [%]
a	H	H	**a**	62	**a**	4
bα	H	Me	**bα**	32	**b**	39
bβ	Me	H	**bβ**	72	**b**	6
c	Me	Me	**c**	80		---
e	-$(CH_2)_4$-		**e**	15		---

[a]Only one enantiomeric dioxadienone shown

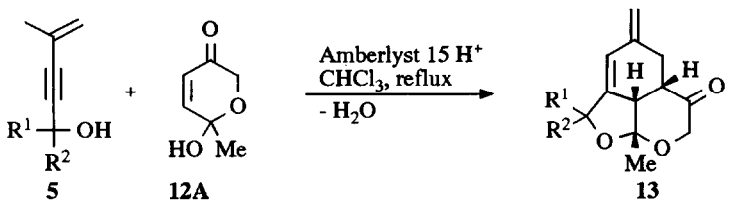
Further light on the formation of isomeric type I (**7**) and type II dienes **11** was cast by studying the diastereomeric pairs **9b**α and **9b**β and, respectively, **10b**α and **10b**β. On chromatography diastereomers **9b**α and **9b**β showed markedly different polarity. The higher melting diastereomer, m.p. 85 °C, was also more polar than the lower melting diastereomer, m.p. 45 °C. An MMX calculation of the theoretical polar surface and the dipole moment suggested the more polar acetal to be the (2'S,6R) and (2'R,6S) enantiomeric pair **9b**β (Scheme 2). The assignment of **9b**α and **9b**β was confirmed by elucidating the structure of the resulting rigid tricycles **7b**α and **7b**β (Scheme 2).



Scheme 2. Tricyclization of Diastereomeric Pair **10b**α and **10b**β: Discrete Starting Materials Afford Discrete Products (as in Tables 1,3 and below, only one enantiomeric dioxadienone with (1R,8S,12S)-configuration is shown).

Detailed NMR studies revealed the bowl-shaped structure of the tricycles. All of the bridgehead hydrogen atoms were on the same face of the molecule (NOE; H,H COSY; H,C COSY). Thus, the configuration at carbon C(1) determines the configuration at C(8) and C(12), irrespective of the configuration at carbon C(3), and the tricyclization is stereoselective. In the case of **7b**α the C-H bond at C(3) is perpendicular to the nodal plane of the neighbouring carbon-carbon double bond. For this reason the isomerization **7b**α → **11b** is stereoelectronically favoured. On the other hand, in diastereomer **7b**β the corresponding C-H σ bond can overlap the π system only after a deformation of the tricycle. Thus formation of **11b** is stereoelectronically more difficult. In a typical experiment **10b**β furnished 72% of type I diene **7b**β and only 6% of isomeric diene **11b** (Table 3). In contrast glycoside **10b**α afforded 32% of type I diene **7b**α and 39% of more highly substituted type II diene **11b**.

Table 4. Amberlyst 15 H^+ Promoted Formation of Dioxatricyclic Dienones **13** Containing an Angular Methyl Group.



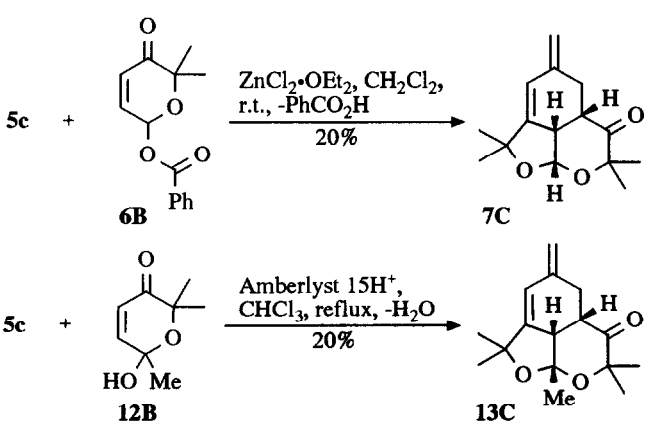
5	R^1	R^2	13	Yield [%]
a	H	H	**a**	35
c	Me	Me	**c**	10
h	Ph	H	**h**[a]	12
i	2-Thienyl	H	**i**[a]	20
j	3-Thienyl	H	**j**[a]	10

[a]Diastereomers (ca. 1 : 1) not assigned

Hemiacetal **12A** (Table 4) contains a sterically hindered hydroxy group. As a result formation of the acetal is more difficult and even the benzoate could not be prepared by the standard method. We were pleased to find, however, that formation of glycoside and subsequent tricyclization took place under forcing conditions, i.e. in the two phase system Amberlyst 15 $H^+/CHCl_3$ at ca. 60°C. Under these conditions the water formed was removed azeotropically.[6] An acetal analogous to glycoside **10** could not be isolated. Instead, bis-annulation was rapid due to the elevated temperature.

Mechanistic Investigations

1. Blockade of Enolization of Carbonyl Group. Enolization of oxacyclohexenone derivatives **10** generates a potentially electron-rich 4π system. On the other hand, the enolization is blocked, the strong Michael

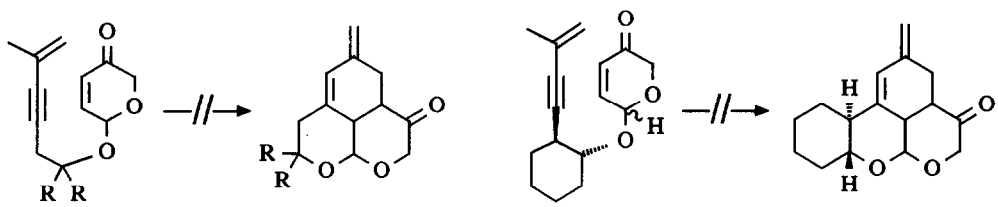


Scheme 3. Blockade of Enolization: Enyne-Ene Cycloisomerization Proceeds Nonetheless.

acceptor character of the enone is retained. Despite the blockade of enolization in precursors **6B** and **12B** tricyclization occurred (Scheme 3). Thus, enolization of the carbonyl system is **not** required for a successful bisannulation. Tricyclic diene **13C** contains even five methyl groups, three of them on the convex face of the molecule. The two inside methyl groups do not clash and the bowl-shaped structure is maintained. As expected, formation of tricycle **13C** requires forcing conditions (see also Table 4).

2. *Variation of Tether.* Substitution at the tether carbon atom shows interesting effects on the yield of the tandem annulation. A marked Thorpe-Ingold effect appears only with the geminal dimethylated **5c** and the spiro-cyclohexyl substituted precursor **5f**. Geminal diethyl groups decrease the yield from 40% to 18 % (Table 1).

Lengthening the tether by an additional carbon atom as in **10f** and **10g** prevents cyclization. In precursor **10h** the rotational entropy of the tether is reduced by the trans-1,2-cyclohexane ring. Nonetheless, cyclization did not take place (Scheme 4; both diastereomers with respect to the chiral acetal carbon were tested).

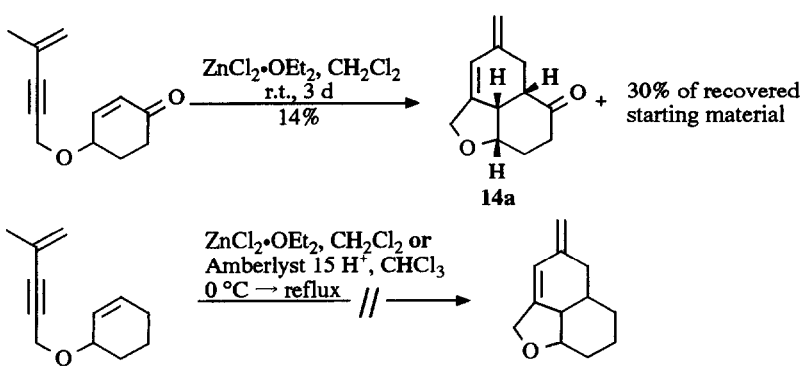


10f R = H
10g R = Me

10h

Scheme 4. Enyne-Ene Tether is Too Long.

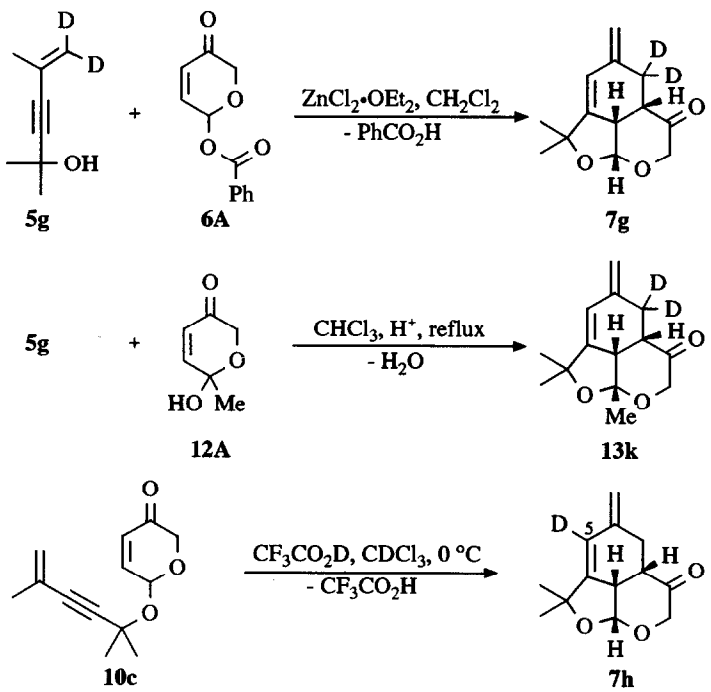
3. *Structural Variation of Heterocycle.* After replacement of the ring ether oxygen atom by a CH_2 group, a $ZnCl_2$•monoetherate promoted tricyclization was still feasible (Scheme 5), although the reaction proceeded more slowly and in lower yield than in the dioxa series (Table 3, cf. **10a** → **7a**). The reaction was stopped after three days in order to obtain pure tricyclic mono-oxadiene **14a**. However, further replacement of the carbonyl oxygen by two hydrogen atoms prohibited the tricyclization. Clearly, the Michael acceptor has now turned into an ordinary carbon-carbon double bond (Scheme 5).



Scheme 5. Tricyclization of a Simple Cyclohexenone Derivative.

Whilst the endocyclic, second oxygen in monocyclic precursors **10** is not decisive, it definitely helps to improve the yield (**7a** 42% vs. **14a** 14%, Scheme 5).[7] Being a σ acceptor the second oxygen activates the dienophile and might also be favourable from a conformational point of view.

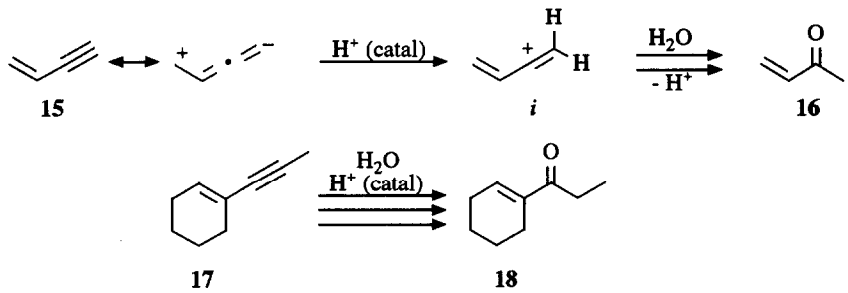
4. Labelling Studies. Since we still had little idea about the mechanism of our tricyclization we used deuterium labelling as a mechanistic probe. The condensations of benzoate **6A** and also of hemiketal **12A** were carried out by the single flask procedure (Scheme 6). Even under the forcing conditions (refluxing $CHCl_3$) which were required for condensation of hemiketal **12A**, the CD_2-group of the pent-4-en-2-yn-1-ol stayed intact. There was no evidence for loss of deuterium or deuterium scrambling in the tricyclic product.



Scheme 6. Tricyclocondensation Does Not Involve Protonation of -C(Me)=CD_2 Terminus.

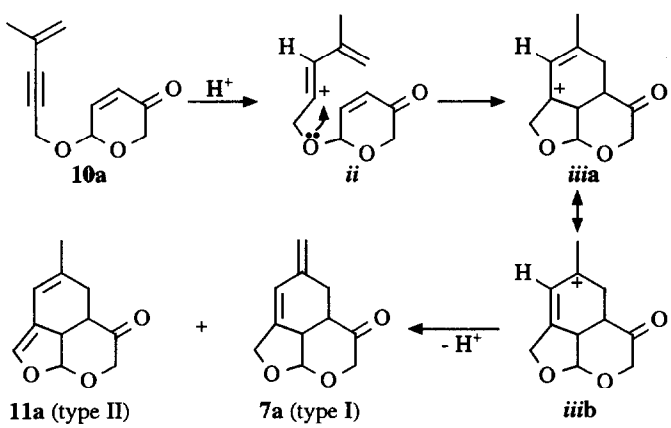
The annulation of preformed acetal **10c** was also triggered with deuterated trifluoroacetic acid CF_3CO_2D at 0°C. In this case, the deuterium label was found cleanly in the vinylic C(5) position. Again, no further scrambling of deuterium within molecule **7h** took place. These experiments rule out a protonation at the olefinic terminus of the enyne and generation of a tertiary propargyl cation intermediate.

Conclusions. Protonation of conventional enynes generally involves attack at the acetylenic terminus and generation of a 1,3-butadien-2-yl cation *i*. For example, acid catalyzed hydration of vinylacetylene (**15**) affords methyl vinyl ketone[8] (**16**) (Scheme 7) and trialkylated enyne **17** furnishes α,β-unsaturated ethyl ketone **18**.[9] Stabilized vinyl cations such as *i* have been generated by various other routes and are generally referred to as "dienyl cations".[10]



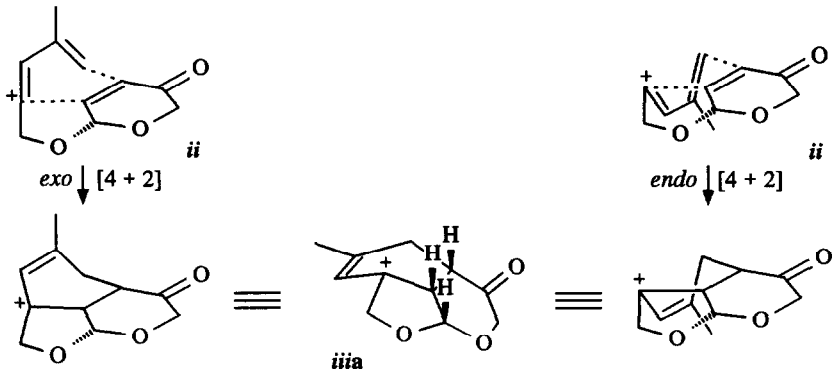
Scheme 7. Regioselectivity of Electrophilic Attack of Typical Enynes.

In contrast, our bis-annulation is proposed to be triggered by an "anti-Markownikow" attack of the enyne and generation of a 1,3-butadien-1-yl cation *ii*. The observed site of deuteration in the cycloisomerization initiated by CF_3CO_2D (Scheme 6, cf. **7h**) agrees with this proposal. The resulting vinyl cation *ii* has a vacant p-orbital which is *orthogonal* to the 1,3-diene π system. The vinyl cation interacts with the nucleophilic auxiliary in the tether, i.e. the ether oxygen atom stabilizes the cation by 1,3-through space interaction. The preceding site-selective protonation of the methylated enyne **10a** is also attributed to the donor in the tether. A 1,3-butadien-1-yl cation *ii* being positively charged, may seem to be a highly improbable 4π partner for a dienophile, which itself is strongly electron-deficient. However, since the diene 4π system and the vacant p-orbital are perpendicular, they are independent of each other. Furthermore, the positive charge is partially transferred to the ether oxygen. In the course of forming the cycloadduct the postulated initial vinyl cation *ii* grows into the stabilized, tetrasubstituted allyl cation (*iiia* ↔ *iiib*) (Scheme 8).



Scheme 8. "Wrongly Oriented" Protonation of Enyne as Key Step of Enyne-Ene Cycloisomerization.

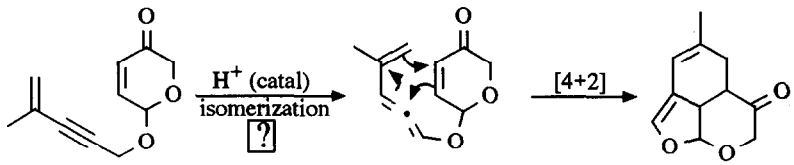
The reaction is terminated by loss of a proton. Type I cycloadduct is formed at least preferentially under kinetic control. Replacement of the olefinic methyl group in glycoside **10c** by hydrogen failed to deliver any tricyclic diene: formation of a semicyclic type I diene is now impossible.



Scheme 9. Exo-Cycloaddition and Endo-Cycloaddition Afford Same Tricyclic, Tetra-substituted Allyl Cation *iii*.

As regards stereochemistry the cycloaddition may proceed in *endo* and *exo* fashion (Scheme 9). However, the primarily generated 1,3-dien-1-yl cation *ii* does not allow a facial distinction at the vinyl cation terminus, and *exo* as well as *endo* cycloaddition afford the **same tricyclic carbonium ion *iii*a**.

Isomerization of enyne **10a** to vinylallene (Scheme 10) and intramolecular Diels-Alder[11] reaction might appear to be a straightforward and plausible alternative to our proposals, especially as a route to type II dienes **11**.



Scheme 10. Intermediate Vinylallenes are not Implicated.

However, several experimental results speak against intermediate vinylallenes. (i) In geminal-dimethylated precursor **10c** formation of an intermediate vinylallene is blocked. Nonetheless, tricyclic diene **7c** is formed in the highest yield (80%). (ii) Isomerization of enynyl glycosides **10b**α and **10b**β would be expected to generate vinylallenes with some loss of stereochemical information at C(3). In fact, the tricyclization is stereoselective: tricycle **7b**α is obtained from precursor **10b**α, and diastereomeric tricycle **7b**β from precursor **10b**β only. A cross-over indicative of an epimerization was not observed (Scheme 2). (iii) The single flask condensation (Table 1) which might again promote equilibration of tricyclic products, gives no evidence for type II cycloadducts. (iv) Tricyclization of the cyclohexenone derivative (Scheme 5) furnishes type I cycloadduct **14a** only. A type II cycloadduct, which would be expected from a vinylallene, is not formed. In our experience type II adducts, if they are formed at all, arise by other routes, namely by deprotonation of allyl cation *iii*a ↔ *iii*b and by equilibration of primarily formed type I dienes **7**. In fact, when diene **7b**α is stirred overnight with $ZnCl_2$•OEt_2, type II diene **11b** is formed quantitatively.

MMX calculations suggest that type II diene **11a** is more stable than type I diene **7a** by ca. 2 kcal/mol and should therefore accumulate on equilibration.[12]

Although the tricyclization may be formulated with a generalized electrophile E^+ as a trigger, in our experiments the initiating species is usually a proton which is supplied, e.g., by Amberlyst 15 H^+. In the terminating step (*iii* → dienes) a proton is regenerated (autocatalysis). Therefore, the tricyclization initiated with deuterated trifluoroacetic acid CF_3CO_2D (equimolar, Scheme 6) affords unlabelled trifluoroacetic acid CF_3CO_2H, and deuterated tricycle **7h** (70%) is accompanied by undeuterated tricycle **7c** (30%, NMR analysis). Furthermore in the single flask condensation (Table 1), stoichiometric amounts of benzoic acid are liberated.

Finally, the mechanistic sequence proposed by us goes beyond the examples described herein. Experimental observations which have been reported over a span of almost 100 years[13] can be interpreted as electrophile-mediated, intramolecular enyne-ene cycloisomerizations, which are triggered by a "wrongly oriented" protonation of the enyne.

Acknowledgements. We thank *Ulrike Eggert* for experimental contributions, *Kirsten Hartmann* for an experimental hint and the *Deutsche Forschungsgemeinschaft* and *Fonds der Chemischen Industrie* for financial support of our work. *Solvay Deutschland GmbH (Hannover)* kindly provided high resolution NMR spectra.

EXPERIMENTAL

General. Melting points: uncorrected, Büchi apparatus. - Infrared spectra: Perkin-Elmer 1710 spectrometer. - ^1H NMR spectra: At 80, 90 and 200 MHz, Bruker WP 80, WH 90 or WP 200 SY spectrometer, solvent $CDCl_3$ unless stated otherwise. - ^{13}C NMR spectra: Bruker WP 200 SY at 50 MHz. APT (attached proton test): spin echo based 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 (-).[14] - MS: Low and high resolution electron impact mass spectra, Finnigan MAT 312 spectrometer, 70 eV, room temperature, unless otherwise stated. Relative intensities in parentheses. - Microanalysis: Department of Organic Chemistry of the University of Hannover. - 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). - THF and diethyl ether (E) were distilled from sodium benzophenone ketyl prior to use, CH_2Cl_2 from P_4O_{10}. PE refers to light petroleum, bp 30 - 60 °C, redistilled prior to use.

Improved Procedure for the Preparation of Substituted 6-Hydroxy-2,3-dihydro-6H-pyran-3-ones. The (substituted) furfuryl alcohol is dissolved in CH_2Cl_2 (5% solution, g/mL) at 0 °C and *m*-chloroperbenzoic acid (1.3 eq, 70 - 75%) is added in portions with stirring. The mixture is allowed to reach r.t., and the reaction (usually ~ 1 h) is monitored by TLC, whilst *m*-chlorobenzoic acid precipitates as a white solid. After the starting material has disappeared, the mixture is cooled to -78 °C (CO_2(s)/MeOH). Water (from *m*-chloroperbenzoic acid) freezes out and is filtered off with suction. Cooling to -78 °C is repeated until no more *m*-chlorobenzoic acid precipitates. The resulting solution is concentrated on a rotavap and the product is purified by crystallization or column chromatography.

6-Hydroxy-2,3-dihydro-6H-pyran-3-one (**2**). 2-Hydroxymethylfuran (4.5 g, 44 mmol) is treated with *m*-chloroperbenzoic acid (9.8 g, 75 mmol). Usual work up and crystallization (E/PE, 1 : 1) affords 4.4 g (88%) of a white solid, m.p. 53 - 54 °C. IR ($CHCl_3$) ν 3590, 3380, 3020, 2940, 1705, 1685, 1425, 1375, 1265, 1160, 1095, 1035, 1010, 925, 850 cm^{-1}; ^1H NMR δ 2.29 (br. s, 1 H, OH), 4.14 (d, ^2J = 17 Hz, 1 H, H-2), 4.58

(d, ^2J = 17 Hz, 1 H, H-2), 5.63 (br. s, 1 H, H-6), 6.17 (d, $J_{4,5}$ = 10 Hz, 1 H, H-4), 6.98 (dd, $J_{4,5}$ = 10 Hz, $J_{5,6}$ = 3.5 Hz, 1 H, H-5); MS *m/z* 114 (M^+, 5), 97 (5), 84 (100), 55 (76).

4-Methylpent-4-en-2-yn-1-ols (**5**). Alcohols **5** were prepared by combination of Li-C≡C-C(CH_3)=CH_2 with the corresponding aldehyde and ketone, respectively.

Deuterated derivative **5g** was obtained as follows: To a solution of tetrahydropyran protected 2-methylbut-4-yn-2-ol (5 g, 29 mmol) in abs. THF (15 mL) is added BuLi (20 mL, 29 mmol, 1.6 M solution in hexane) at -78 °C. A white solid precipitates. After complete addition stirring is continued for 0.5 h. The light greenish, cloudy solution is transferred to a precooled funnel and dropped slowly to a solution of acetic anhydride (3.5 g, 29 mmol) in abs. THF (15 mL). After complete addition the reaction mixture is allowed to reach r.t. and stirred for 20 h at this temperature. The mixture is quenched with aq. NH_4Cl (15 mL). After stirring for 0.5 h conc. aq. NH_3 is added. The organic layer is washed with aq. NH_4Cl and H_2O, dried and evaporated. Distillation (90 °C/1 mm) of the crude product affords 6.2 g (27%) of 5-pyranyloxy(2)-5-methyl-2-oxo-hex-3-yne as a clear liquid (^{1}H NMR δ 1.55 (s, 6 H, 1.6, m, 6 H, 2.35 (t, 3 H), 3.55 (m, 1 H), 3.90 (m, 1 H, 5.00 (m, 1 H), 5.20 (m, 2 H). To a solution of methyl(D_3)triphenylphosphonium bromide (Fluka) (3.07 g, 8.6 mmol) in abs. THF (20 mL) is added BuLi (6.0 mL, 8.6 mmol, 1.6 M solution in hexane) at 0 °C with vigorous stirring. After 0.5 h the reaction mixture is cooled to -78 °C and 5-pyranyloxy-5-methyl-2-oxo-hex-3-yne (1.8 g, 8.6 mmol) in abs. THF (10 mL) is added dropwise. After complete addition the mixture is allowed to reach r.t. and stirring is continued for 20 h. Aq. $NaHCO_3$ is added and the aqueous phase is extracted with E. The combined organic layer is washed with aq. $NaHCO_3$ and H_2O and dried ($MgSO_4$). After removal of the solvent the red-brown solid is purified by chromatography (E/PE, 1 : 1). The resulting clear liquid is dissolved in MeOH (10 mL) and Amberlyst 15 H^+ (50 mg) is added. After complete reaction (TLC control) the mixture is filtrated. Removal of the solvent and purification of the crude product by chromatography (E/PE, 1 : 1) afford **5g** (200 mg, 17%), clear liquid. ^{1}H NMR δ 1.50 (s, 6 H, 1.85 (s, 3 H), 2.05 (s, 1). *NB*: The yield of deuterated enynol **5g** is clearly inferior to the yield of **5a** (>50%) when prepared by the analogous Wittig reaction and deprotection.

6-Benzoyloxy-2,3-dihydro-6H-pyran-3-one (**6A**). A solution of hemiacetal **2** (9.3 g, 8.2 mmol) in CH_2Cl_2 (80 mL) and pyridine (41 mL) is cooled to 0 °C. Freshly distilled benzoyl chloride (11 mL, 65 mmol) in CH_2Cl_2 (40 mL) is added slowly, so that the temperature does not exceed 5 °C. After complete reaction the organic phase is washed several times with water, dried ($MgSO_4$), concentrated and chromatographed (E/PE, 1 : 2) to give colourless crystals of **6A** (13.9 g, 78%), m.p. 82 - 83 °C. IR (KBr) ν 1732, 1705, 1452, 1397, 1279, 1257, 1176, 1118, 1085, 1065, 1026, 920, 714 cm^{-1}; ^{1}H NMR (200 MHz) δ 4.30 (dd, ^2J = 17 Hz, ^4J < 1 Hz, 1 H, H-2), 4.62 (d, ^2J = 17 Hz, 1 H, H-2), 6.32 (d, ^3J = 10 Hz, 1 H, H-4), 6.75 (dd, ^3J = 4 Hz, ^4J < 1 Hz, 1 H, H-6), 7.08 (dd, ^3J = 10 Hz, ^3J = 4 Hz, 1 H, H-5), 7.40 - 7.70 (m, 3 H, arom. H), 8.05 (m, 2 H, arom. H); MS *m/z* 218 (M^+, 5), 188 (3), 145 (3), 123 (5), 105 (100), 97 (72), 77 (35).

6-Benzoyloxy-2,2-dimethyl-2,3-dihydro-6H-pyran-3-one (**6B**). 2-(1'-hydroxy-1'-methylethyl)furan (5 g, 40 mmol) is treated with *m*-chloroperbenzoic acid (10.2 g, 60 mmol). Usual work up and chromatography (MTB-ether/cyclohexane, 1 : 2) affords 6-hydroxy-2,2-dimethyl-2,3-dihydro-6*H*-pyran-3-one (4.3 g, 85%). IR (film) ν 3550 - 3200, 2877, 2840, 2600 - 2500, 1680, 1630, 1470, 1440, 1380, 1290, 1200, 1170, 1130, 1080, 1040, 970, 920, 880, 820 cm^{-1}; ^{1}H NMR (90 MHz) δ 1.40 (2, 3 H, CH_3), 1.50 (s, 3 H, CH_3), 3.60 (br. s, 1 H, OH), 5.80 (br. m, 1 H, H-6), 6.10 (dd, ^3J = 10 Hz, ^4J = 1.5 Hz, 1 H, H-4), 6.90 (dd, ^3J = 10 Hz, ^4J = 2.0 Hz, 1 H, H-5). Benzoate **6B** was obtained by standard benzoylation. Yield 74%, m.p. 110 - 115 °C. IR (KBr) ν

2986, 1729, 1689, 1602, 1456, 1386, 1334, 1273, 1200, 1108, 1088, 1068, 909, 712 cm^{-1}; ^1H NMR (200 MHz) δ 1.45 (s, 3 H, CH_3), 1.58 (s, 3 H, CH_3), 6.24 (dd, ^3J = 10 Hz, ^4J < 1 Hz, 1 H, H-4), 6.83 (dd, ^3J = 3.8 Hz, ^4J < 1 Hz, 1 H, H-6), 6.98 (dd, ^3J = 10 Hz, ^3J = 3.8 Hz, 1 H, H-5), 7.40 - 7.70 (m, 3 H, arom. H), 8.06 (m, 2 H, arom. H); ^{13}C NMR (APT) δ 24.71 (+, CH_3), 27.45 (+, CH_3), 79.97 (+, C-2), 87.41 (-, C-6), 126.95 (-, C-4), 128.58 (-, arom. C), 129.38 (+, arom. C), 129.83 (-, arom. C), 133.60 (-, arom. C), 141.50 (-, C-5), 165.07 (+, CO_2R), 198.23 (+, C-3).

6-Hydroxy-6-methyl-2,3-dihydro-6H-pyran-3-one (**12A**). 2-Hydroxymethyl-5-methylfuran (10 g, 89 mmol) is allowed to react with *m*-chloroperbenzoic acid (23 g, 134 mmol) in CH_2Cl_2 (200 mL). After water has been frozen out, the solvent is removed to leave **12A** (10.8 g, >95%), yellow solid, m.p. 40 °C. IR (KBr) ν 3313, 2991, 2892, 1680, 1631, 1470, 1405, 1384, 1373, 1338, 1274, 1247, 1200, 1164, 1134, 1097, 1083, 1005, 936, 865 cm^{-1}; ^1H NMR δ 1.62 (s, 3 H, CH_3), 4.10 (d, ^2J = 17 Hz, 1 H, H-2), 4.55 (d, ^2J = 17 Hz, 1 H, H-2), 4.20 - 4.60 (br. s, 1 H, OH), 6.05 (d, ^3J = 10 Hz, 1 H, H-4), 6.93 (d, ^3J = 10 Hz, 1 H, H-5); ^{13}C NMR δ 27.45 (CH_3), 66.38 (C-2), 92.70 (C-6), 125.99 (C-4), 150.07 (C-5), 195.91 (C-3); MS *m/z* 128 (M^+, 5), 113 (13), 98 (100), 83 (5), 70 (27), 55 (61).

6-Hydroxy-2,2,6-trimethyl-2,3-dihydro-6H-pyran-3-one (**12B**). Oxidative rearrangement of 2-(1'-hydroxy-1'-methylethyl)-5-methylfuran by standard procedure furnished **12B**, which was not purified, but used directly in the single flask condensation (Table 4).

General Procedure for the Preparation of 6-Propargyloxy-2,3-dihydro-6H-pyran-3-ones (**9**). Benzoate **6** is dissolved in dichloroethane (2 mol/L) in an oven-dried flask and an excess of propargyl alcohol (1.5 - 3 eq) is added. After addition of $ZnCl_2 \cdot OEt_2$[5] (10 mol% w. r. t. **6**) the reaction is followed by TLC. The mixture is worked up by addition of aq. $NaHCO_3$ and back extraction with E or CH_2Cl_2. The combined organic phase is washed with H_2O and dried ($MgSO_4$). The crude product is purified by chromatography on silica gel or distilled. The acetals are worked up without delay in order to avoid decomposition.

6-Propargyloxy-2,3-dihydro-6H-pyran-3-one (**9a**). Benzoate **6A** (2 g, 9.2 mmol) and propargyl alcohol (1.03 g, 18.4 mmol) in 1,2-dichloroethane (4 mL) are allowed to react in the presence of $ZnCl_2 \cdot OEt_2$ (10 mol%; 516 μL of a 2.2 M solution). Work up after 2 h and a Kugelrohr distillation afford **9a** (1.0 g, 78%), clear liquid. IR ($CHCl_3$) ν 3310, 3020, 2950, 2120, 1710, 1685, 1400, 1270, 1160, 1105, 1040, 955, 920 cm^{-1}; ^1H NMR δ 2.77 (t, $J_{7,9}$ = 2.0 Hz, 1 H, H-9), 4.21 (d, ^2J = 17 Hz, 1 H, H-2), 4.48 (d, $J_{7,9}$ = 2.0 Hz, 2 H, H-7), 4.56 (d, ^2J = 17 Hz, 1 H, H-2), 5.64 (d, $J_{5,6}$ = 3.8 Hz, 1 H, H-6), 6.27 (d, $J_{4,5}$ = 10 Hz, 1 H, H-4), 7.05 (dd, $J_{4,5}$ = 10 Hz, $J_{5,6}$ = 3.5 Hz, 1 H, H-5); ^{13}C NMR δ 55.60 (t, C-7), 66.28 (t, C-2), 75.72 (d, C-9), 78.89 (d, C-8), 91.49 (d, C-6), 128.11 (d, C-4), 143.86 (d, C-5), 194.07 (s, C-3); MS *m/z* 152 (M^+, 14), 122 (89), 97 (73), 84 (100), 69 (19), 55 (23), 40 (46). HRMS calcd for $C_8H_8O_3$ 152.0734, found 152.0734.

6-(3-Butyn-2-oxy)-2,3-dihydro-6H-pyran-3-one [(2'RS,6RS)-**9bα**, (2'SR,6RS)-**9bβ**]. Benzoate **6A** (2 g, 9.2 mmol) and d,l-3-butyn-2-ol (1.3 g, 18.4 mmol) in 1,2-dichloroethane (5 mL) are treated with catalytic $ZnCl_2 \cdot OEt_2$ (10 mol%; 516 μL of a 2.2 M solution in CH_2Cl_2). After 3 h the mixture is worked up and chromatographed (E/PE, 1 : 3), giving diastereomers, **9bα** (nonpolar, 660 mg, 43%) and **9bβ** (polar, 690 mg, 45%), colorless solids. Data for **9bα**, m.p. 45 °C. IR (KBr) ν 3261, 2978, 2932, 2880, 2111, 1698, 1683, 1425, 1396, 1359, 1332, 1266, 1166, 1139, 1103, 1046, 1028, 1014, 1003, 910, 856 cm^{-1}; ^1H NMR δ 1.51 (d, ^3J = 6.7 Hz, 3 H, CH_3), 2.53 (d, ^4J = 2 Hz, 1 H, H-9), 4.10 (dd, ^2J = 16.8 Hz, ^4J = 0.7 Hz, 1 H, H-2), 4.42 (d, ^2J = 16.8 Hz, 1 H, H-2), 4.62 (dq, ^3J = 6 Hz, ^4J = 2 Hz, 1 H, H-7), 5.59 (dd, ^3J = 3.4 Hz, ^4J = 0.8 Hz, 1 H, H-6), 6.17 (ddd, ^3J = 10.3 Hz, ^4J = 0.8 Hz, ^4J = 0.7 Hz, 1 H, H-4), 6.92 (dd, ^3J = 10.3 Hz, ^4J = 3.4 Hz, 1 H,

H-5); ^{13}C NMR δ (21.77 (C-11), 62.68 (C-8), 66.31 (C-2), 74.23 (C-10), 84.41 (C-9), 90.37 (C-6), 127.99 (C-4), 144.41 (C-5), 194.43 (C-3); MS (50 °C) *m/z* 166 (M^+, 9), 136 (28), 97 (63), 84 (100), 69 (31), 55 (33), 53 (75). Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 64.44; H, 6.06. Data for **9bβ**, m.p. 85 °C. IR (KBr) ν 3275, 2990, 2937, 2113, 1688, 1435, 1398, 1376, 1323, 1271, 1164, 1107, 1042, 1029, 1002, 908, 857 cm^{-1}; ^{1}H NMR δ 1.52 (d, ^3J = 6.7 Hz, 3 H, CH_3), 2.55 (d, ^4J = 2 Hz, 1 H, H-9), 4.18 (dd, ^2J = 17.1 Hz, ^4J = 0.7 Hz, 1 H, H-2), 4.53 (dq, ^3J = 6.7 Hz, ^4J = 2 Hz, 1 H, H-7), 4.61 (d, ^2J = 17.1 Hz, 1 H, H-2), 5.40 (dd, ^3J = 3.5 Hz, ^4J = 0.8 Hz, 1 H, H-6), 6.17 (ddd, ^3J = 10.3 Hz, ^4J = 0.8 Hz, ^4J = 0.7 Hz, 1 H, H-4), 6.89 (dd, ^3J = 10.3 Hz, ^4J = 3.5 Hz, 1 H, H-5); ^{13}C NMR δ 22.23 (C-11), 64.83 (C-8), 66.49 (C-2), 73.40 (C-10), 83.38 (C-9), 92.19 (C-6), 128.09 (C-4), 143.82 (C-5), 194.62 (C-3); MS (50 °C) *m/z* 166 (M^+, 3), 136 (28), 97 (64), 84 (100), 69 (32), 55 (28). Anal. Calcd for $C_9H_{10}O_3$: C, 65.05; H, 6.07. Found: C, 64.85; H, 6.08.

6-(2-Methyl-3-butyn-2-oxy)-2,3-dihydro-6H-pyran-3-one (**9c**). Benzoate **6A** (3 g, 13.8 mmol) and 2-methyl-3-butyn-2-ol (2.3 g, 27.6 mmol) in 1,2-dichloroethane (6 mL) are treated with $ZnCl_2$•OEt_2 (10 mol%; 774 μL of a 2.2 M solution in CH_2Cl_2). Distillation (Kugelrohr, 120 °C/0.05 Torr) affords **9c** (2.1 g, 84%), clear liquid. IR (film) ν 3295, 2950, 2110, 1710, 1690, 1630, 1430, 1390, 1370, 1260, 1235, 1190, 1150, 1100, 1030, 1020, 880 cm^{-1}; ^{1}H NMR (80 MHz) δ 1.55 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 2.57 (s, 1 H, H-9), 4.06 (d, ^2J = 17 Hz, H-2), 4.54 (d, ^2J = 17 Hz, H-2), 5.81 (d, $J_{5,6}$ = 3.8 Hz, 1 H, H-6), 6.12 (d, $J_{4,5}$ = 10 Hz, 1 H, H-4), 6.85 (dd, $J_{4,5}$ = 10 Hz, $J_{5,6}$ = 4 Hz, 1 H, H-5); MS *m/z* 180 (M^+, 5), 165 (5), 150 (21), 97 (100), 84 (90), 67 (67).

6-(1-Ethynyl-1-cyclopentan-1-oxy)-2,3-dihydro-6H-pyran-3-one (**9e**). Benzoate **6A** (1.3 g, 6 mmol) and 1-ethynyl-cyclopentan-1-ol (2 g, 18 mmol) in 1,2-dichloroethane (4 mL) are treated with $ZnCl_2$•OEt_2 (0.3 mL of a 2.2 M solution in CH_2Cl_2) for 6 h. Chromatography (E/PE, 1 : 2) gives **9e** (840 mg, 68%), colorless solid, m.p. 48 °C. IR (KBr) ν 3252, 2978, 2880, 2108, 1688, 1451, 1427, 1390, 1267, 1200, 1163, 1098, 1028, 1010, 994, 984 cm^{-1}; ^{1}H NMR δ 2.12 (m, 8 H, cycloalkyl H), 2.60 (s, 1 H, acetylene H), 4.08 (d, ^2J = 17 Hz, 1 H, H-2), 4.50 (d, ^2J = 17 Hz, 1 H, H-2), 5.63 (dd, ^3J = 3.5 Hz, ^4J = 1.0 Hz, 1 H, H-6), 6.11 (d, ^3J = 10 Hz, 1 H, H-4), 6.84 (dd, ^3J = 10 Hz, ^4J = 3.5 Hz, 1 H, H-5); MS *m/z* 206 (M^+, 3), 135 (14), 109 (10), 97 (100), 93 (28), 84 (25), 77 (29), 69 (23). HRMS calcd for $C_5H_5O_2$ 97.0290, found 97.0290. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.95; H, 6.95.

General Procedure for Pd-Catalyzed Cross Coupling. $PdCl_2$ (10 mg, 0.06 mmol) and PPh_3 (62 mg, 0.24 mmol) in Et_2NH (4 mL) are stirred for 30 min at r.t. After addition of propargylacetal (3.2 mmol) and CuI (76 mg, 0.4 mmol) the mixture is warmed to 45 °C and 2-bromopropene (545 mg, 4.5 mmol) is added dropwise. After completed reaction (TLC monitoring) the mixture is purified by column filtration and column chromatography.

(6RS,2'RS)-6-(5-Methyl-3-hexyn-5-en-2-oxy)-2,3-dihydro-6H-pyran-3-one (**10bα**). $PdCl_2$ (1.4 mg, 0.008 mmol), PPh_3 (8.3 mg, 0.032 mmol), CuI (9 mg, 0.047 mmol), 2-bromopropene (870 mg, 7.22 mmol) and **9bα** (600 mg, 3.6 mmol) are allowed to react according to the general procedure. Yield: 362 mg (49%). ^{1}H NMR δ 1.51 (d, ^3J = 7 Hz, 3 H, CH_3), 1.90 (dd, ^4J = 1.6 Hz, ^4J = 1.0 Hz, 3 H, CH_3), 4.10 (d, ^2J = 16 Hz, 1 H, H-2), 4.42 (d, ^2J = 16 Hz, 1 H, H-2), 4.73 (q, ^3J = 7 Hz, 1 H, H-2'), 5.27 (dq, ^2J = ^4J = 1.6 Hz, 1 H, H-5'), 5.33 (m, 1 H, H-5'), 5.58 (dd, ^3J = 3.5 Hz, ^4J = 0.8 Hz, 1 H, H-6), 6.16 (d, ^3J = 10 Hz, 1 H, H-4), 6.92 (dd, ^3J = 10 Hz, ^3J = 3.5 Hz, 1 H, H-5); ^{13}C NMR δ 21.96 (CH_3), 23.38 (CH_3), 63.29 (C-2'), 66.36, 86.54, 87.30, 90.36, 122.75, 126.02, 127.94, 144.62, 194.41.

(6RS,2'SR)-6-(5-Methyl-3-hexyn-5-en-2-oxy)-2,3-dihydro-6H-pyran-3-one (**10bβ**). 2-Bromopropene (870 mg, 7.2 mmol) and **9bβ** (560 mg, 3.4 mmol) are allowed to react according to the general procedure. Yield: 300 mg (43%). ^{1}H NMR δ 1.52 (d, ^3J = 7 Hz, 3 H, CH_3), 1.89 (dd, ^4J = 1.0 Hz, ^4J = 1.6 Hz, 3 H, CH_3), 4.11 (dd, ^2J = 17 Hz, ^4J = 1 Hz, 1 H, H-2), 4.62 (d, ^2J = 17 Hz, 1 H, H-2), 4.64 (q, ^3J = 7 Hz, 1 H, H-2'), 5.25 (m, 1 H, H-5'), 5.30 (m, 1 H, H-5'), 5.41 (dd, ^3J = 3.6 Hz, ^4J = 1.6 Hz, 1 H, H-6), 6.16 (d, ^3J = 10 Hz, 1 H, H-4), 6.89 (dd, ^3J = 10 Hz, ^3J = 3.6 Hz, 1 H, H-5); ^{13}C NMR δ 22.36, 23.32, 65.54, 66.46, 86.44, 87.72, 92.20, 122.39, 126.12, 128.02, 144.03, 194.79.

6-(2,5-Dimethyl-3-hexyn-5-en-2-oxy)-2,3-dihydro-6H-pyran-3-one (**10c**). 2-Bromopropene (2 g, 16.2 mmol) and **9c** (2 g, 10.8 mmol) are allowed to react according to the general procedure. Yield: 964 mg (41%). IR ($CHCl_3$) ν 2989, 2937, 2220, 1704, 1688, 1615, 1383, 1366, 1298, 1266, 1234, 1210, 1148, 1101, 1079, 1020, 994, 908, 855 cm^{-1}; ^{1}H NMR δ 1.54 (s, 3 H, CH_3), 1.61 (s, 3 H, CH_3), 1.89 (dd, ^4J = 1.5 Hz, ^4J = 1.0 Hz, 3 H, CH_3), 4.06 (dd, ^2J = 17 Hz, ^4J = 0.6 Hz, 1 H, H-2), 4.53 (d, ^2J = 17 Hz, 1 H, H-2), 5.25 (m, 2 H, H-5'), 5.78 (dd, ^3J = 3.5 Hz, ^4J = 1 Hz, 1 H, H-4), 6.11 (d, ^3J = 10 Hz, 1 H, H-6), 6.86 (dd, ^3J = 10 Hz, ^3J = 3.5 Hz, 1 H, H-5).

General Procedure for the Preparation of Tricyclic Dioxadienes[15] *via Single Flask Condensation-Cycloisomerization (Table 1) with Zinc Chloride•Monoetherate.* To a solution of benzoate and alcohol in dichloroethane is added $ZnCl_2$•OEt_2 (2.2 M solution in CH_2Cl_2) at r.t under N_2 atmosphere. After complete reaction (TLC control) the mixture is diluted with E and quenched with aq. $NaHCO_3$. The organic layer is washed with aq. $NaHCO_3$ (3x) and H_2O. The combined aq. layer is reextracted with E and the combined organic layer is dried ($MgSO_4$) and evaporated. The crude product is purified by chromatography. Cyclization of enynyl glycosides **10** (Table 3) is carried out under the same conditions.

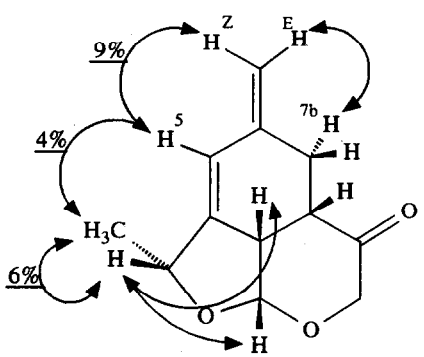
6-Methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one[15] (**7a**). A suspension of enynyl glycoside **10a** (0.19 g, 1 mmol) and $ZnCl_2$ (0.34 g, 2.5 mmol) in CH_2Cl_2 (5 mL) is stirred for 5 d at r.t. Then H_2O is added and the aqueous layer is extracted with CH_2Cl_2. The combined organic layer is dried ($MgSO_4$), evaporated and purified by chromatography (E/PE, 1 : 2) to give **7a** (118 mg (62%), white crystals, m.p. 94 °C. IR ($CHCl_3$) ν 3010, 2980, 1730, 1615, 1560, 1420, 1155, 1130, 1015, 890 cm^{-1}; ^{1}H NMR δ 2.39 (m, ^2J = 15 Hz, 1 H, H-7), 3.15 (m, ^2J = 15 Hz, 1 H, H-7), 2.97 (m, H-8), 3.36 (br. m, 1 H, H-12), 3.91 (d, ^2J = 18 Hz, 1 H, H-10), 4.00 (d, ^2J = 18 Hz, 1 H, H-10), 4.51 (d, ^2J = 13 Hz, 1 H, H-3), 4.63 (d, ^2J = 13 Hz, 1 H, H-3), 5.01 (br. s, 1 H, H-13), 5.12 (br. s, 1 H, H-13), 5.70 (d, $J_{1,12}$ = 7 Hz, 1 H, H-1), 6.12 (br. s, 1 H, H-5); ^{13}C NMR δ 28.32 (t, C-7), 40.39 (d, C-8), 41.16 (d, C-12), 66.43 (t, C-3), 71.06 (t, C-10), 100.72 (d, C-1), 115.15 (t, C-13), 122.94 (d, C-5), 139.12 (s, C-6), 139.95 (s, C-4), 208.31 (s, C-9); MS (40 °C) *m/z* 192 (M^+, 100), 163 (1), 161 (1), 144 (26), 113 (3), 105 (70), 104 (18), 97 (22), 91 (26), 79 (11), 77 (13). HRMS calcd for $C_{11}H_{12}O_3$ 192.0786, founf 192.0785.

(1RS,3RS,8SR,12SR)-3-Methyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**7bα**) *and 3,6-Dimethyl-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodeca-3,5-dien-9-one* (**11b**). Enynyl glycoside **10bα** (206 mg, 1 mmol) in dichloroethane (5 mL) is treated with $ZnCl_2$•OEt_2 (100 µL, 2.2 M solution). Chromatography affords **7bα** (65 mg, 32%) and **11b** (81 mg, 39%). Data for **7bα**, colorless crystals, m.p. 95 °C. IR ($CHCl_3$) ν 3000, 2975, 2927, 2894, 1731, 1615, 1451, 1426, 1385, 1371, 1361, 1339, 1305, 1283, 1240, 1163, 1125, 1099, 1075, 1054, 1041, 1032, 1015, 993, 977, 949, 900, 871, 855 cm^{-1}; ^{1}H NMR δ = 1.40 (d, ^3J = 6 Hz, 3 H, CH_3), 2.36 (dm, ^2J = 16 Hz, 1 H, H-7), 2.94 (m, 1 H, H-8), 3.13 (dd, ^2J = 16 Hz, ^3J = 2.5 Hz, 1 H, H-7), 3.41 (m, 1 H, H-12), 3.86 (d, ^2J = 18 Hz, 1 H, H-10), 3.98 (d, ^2J = 18 Hz, 1 H, H-10), 4.63 (m, 1 H, H-3), 5.03 (br. s, 1

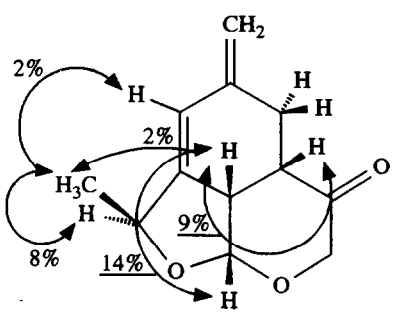
H, H-13), 5.11 (br. s, 1 H, H-13), 5.77 (d, ^3J = 7 Hz, 1 H, H-1), 5.97 (m, 1 H, H-5); ^{13}C NMR δ 17.68 (q, CH_3), 28.50 (t, C-7), 41.10 (d, C-8) 41.40 (d, C-12), 65.68 (t, C-10), 75.76 (d, C-3), 99.21 (d, C-1), 115.45 (t, C-13), 121.76 (d, C-5), 138.18 (s, C-6), 142.77 (s, C-4), 208.93 (s, C-9); MS (60 °C) *m/z* 206 (M^+, 76), 191 (21), 163 (17), 133 (22), 119 (92), 109 (88), 97 (93), 91 (100), 77 (48). HRMS calcd for $C_{12}H_{14}O_3$ 206.0943, found 206.0943. Data for **11b**, colourless crystals, m.p. 72 °C. IR (KBr) ν 2997, 2962, 2912, 2893, 1726, 1694, 1626, 1448, 1422, 1387, 1347, 1297, 1255, 1229, 1208, 1181, 1156, 1122, 1101, 1032, 1013, 995, 944, 932, 856, 786, 695 cm^{-1}; ^{1}H NMR δ 1.78 (s, 3 H, CH_3), 1.86 (d, ^4J = 2.4 Hz, 3 H, CH_3), 2.19 (dm, ^2J = 18 Hz, 1 H, H-7), 2.78 (d, ^2J = 18 Hz, 1 H, H-7), 3.04 (dd, ^3J = 7 Hz, ^3J = 6 Hz, 1 H, H-8), 3.48 (m, 1 H, H-12), 3.91 (d, ^2J = 18 Hz, 1 H, H-10), 4.03 (d, ^2J = 18 Hz, 1 H, H-10), 5.84 (br. s, 1 H, H-5), 5.93 (d, ^3J = 8 Hz, 1 H, H-1); ^{13}C NMR δ 10.92, 23.38, 29.03, 40.67, 42.11, 66.96, 99.94, 105.84, 113.95, 131.33, 146.57, 209.57; MS *m/z* 206 (M^+, 92), 161 (16), 147 (86), 133 (100), 117 (24), 105 (57), 91 (33), 77 (23), 44 (83). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.42; H. 7.07.

(1RS,3SR,8SR,12SR)-3-Methyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**7bβ**). Enynyl glycoside **10bβ** (180 mg, 0.9 mmol) in dichloroethane (5 mL) is treated with $ZnCl_2$•OEt_2 (100 μL, 2.2 M solution) to give after chromatography **7bβ** (130 mg, 72%) and **11b** (10 mg, 6%). Data for **7bβ**, colorless crystals, m.p. 96°C. IR ($CHCl_3$) ν 3000, 2975, 2927, 2894, 1731, 1615, 1451, 1371, 1339, 1305, 1283, 1240, 1163, 1125, 1099, 1075, 1054, 1041, 1032, 1015, 993, 949, 900, 855 cm^{-1}; ^{1}H NMR δ 1.32 (d, ^3J = 7 Hz, 3 H, CH_3), 2.37 (dm, ^3J = 16 Hz, 1 H, H-7), 2.96 (m, 1 H, H-8), 3.14 (ddddd, ^2J = 15.8 Hz, ^3J = 2.7 Hz, ^4J = 0.7 Hz, ^4J = 0.7 Hz, ^4J = 0.7 Hz, 1 H, H-7), 3.44 (m, 1 H, H-12), 3.87 (d, ^2J = 18 Hz, 1 H, H-10), 3.96 (d, ^2J = 18 Hz, 1 H, H-10), 4.88 (bq, ^3J = 7 Hz, 1 H, H-3), 4.98 (bs, 1 H, H-13), 5.08 (bs, 1 H, H-13), 5.82 (d, ^3J = 7 Hz, 1 H, H-1), 6.07 (dddd, ^4J = 3.0 Hz, ^4J = 1.8 Hz, ^4J = 0.7 Hz, ^5J = 0.5 Hz, 1 H, H-5); ^{13}C NMR δ 22.82, 28.90, 40.16, 41.17, 68.70, 100.20, 115.07, 122.33, 128.13, 142.34, 208.52; MS (60 °C) *m/z* 206 (M^+, 59), 191 (9), 163 (70) , 147 (15), 133 (51), 119 (100), 105 (71), 91 (14), 77 (40). HRMS calcd for $C_{12}H_{14}O_3$ 126.0943, found 126.0943.

The relative configuration of **7bα** and **7bβ** was assigned by NOE experiments and by H,H COSY and H,C COSY spectra.



7bα



7bβ

3,3-Dimethyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**7c**). Benzoate **6A** (500 mg, 2.3 mmol) and alcohol **5c** (340 mg, 2.75 mmol) in dichloroethane (10 mL) are treated with $ZnCl_2$•OEt_2 (104

μL, 2.2 M solution) to give after chromatography **7c** (200 mg, 40%), colorless crystals, m.p. 124 °C. IR ($CHCl_3$) ν 3005, 2980, 2900, 1725, 1610, 1460, 1420, 1380, 1365, 1335, 1320, 1305, 1265, 1190, 1145, 1120, 1100, 1050, 1030, 1010, 990, 960, 900 cm^{-1}; ^1H NMR δ 1.32 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 2.35 (dm, ^2J = 16 Hz, 1 H, H-7), 2.96 (m, 1 H, H-8), 3.13 (dd, ^2J = 16 Hz, ^3J = 3 Hz, 1 H, H-7), 3.54 (m, 1 H, H-12), 3.87 (d, ^2J = 18 Hz, 1 H, H-10), 3.98 (d, ^2J = 18 Hz, 1 H, H-10), 5.01 (br. s, 1 H, H-13), 5.10 (br. s, 1 H, H-13), 5.78 (d, ^3J = 7 Hz, 1 H, H-1), 5.97 (d, ^4J = 3 Hz, 1 H, H-5); ^{13}C NMR δ 25.27, 28.46, 28.93, 40.76, 41.07, 65.78, 82.52, 98.54, 115.19, 120.74, 138.28, 145.92, 208.98; MS *m/z* 220 (M^+, 7), 219 (47), 204 (69), 182 (10), 154 (24), 146 (100), 133 (76), 123 (38), 119 (23), 112 (38), 105 (50), 91 (54), 84 (47). HRMS calcd for $C_{13}H_{16}O_3$ 220.1099, found 220.1099. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.77; H, 7.33.

3,3,10,10-Tetramethyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**7C**). Yield 198 mg (20%), yellowish oil. IR ($CHCl_3$) 2976, 2932, 2872, 1720, 1616, 1464, 1380, 1184, 1160, 1120, 1088, 1064, 940, 896, 830 cm^{-1}; ^1H NMR δ 1.25 (s, 3 H, H-13), 1.33 (s, 3 H, H-14), 1.41 (s, 3 H, H-16), 1.48 (s, 3 H, H-17), 2.25 (dm, ^2J = 15 Hz, 1 H, H-7), 3.06 (dd, ^2J = 15 Hz, ^3J = 2 Hz, 1 H, H-7), 3.32 (m, 1 H, H-8), 3.52 (m, 1 H, H-12), 4.98 (m, 1 H, H-15), 5.05 (m, 1 H, H-15), 5.77 (d, ^3J = 5 Hz, 1 H, H-1), 6.07 (d, ^4J = 2 Hz, 1 H, H-5). ^{13}CNMR (APT) δ 24.26 (-, C-14), 24.53 (-, C-14), 27.70 (-, H-13), 28.20 (+, C-7), 28.87 (-, C-13), 38.45 (-, C-12), 45.19 (-, C-8), 79.33 (+, C-3), 82.76 (+, C-10), 96.19 (-, C-1), 113.87 (+, C-15), 121.30 (-, C-5), 138.57 (+, C-4), 146.12 (+, C-6), 209.48 (+, C-9); MS *m/z* 248 (M^+, 27), 233 (7), 190 (44), 162 (50), 147 (38), 134 (30), 133 (100), 119 (34), 91 (45).

3,3-Diethyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**7d**). Benzoate **6A** (500 mg, 2.3 mmol) and alcohol **5d** (700 mg, 4.6 mmol) in dichloroethane (2 mL) are treated with $ZnCl_2$•OEt_2 (130 μL, 0.29 mmol, 2.2 M solution) to give after chromatography **7d** (100 mg, 18%), colorless solid, m.p. 120 °C. ^1H NMR δ 0.81 (t, ^3J = 7 Hz, 3 H, CH_3), 1.00 (t, ^3J = 7 Hz, 3 H, CH_3), 1.41-1.96 (m, 4 H, CH_2CH_3), 2.35 (dm, ^2J = 15 Hz, 1 H, H-7), 2.95 (m, 1 H, H-8), 3.12 (dd, ^2J = 15 Hz, ^3J = 2.4 Hz, 1 H, H-7), 3.48 (m, 1 H, H-12), 3.87 (d, ^2J = 18 Hz, 1 H, H-10), 4.04 (d, ^2J = 18 Hz, 1 H, H-10), 5.01 (br. s, 1 H, H-13), 5.10 (br. s, 1 H, H-13), 5.79 (d, ^3J = 7.5, 1 H, H-1), 5.90 (d, ^4J = 3 Hz, 1 H, H-5); ^{13}C NMR δ 8.06, 8.95, 28.34, 28.39, 30.66, 41.06, 41.56, 66.07, 88.00, 98.51, 115.09, 122.24, 138.40, 143.75, 209.20.

6-Methylene-3-spirocyclopentan-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**7e**). Benzoate **6A** (500 mg, 2.3 mmol) and alcohol **5e** (600 mg, 2.9 mmol) in dichloroethane (10 mL) are treated with $ZnCl_2$•OEt_2 (105 μL, 0.23 mmol, 2.2 M solution) to give after chromatography **7e** (44 mg, 8%), colorless solid, m.p. 115 °C. ^1H NMR δ 1.8 (br. m, 8 H, cyclopentyl), 2.36 (dm, ^2J = 16 Hz, 1 H, H-7), 2.96 (m, 1 H, H-8), 3.13 (dd, ^2J = 16 Hz, ^3J = 2 Hz, 1 H, H-7), 3.48 (m, 1 H, H-12), 3.86 (d, ^2J = 18 Hz, 1 H, H-10), 3.98 (d, ^2J = 18 Hz, 1 H, H-10), 5.02 (br. s, 1 H, H-13), 5.10 (br. s, 1 H, H-13), 5.75 (d, ^3J = 7 Hz, 1 H, H-1), 5.99 (d, ^4J = 3 Hz, 1 H, H-5).

6-Methylene-3-spirocyclohexan-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**7f**). Benzoate **6A** (6.0 g, 27 mmol) and alcohol **5f** (13.1 g, 80 mmol) in dichloroethane (20 mL) are treated with $ZnCl_2$•OEt_2 (1.3 mL, 2.9 mmol, 2.2 M solution) to give after chromatography **7f** (2.6 g, 40%), colorless crystals, m.p. 110 °C. IR ($CHCl_3$) ν 3000, 2940, 2900, 2860, 1730, 1610, 1445, 1420, 1160, 1120, 1080, 1045, 1035, 1020, 990, 960, 935, 910, 890 cm^{-1}; ^1H NMR δ 1.68 (m, 10 H, cyclohexyl), 2.35 (dm, ^2J = 15 Hz, 1 H, H-7), 2.94 (m, 1 H, H-8), 3.13 (dd, ^2J = 15 Hz, ^3J = 3 Hz, 1 H, H-7), 3.51 (m, 1 H, H-12), 3.86 (d, ^2J = 18 Hz, 1 H, H-10), 3.99 (d, ^2J = 18 Hz, 1 H, H-10), 5.0 (br. s, 1 H, H-13), 5.09 (br. s, 1 H, H-13), 5.78 (d, ^3J = 7 Hz, 1 H, H-1), 5.97 (d, ^4J = 3 Hz, 1 H, H-5); MS (50 °C) *m/z* 260 (M^+, 15), 259 (79), 217 (17), 216 (100), 172 (27), 162 (19), 158 (54),

130 (33), 115 (24), 105 (36), 91 (42), 81 (20), 79 (20), 77 (24), 55 (27). HRMS calcd for $C_{16}H_{20}O_3$ 260.1413, found 260.1412.

3,3-Dimethyl-5-deuterio-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**7h**). To a solution of enynyl glycoside **10c** (157 mg, 0.72 mmol) in $CDCl_3$ (5 mL) is added CF_3CO_2D (55 μL, 0.72 mmol) at 0 °C. Immediately after addition of the catalyst the mixture turns emerald green. After 2 h (TLC control) the reaction mixture is quenched with aq. $NaHCO_3$. The aq. layer is extracted with E (3x), dried ($MgSO_4$) and evaporated. The crude product is purified by chromatography (E/PE, 1 : 3) to give **7h** (38 mg, 24%). ^{1}H NMR δ 1.32 (s, 3 H, CH_3), 1.46 (s, 3 H, CH_3), 2.35 (m, ^2J = 16 Hz, 1 H, H-7), 2.96 (m, 1 H, H-8), 3.13 (dd, (m, ^2J = 16 Hz, $J_{7,8}$ = 2.5 Hz, 1 H, H-7), 3.54 (m, 1 H, H-12), 3.87 (d, ^2J = 18 Hz, 1 H, H-10), 3.98 (d, ^2J = 18 Hz, 1 H, H-10), 5.01 (br. s, 1 H, H-13), 5.10 (br. s, 1 H, H-13), 5.78 (d, $J_{1,12}$ = 7 Hz, 1 H, H-1); ^{13}C NMR (APT) δ 25.27 (-, CH_3), 28.45 (+, C-7), 28.93 (-, CH_3), 40.76 (-, C-8), 41.09 (-, C-12), 65.79 (+, C-3), 82.56 (+, C-10), 98.55 (-, C-1), 115.19 (+, C-13), 120.77 (-, C-5), 138.21 (+, C-6), 145.78 (+, C-4), 209.04 (+, C-9); MS *m/z* 221 (M^+, 53), 206 (60), 148 (73), 134 (100), 124 (31), 120 (19), 106 (16), 92 (30).

6-Methyl-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodeca-3,5-dien-9-one (**11a**). Enynyl glycoside **10a** (190 mg, 1 mmol) was treated with $ZnCl_2$•OEt_2 (90 μL, 0.2 mmol, 2.2 M solution) to afford after chromatography **11a** (70 mg, 37%), colorless solid. ^{1}H NMR δ 1.79 (s, 1 H, CH_3), 2.22 (dm, ^2J = 18 Hz, 1 H, H-7), 2.82 (d, ^2J = 18 Hz, 1 H, H-7), 3.10 (ddd, ^3J = 8 Hz,^3J = 8 Hz,^3J = 2.4 Hz, 1 H, H-7), 3.50 (ddd, ^3J = ^3J = 8 Hz, ^4J = 2 Hz, 1 H, H-12), 4.05 (s, 2 H, H-10), 5.89 (br. s, 1 H, H-5), 6.02 (d, ^3J = 8 Hz, 1 H, H-1), 6.38 (d, ^4J = 2 Hz, 1 H, H-3).

1-Methyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**13a**). Enynyl glycoside (30 mg, 0.15 mmol) is treated with $ZnCl_2$•OEt_2 (14 μL, 0.03 mmol, 2.2 M solution) to give after chromatography **13a** (10 mg, 35%). ^{1}H NMR δ 1.68 (s, 3 H, CH_3), 2.36 (dm, ^2J = 16 Hz, 1 H, H-7), 3.06 (m, 1 H, H-8), 3.13 (dd, ^2J = 16 Hz, ^3J = 2 Hz, 1 H, H-7), 3.13 (m, 1 H, H-12), 3.88 (d, ^2J = 18 Hz, 1 H, H-10), 4.03 (d, ^2J = 18 Hz, H-10), 4.55 (br. s, 2 H, H-3), 5.00 (br. s, 1 H, H-13), 5.10 (br. s, 1 H, H-13), 6.07 (br. s, 1 H, H-5).

General Procedure for the Amberlyst Promoted Tricyclocondensation. To a solution of methylpyranone or trimethylpyranone in $CHCl_3$ (0.1 mol/L) is added the alcohol. The mixture is warmed to 60 °C and amberlyst 15 H^+ (20 mg/mmol) was added. The water is removed by a Dean-Stark separator. After complete reaction silica gel is added, the solvent is evaporated and the resulting mixture is purified by chromatography.

1,3,3-Trimethyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**13c**). Pyranone **12B** (312 mg, 2 mmol) and alcohol **5c** (192 mg, 2 mmol) are treated with Amberlyst 15 H^+ to give **13c** (93 mg, 20%), yellow solid. IR ($CHCl_3$) ν 2980, 2932, 2892, 1732, 1380, 1276, 1248, 1188, 1160, 1140, 1108, 1092, 1064, 932, 912, 892 cm^{-1}; ^{1}H NMR δ 1.34 (s, 3 H, H-14), 1.43 (s, 3 H, H-14), 1.69 (s, 3 H, H-13), 2.32 (dm, ^{2}J = 16 Hz, 1 H, H-7), 2.94 (m, 1 H, H-8), 3.1 (dm, ^{2}J = 16 Hz, 1 H, H-7), 3.34 (m, 1 H, H-12), 3.82 (d, ^{2}J = 18 Hz, 1 H, H-10), 3.93 (d, ^{2}J = 18 Hz, 1 H, H-10), 4.98 (m, 1 H, H-16), 5.08 (m, 1 H, H-16), 5.91 (d, ^{4}J = 3 Hz, 1 H, H-5); ^{13}C NMR δ 25.56 (q, C-14), 28.29 (q, C-15), 28.76 (t, C-7), 29.02 (q, C-13), 41.45 and 45.67 (d, C-8 and C-12), 66.36 (t, C-10), 82.00 (s, C-3), 104.86 (s, C-1), 114.88 (t, C-16), 120.25 (d, C-5), 138.42 (s, C-4), 147.80 (s, C-6), 208 (s, C-9); MS *m/z* 234 (35), 220 (8), 219 (49), 191 (10), 161 (34), 133 (100), 111 (18), 91 (21).

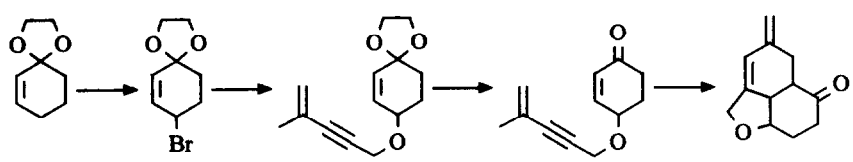
1,3,3,10,10-Pentamethyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**13C**). Pyranone **12B** (743 mg, 4.7 mmol) and alcohol **5c** (580 mg, 4.7 mmol) are treated with amberlyst 15 H^+ to give **13C** (123 mg, 10%), yellow oil. ^{1}H NMR δ 1.29 (s, 3 H, H-17), 1.31 (s, 3 H, H-18), 1.32 (s, 3 H, H-14), 1.46 (s, 3 H, H-15), 1.73 (s, 3 H, H-13), 2.25 (m, 1 H, H-7), 3.05 (m, 1 H, H-7), 3.08 (m, 1 H, H-8), 3.40 (m, 1 H, H-12),

5.00 (m, 1 H, H-16), 5.10 (m, 1 H, H-16), 5.98 (d, ^4J = 3 Hz, 1 H, H-5); ^{13}C NMR (APT) δ 23.46 (-, C-13), 26.04 (-, C-17), 26.23 (-, C-18), 28.49 (-, C-14), 28.68 (+, C-7), 31.46 (-, C-15), 38.67 (-,C-12), 47.57 (-, C-8), 79.84 (+, C-3), 81.50 (+, C-10), 103.53 (+, C-1), 114.25 (+, C-16), 121.64 (-, C-5), 138.60 (+, C-4), 147.82 (+, C-6), 212.22 (+, C-9); MS *m/z* 262 (6), 248 (7), 236 (3), 204 (4), 176 (27), 134 (100), 119 (9), 91 (11).

1-Methyl-3-phenyl-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**13h**). Pyranone **12A** (256 mg, 2 mmol) and alcohol **5h** (376 mg, 2 mmol) are treated with amberlyst 15 H^+ to give **13h** (67 mg, 12%), yellow oil. IR ($CHCl_3$) 3512, 3496, 3304, 3088, 3064, 2996, 2936, 2892, 1732, 1612, 1492, 1448, 1424, 1384, 1356, 1332, 1312, 1236, 1160, 1104, 1084, 1012, 956, 908, 888, 832 cm^{-1}; ^{1}H NMR δ 1.3 (s, 3 H, H-13), 2.35 (m, 1 H, H-7), 3.0 (m, 1 H, H-8), 3.15 (m, 1 H, H-7), 3.95 (d, ^2J = 18 Hz, 1 H, H-10), 4.15 (dd, ^2J = 18 Hz, ^4J < 1 Hz, 1 H, H-10), 5.05 (m, 1 H, H-14), 5.13 (m, 1 H, H-14), 5.75 (s, 1 H, H-3), 6.2 (m, 1 H, H-5), 7.35 (m, 5 H, arom. H).

1-Methyl-3-(3'-thienyl)-6-methylene-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**13j**). Pyranone **12A** (140 mg, 1.1 mmol) and alcohol **5j** (500 mg, 1.1 mmol) are treated with amberlyst 15 H^+ to give **13j** (63 mg, 20%), yellow oil. ^{1}H NMR δ 1.67 (s, 3 H, H-13), 2.4 (m, 1 H, H-7), 3.0 (m, 1 H, H-8), 3.15 (m, 1 H, H-7), 3.22 (m, 1 H, H-12), 3.93 (d, ^2J = 18 Hz, 1 H, H-10), 4.1 (d, ^2J = 18 Hz, 1 H, H-10), 5.04 (s, 1 H, H-14), 5.15 (s, 1 H, H-14), 5.77 (s, 1 H, H-3), 6.2 (d, ^4J = 2 Hz, 1 H, H-5), 7.1 (m, 1 H, H-16), 7.2 (m, 1 H, H-17), 7.35 (m, 1 H, H-18); MS (90 °C) *m/z* 288 (34), 245 (15), 229 (6), 187 (43), 170 (18), 149 (18), 113 (100), 97 (25), 85 (35).

1,3,3-Trimethyl-6-methylene-7,7-dideuterio-2,11-dioxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**13k**). Deuterated enynol **5g** (252 mg, 2 mmol) and pyranone **12A** (256 mg, 2 mmol) are treated with amberlyst 15 H^+ to give **13k** (47 mg, 10%), viscous yellow oil. ^{1}H NMR δ 1.35 (s, 3 H, H-14), 1.45 (s, 3 H, H-15), 1.7 (s, 3 H, H-13), 2.93 (d, ^3J = 6 Hz, 1 H, H-8), 3.33 (m, 1 H, H-12), 3.85 (d, ^2J = 18 Hz, 1 H, H-10), 3.95 3.85 (dd, ^2J = 18 Hz, ^4J < 1 Hz, 1 H, H-10), 5.01 (s, 1 H, H-16), 5.09 (d, ^4J < 1 Hz, 1 H, H-16), 5.92 (d, ^4J = 3 Hz, 1 H); MS (80 °C) *m/z* 236 (43), 222 (10), 193 (13), 178 (9), 163 (37), 135 (100), 111 (21), 93 (15).



19 **20** **21** **22** **14a**

6-Methylene-2-oxatricyclo[6.3.1.0^{4,12}]dodec-4-en-9-one (**14a**). A suspension of *N*-bromosuccinimide (2.14 g, 12 mmol) and 2-cyclohexenone ethyleneketal (**19**) in CCl_4 (20 mL) is refluxed for 1 h. After cooling, the reaction mixture is suctionfiltered and extracted with CCl_4 (2x). The combined organic layers are washed with water and dried ($MgSO_4$). The solution of the sensitive allylic bromide **20** is not isolated, but directly used in the next step. Enynol **5a** (0.96 g, 10 mmol) is added slowly to a solution of aq. KOH [5 eq; KOH (2.8 g, 50 mmol), water (2.8 mL)]. The mixture is stirred for 0.5 h and cooled to 0 °C. After addition of Bu_4NHSO_4 (340 mg, 1 mmol, 0.1 eq) the solution of the allylic bromide in CCl_4 is added slowly during 30 min at 0 °C. After 2 days' stirring at r.t. the reaction mixture is washed with sat. aq. NH_4Cl (2x). The aq. layer is backextracted with CH_2Cl_2 and the combined organic layers are dried ($MgSO_4$). Column chromatography (PE/E, 10 : 1) gives ether acetal **21** (1.23 g, 53% yield overall), pale yellow oil. IR (film) ν 2953, 1614, 1439,

1399, 1290, 1117, 1088, 1025, 938 cm^{-1}; ^1H NMR δ 1.88 (dd, J < 1 Hz, 3 H, H-12), 1.70 - 2.20 (m, 4 H, H-5, H-6), 3.97 (m, 4 H, H-13, H-14), 4.11 (m, 1 H, H-4), 4.35 (d, ^2J = 10 Hz, 2 H, H-7), 5.27 (m, 2 H, H-13), 5.68 (m, 1 H, H-3), 6.01 (m, 1 H, H-2); ^{13}C NMR δ 23.33 (-, C-12), 26.97 (+, C-5), 30.87 (+, C-6), 56.24 (+, C-4), 64.65 (+, C-13, C-14), 71.80 (-, C-4), 84.31 (+, C-8), 86.51 (+, C-9), 105.17 (+, C-1), 122.32 (+, C-11), 126.26 (+, C-10), 129.87 (-, C-3), 132.37 (-, C-2); MS *m/z* 219 (M^+-CH_3, 1), 139 (2), 96 (81), 95 (80), 81 (100), 77 (51), 67 (99), 65 (56).

Acetal **21** is added to a stirred suspension of silica gel (3 g), aq. oxalic acid (0.3 g, 10% w/v) and CH_2Cl_2 (10 mL) at r.t. Stirring is continued for 2 h and the solid phase is separated by suction-filtration. The solid is washed several times with CH_2Cl_2. The solvent is removed on a rotavap leaving an oil, which is purified by column chromatography (PE/E, 10 : 1); **22** (465 mg, 54%), colorless oil. IR ($CHCl_3$) ν 2954, 2924, 2224, 1685, 1614, 1377, 1094, 1012, 905, 867 cm^{-1}; ^1H NMR δ 1.90 (m, 3 H, H-12), 1.90 - 2.70 (m, 4 H, H-4, H-5), 4.41 (d, J = 2 Hz, 2 H, H-7), 4.45 (m, 1 H, H-4), 5.30 (m, 2 H, H-11), 6.01 (m, 1 H, H-2), 7.00 (m, 1 H, H-3); ^{13}C NMR δ 23.19 (-, C-12), 28.83 (+, C-5), 35.11 (+, C-6), 56.83 (+, C-7), 71.90 (-, C-4), 83.46 (+, C-8), 87.92 (+, C-9), 122.65 (+, C-11), 125.54 (+, C-10), 129.77 (-, C-2), 150.02 (-, C-3), 198.51 (+, C-1); MS *m/z* 190 (M^+, 2), 161 (7), 134 (13), 133 (16), 105 (13), 95 (30), 91 (17), 79 (88), 77 (100), 67 (40).

Keto ether **22** (390 mg, 2.05 mmol) in CH_2Cl_2 (10 mL) is treated with $ZnCl_2$•OEt_2 (0.36 mL, 4 mol%, 2.2 M solution in CH_2Cl_2). The resulting suspension is being stirred at for 3 d at r.t., then the reaction is stopped in order to obtain pure cyclization product. The organic layer is washed with sat. aq. $NaHCO_3$ (2x) and H_2O, dried ($MgSO_4$) and evaporated. Column chromatography (PE/E, 1 : 1) gives **14a** (55 mg, 14%), colorless solid. Starting material **22** (96 mg, 30%) is recovered. IR (KBr) ν 2932, 2904, 1700, 1613, 1354, 1046, 1023, 1002, 990, 894 cm^{-1}; ^1H NMR δ 1.93 (m, 2 H, H-10), 2.27 (m, 3 H, H-11, H-3), 2.77 (m, 1 H, H-2), 3.09 (dd, $J_{2,3}$ = 2.5 Hz, ^2J = 15 Hz, 1 H, H-3), 3.33 (m, 1 H, H-12), 4.37 (br. s, 2 H, H-7), 4.65 (dt, $J_{9,12}$ = 9 Hz, $J_{9,10}$ = 4.5 Hz, 1 H, H-9), 4.99 (d, ^2J = 23 Hz, 2 H, H-13), 6.07 (br. s, 1 H, H-5); ^{13}C NMR δ 27.06 (+, C-10), 29.15 (+, C-3), 34.66 (+, C-11), 41.86 (-, C-2), 43.00 (-, C-12), 69.39 (+, C-7), 75.43 (-, C-9), 113.57 (+, C-13), 121.80 (-, C-5), 138.91 (+, C-4), 141.05 (+, C-6), 210.30 (+, C-1); MS *m/z* 190 (M^+, 100), 161 (15), 146 (19), 143 (27), 129 (23), 117 (18), 105 (53), 91 (57).

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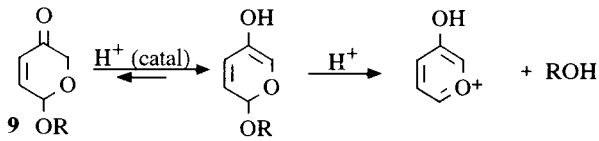
5. (a) Mayr, H.; Striefe, W. *J. Org. Chem.* **1985**, *50*, 2995. A 2.2 M solution in CH_2Cl_2 is commercially available (E. Merck, Darmstadt); (b) Presumably, glycosides **9** suffers acid catalyzed enolization and then decompose to the aromatic 3-hydroxypyrylium ion. (In solvent DMF, a hydrogen bonding solvent, formation of the pyrylium ion is suppressed and electrocyclic opening is feasible with eventual formation of functionalized cyclopentenone, **3** → **4**).[2] Furthermore oxacycle **9** (e.g., R = Me) is a strong Michael acceptor, due to the two ether oxygen atoms acting as σ acceptors. With alcohols such as methanol the oxacycle suffers ready conjugate addition to the enone double bond, even at room temperature.



6. The $CHCl_3$-H_2O azeotrope boils at 56.3°C and contains 3% of water.
7. Starting material (30%) recovered.
8. Beilsteins Handbuch der Organischen Chemie, E IV 1, 1085, Springer, Berlin, 1973; see also E III 1, 1035.
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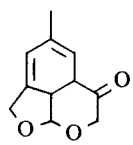
12. Type III diene (which was not observed) is the least stable of these diene isomers (7 kcal/mol less than type II diene **11a** by MMX).

type III diene 

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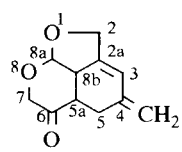
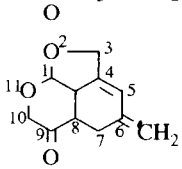
14. APT is a time saving alternative to DEPT sequence, when used with care. See Günther, H. *NMR-Spektroskopie*; Georg Thieme Verlag: Stuttgart **1992**, p. 423. Atta-ur-Rahman. *One and Two Dimensional NMR Spectroscopy*; Elsevier: Amsterdam **1989**, p. 82.
15. Other names for the basic tricyclic skeleton of **7a-h**:



1) IUPAC: 4-methylene-4,5,5a,7,8a,8b-hexahydro-furo[4,3,2-ij]isochromen-6(2*H*)-one

2) CAS: 4,5,5a,7,8a,8b-hexahydro-4-methylene-furo[4,3,2-ij][2]benzopyran-6(2*H*)-one



3) 6-methylene-2,11-dioxatricyclo[6.3.1.$0^{4,12}$]-dodec-4-en-9-one