Intramolecular Ni-Mediated Cyclizations with α,ω-Dienals

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Fifteen α,ω-dienals and one α-en-ω-ynal were prepared. These substrates were treated with $Ni(COD)_2$/TMSCl under carbonylative and noncarbonylative conditions, with subsequent methanol quenching of the resulting metal intermediates to afford different types of cycloadducts. From the compounds thus obtained, it is concluded that the reaction proceeds through an intermediate (π-allyl)Ni complex, which readily cyclises in a "metallo-ene"-type reaction. The different pathways were characterised by further carbonyl insertion or by protonolysis, resulting either in cyclopentanone formation (insertion followed by β-elimination) when under carbon monoxide gas, or in single cyclization when not (or, even better, when in the presence of protic acids). Coordination of the distal olefin has been found essential for either of the two processes to proceed. Thus, coordinating heteroatoms (N,S), excessive tether length and particular substituents hampering satisfactory double bond chelation all disrupt the process, with the ketals of the original aldehyde (occasionally as Michael adducts) largely being recovered in such cases.

Introduction

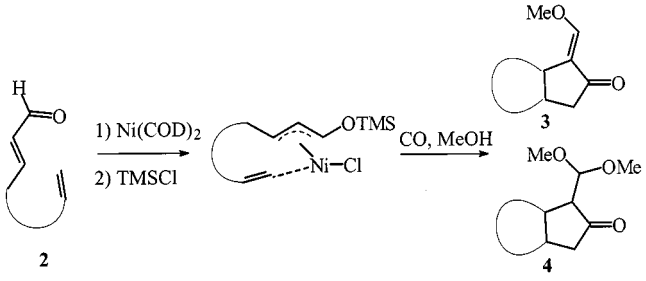
The use of transition metal complexes in organic synthesis has provided not only shortened path sequences to interesting target molecules, by altering the conventional reactivity of the organic substrates, but also, often, the achievement of higher selectivity in the preparation of the intermediates involved in the development of the synthesis.

It should also be stressed that transition metals are able to perform more than one synthetic step in a multicomponent single operation (tandem, cascade or domino processes), usually operate under very mild conditions and display catalytic character (atom economy) in many cases.[1]

Recently, one of the most actively studied processes in this category is the Pauson−Khand reaction, which has been applied to the synthesis of a variety of bioactive compounds.[2]

During the last decade we have been studying the scope and applications of Ni-mediated carbonylative cycloaddition of allyl derivatives and alkynes.[3] Among our more recent contributions in the field are the use of a ready-made and low-risk Ni mediator, and also the replacement of allyl halides by α,β unsaturated aldehydes, a system in which acetylenes have also been found to be susceptible to replacement by olefins in the intramolecular version of the process.[4] In this version, the allyl derivative (prepared in situ by addition of a Lewis acid, namely TMSCl, to the aldehyde) underwent an oxidative addition with $Ni(COD)_2$ to afford the corresponding π-allyl complex (Mackenzie complexes).

Under CO gas, these complexes react with either strained or tethered olefins to give an enol ether **3** or a ketal **4** (or a mixture of both, depending on reaction conditions). After hydrolysis, a single oxocyclopentenylcarboxaldehyde is obtained from these. We report here on the results of our studies concerning the carbonylative cycloaddition of olefin-tethered acrylaldehydes (Scheme 1).



Scheme 1. Ni-mediated carbonylative cycloaddition of α,ω-dienals

Preparation of the Substrates and General Procedure for the Cycloaddition

Sixteen different acrylaldehydes with a distal double bond (one of them, exceptionally, with a triple bond) were prepared through the corresponding intermediate allyl alcohol **1**, according to two general methods. The first involved treatment of an *O*-monoprotected (*Z*)-but-2-ene-1,4-diol derivative (for **1f** and **1g**) or the unprotected compound (for **1a−e, h**, **i**, **l**, **m**) with a base (NaH) in THF, followed by the addition of the corresponding allyl halide (and, when applicable, deprotection), affording the corresponding alcohols **1**. The second was based on treatment of the alkoxide (for **1j** and **1k**), carbanion (**1n**), thiol or amine (**1o** and **1p**, respectively) with an *O*-protected (*Z*)-4-halobut-2-en-1-ol derivative, followed by deprotection, also giving the alcohols **1** corresponding to this group of substrates**.** The resulting alcohols were then oxidised to the corresponding

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aldehydes **2** by using pyridinium chlorochromate, with yields ranging from 40 to 90%. In the design of these, we mainly paid attention to three aspects: the type of tether, the length of the tether, and the substitution of the distal double bond. These are listed in Figure 1.

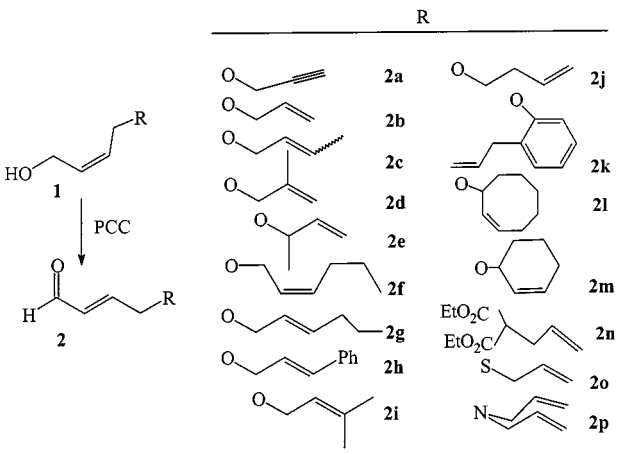


Figure 1. Preparation of the substrates

The obtained dienal was added to an equimolar amount of $Ni(COD)_2$ in toluene at low temperature. A red precipitate (or solution) was thus formed. In this work, we changed the original stoichiometry (2 mols of acryl derivative per mol of Ni),[4b] since we supposed that the distal olefin could replace in its ligand role the extra mol of acrylaldehyde required in the original methodology. After addition of TMSCl, the red precipitate dissolved and CO was let in. Finally, methanol was added to quench the organometallic intermediate and the contents of the flask were concentrated to dryness. The residue was then worked up as indicated for each of the cases. The results obtained are given in Table 1.

Results and Discussion

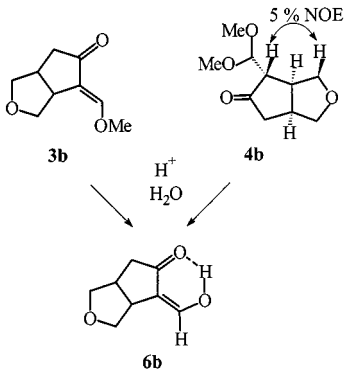
The first substrate to be treated with $Ni(COD)_2$ was enyne **2a**. We had already successfully performed the intramolecular cycloaddition with the corresponding halides[5] and did not expect to meet any problem in this. However, we could not isolate any defined product from the analogous acryl derivatives. In this methodology, the triple bond was allowed to interact with Ni^0 [6] first, since the formation of the π-allyl complex would be delayed until the introduction of TMSCl, and reaction would take place without the protective presence of CO. We attributed our failure to alkyne polymerization and reasoned that, since olefins were less reactive towards Ni^0 complexes, they would remain unaltered until the π-allyl complex was formed. Accordingly, we started out from a 1:1 mixture of **2b** and $Ni(COD)_2$ in toluene, at which point a deep red, insoluble complex was formed, turning orange after the addition of TMSCl and the introduction of CO by means of bubbling under atmospheric pressure. Further addition of the quencher (methanol) and workup of the crude product afforded a 41% yield of the cyclopentanone **3b.** No ketal was produced under these conditions. A single isomer of the enol ether **3b** was obtained, the stereochemistry of which, as depicted, had arisen from two stereodefined processes: *syn*-carbometallation and *syn*-periplanar β-H elimination.[7] In the pres-

Table 1. Reaction of substrates **2a**−**2p** with $Ni(COD)_2$, TMSCl and methanol

Entry	Dienal	Solvent	Reaction products with CO bubbling	Reaction products without CO
1	**2a**	toluene	–[a]	–
2	**2b**	toluene	**3b** (56%), **4b** (4%)	–
3	**2b**	acetonitrile	**3b** (55%), **4b** (18%)	–
4	**2b**	methanol + TFA	**7b** (15%), **8b** (25%)	–
5	**2b**	toluene	–	**9b** (20%), **10b** (40%)
6	**2c**[b]	toluene	**3c** (52%)[b]	–
7	**2d**	toluene	–	–
8	**2e**	toluene	**3e** (60%)[c]	–
9	**2f**	toluene	**3f** (69%)[d]	–
10	**2g**	toluene	**5g** (40%), **12g** (15%)	–
11	**2h**	toluene	–	–
12	**2i**	toluene	–	**2i** (60%)
13	**2j**	toluene	**12j** (37%)	–
14	**2k**	toluene	–	–
15	**2l**	toluene	**3l** (85%)	–
16	**2m**	toluene	**5m** (42%)	–
17	**2n**	acetonitrile	**3n** (65%), **5n** (8%)	**11n** (52%)
18	**2o**	toluene	decomposition	–
19	**2p**	toluene	**5p** (10%)	–

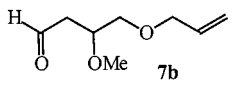
[a] Although only polymers could be obtained from the substrate **2a**, the corresponding allyl halide (2*E*)-4-bromobut-2-enyl prop-2-ynyl ether was prepared and the analogous carbonylated ene product, methyl (2*E*)-4-vinyldihydrofuran-3(2*H*)-ylideneacetate, was obtained from this in 84% yield. – [b] Isomeric *cis*/*trans* mixture (1:4) and diastereomeric ratio 75:25 for **3c**. – [c] Diastereomeric ratio 95:5. – [d] Diastereomeric ratio 75:25.

ence of 2 mol of TMSCl, however, the reaction gave a 56% yield of cycloadduct **3b** and 4% of the ketal **4b** (Table 1, Entry 2). Both products converged after hydrolysis to the common α-oxocarbaldehyde **6b**.

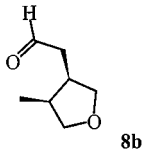


The ketal **4b** was obtained as a diastereomeric mixture (93:7). The formation of the major stereoisomer with the dimethoxymethyl group in *exo* orientation, as deduced from NOE experiments, most probably arises from the different arrangement of the substituent bearing the TMSO moiety in the two possible coordination faces of the double bond in the (acyl)Ni intermediate. Obviously, the one disposing this substituent in a pseudoequatorial arrangement will be favoured over that positioning it with the pseudoaxial geometry (Scheme 2). The reaction proved to proceed even better (although with lower selectivity) in acetonitrile (replacing the original toluene), and a 55% yield of enol ether **3b** and an 18% yield of the ketal **4b** were obtained in this solvent (Entry 3).

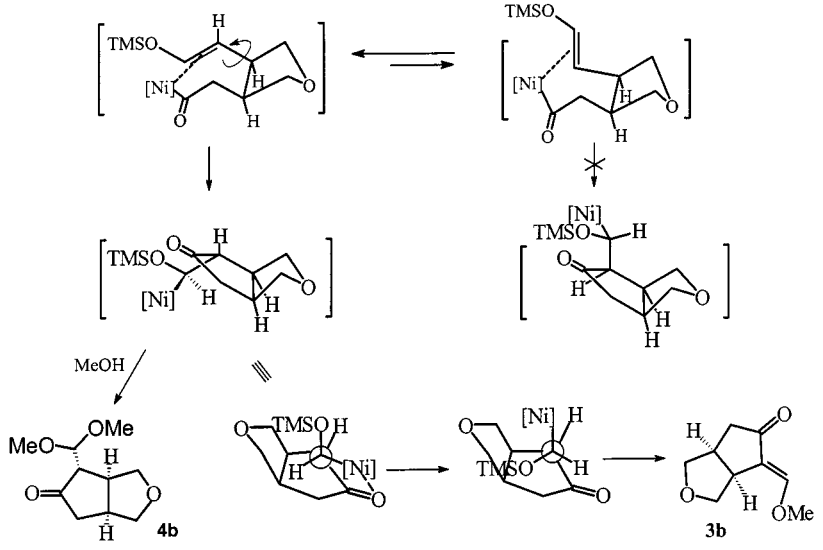
With the aim of making the reaction catalytic in nickel, we then replaced the Lewis acid TMSCl with protic trifluoroacetic acid. No catalytic character resulted, but from the reaction in toluene we were able, after quenching the intermediates with methanol, to isolate the product formally corresponding to the Michael adduct **7b**,[8] with no traces of cycloadducts.



However, when methanol in the presence of TFA was used as the solvent we observed a rapid change as soon as CO was allowed to enter the reaction flask: The original deep red colour, typical of the generated allyl complexes, rapidly turned apple green. After workup of the mixture and purification of the products, we isolated, together with the former product **7b**, a 25% yield of a product **8b** arising from a formal "metallo-ene" reaction.

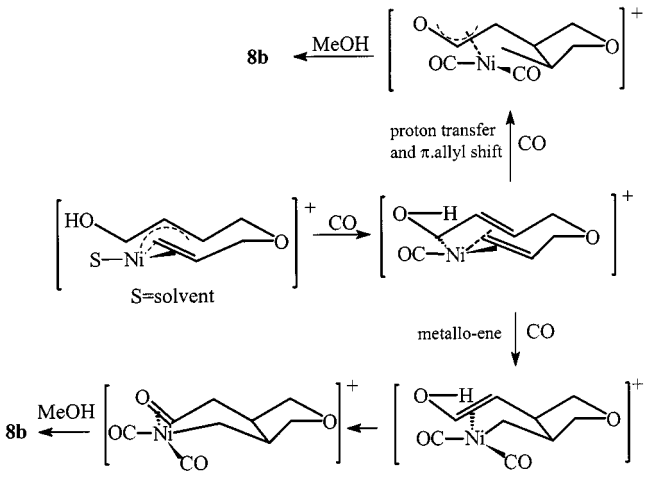


Interestingly, it consisted of only one diastereomer (the *cis* isomer as deduced from the chemical shift of the annular methyne protons).[9a] We interpret this result as a function of a low degree of stabilisation of a putative (π-allyl)Ni cation, brought about by the enol proton. Thus, rapid coordination of carbon monoxide would alter the π-allyl system



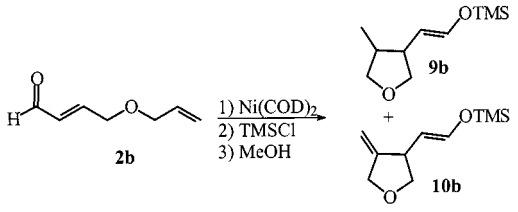
Scheme 2. Origin of the stereoselectivity found in products **3b** and **4b**

to a σ-allyl state, promoting either a "metallo-ene" reaction[9b] or alternatively a shift to a weakly coordinated π-oxaallyl complex (through insertion and proton capture), which would eventually be cleaved by methanol (Scheme 3).



Scheme 3. Two plausible paths for the formation of tetrahydrofuran **8b**

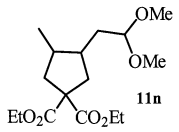
The formation of **8b** represents a diversion of the process leading to cyclopentanones in the presence of a protic acid. It took place even in the presence of CO when TFA was present. The question now arose of whether or not the first C−C insertion, producing the furan ring, actually required CO. After treatment of **2b** with $Ni(COD)_2$, TMSCl and methanol in toluene, we were able to isolate a 60% yield of a 1:2 mixture of **9b** and **10b** (Entry 5).



(global yield 60 %)

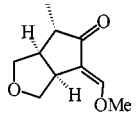
Since the product of β-elimination (**10b**) was the most abundant, we concluded that the role of TFA in the protonation of the aldehyde was very efficient and completely avoided a β-elimination. These last experiments told us that *while the first insertion would not require the presence of CO, its presence and the stabilising role of the TMS group would be essential for the carbonylation and second cyclization to occur.*

We then introduced changes in the tether, and the substrates **2n**, **2o** and **2p** were tested in the carbonylative cycloaddition. Treatment of **2n** and 2 mol of TMSCl in acetonitrile gave similar results to those for **2b**, and a 65% yield of **3n** was isolated (Entry 17). Together with **3n**, an 8% yield of the dimethyl ketal of the original dienal **5n** was produced and also a minor quantity of **4n** (1:12 related to **3n**) that did not permit isolation and characterisation. The same substrate **2n**, in the absence of CO and in the presence of TFA gave a 52% yield of the "ene-type" product **11n**, the dimethylketal of **8n** (Entry 17).



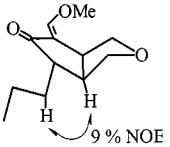
Not only did thioether **2o** not afford any defined product, but it promoted decomposition of the original $Ni(COD)_2$ complex, since the typical red colour of the allyl derivative was not formed and, instead, a black deposition was observed. From the diallylamine **2p**, only a minor amount of the original substrate (10%) could be recovered, as the corresponding ketal, from the reaction mixture and no cycloadduct was detected. Therefore, both nitrogen and sulfur, being strongly coordinating heteroatoms, were found to interact in a detrimental way in the cycloaddition pathway.

In our next move, we investigated the effects of substitution in the distal allylic region. With this aim, we prepared the starting compound **2c**, with a *cis*/*trans* ratio of 75:25 (as in the original crotyl chloride). Treatment of this with $Ni(COD)_2$, TMSCl and CO in toluene gave a 52% yield of two isomeric cyclopentanones **3c** in a molar ratio of 3:1, similar to that in the starting dienal (Entry 6).



3c (major isomer)

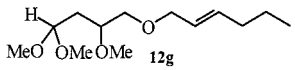
We ruled out the possibility of the presence of a pair of *cis* and *trans* isomers at the enol ether double bond because of the very different ^1H and ^{13}C NMR chemical shifts for the atoms in the neighbourhood of the saturated α-oxo site compared with the similarity of those near the enol ether. We thought that the transformation might have been stereospecific and therefore decided to start from pure isomers. We prepared the *cis*-dienal **2f**, which under the former reaction conditions gave a 69% yield of the oxadiquinane **3f** (Entry 9). This compound, however, consisted of two different diastereomers in a ratio of 75:25. Surprisingly, the relative stereochemistry of the *n*-propyl moiety and the oxa ring in the major isomer is *trans* (as deduced from NOE experiments), exactly the opposite of that expected from the original substrate.



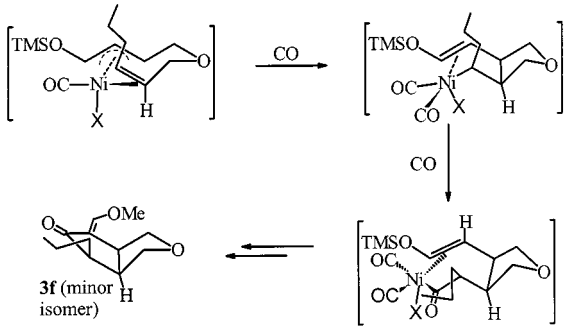
3f (major isomer)

Since the *trans* geometry appeared the most favoured for both the starting dienal and the cyclopentanone, we set out

to discriminate between two different isomerization paths: (*a*) prior to the closure of the cyclopentanone ring (either before coordination or during the process), or (*b*) with the oxadiquinane retaining its original geometry but the epimerizable α-oxo site suffering thermodynamic equilibration after the process. Thus, we prepared the other (*trans*) isomer **2g**, which was tested in the reaction under the same conditions as for **2f**. We were surprised to see that no adduct was detected, but that the ketal derived from the substrate (**5g**) was produced (Entry 10). We tried under more forcing conditions (acetonitrile and 2 mol of TMSCl), but again the cycloaddition failed and we were able only to isolate, together with **5g**, a 15% yield of **12g**.

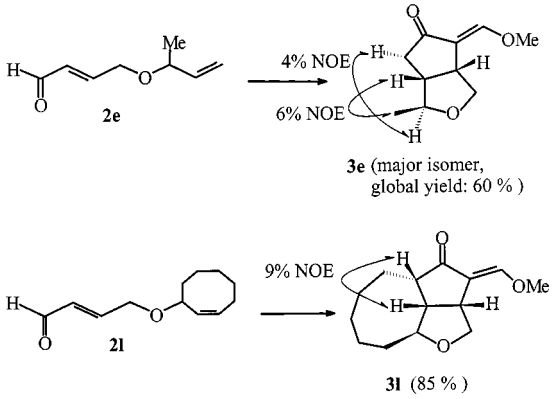


It had become clear that the isomerization occurred when the cyclopentanone ring had already been formed, and that the geometry of the substituents at the double bond was of the utmost importance before ring closure. Therefore, if a substrate does not undergo any cycloaddition (usually reverting to the ketal of the original aldehyde), it is *because the coordination of the distal olefin is somehow hampered*. Searching for the factor that might explain these observations, we came to the conclusion that, in addition to the known fact that (*Z*)-olefins coordinate to transition metal ions more easily than their (*E*) counterparts in this process, those substituents liable to sterically interact with the substituents and ligands placed in the coordination hemisphere opposed to the central (apical) π-allyl carbon atom were completely preventing the chelation of the double bond, and also its activation and final insertion. This conclusion would fit with the known tilting "out-above, in-below" of the π-allyl plane[10] and would very much point to a slanted coordination of the olefin to the nickel centre in a square-pyramidal environment (Scheme 4).



Scheme 4. Putative intermediates involved in the formation of **3f**

Consistently with this, reactions with **2d, 2h** and **2i** also produced uncyclized products (starting products and/or the corresponding ketals). Again, these substrates were liable to bring with them the same kind of steric interactions and we were not surprised by the lack of cyclization. Moreover, corresponding treatment of **2e** and **2l** (Entries 8 and 15, respectively), both with substitution patterns close to that of **2f** and therefore prone to undergo carbonylative cycloaddition, did indeed give good and excellent yields of the expected cycloadducts in highly stereoselective manner (60% and 85% respectively, diastereomeric ratio for **3e** 95:5 and one single diastereomer for **3l**) (Scheme 5).



Scheme 5. Allowed cycloadditions in unhindered dienals

The configuration of the three stereogenic tertiary fusion centres in **3l** was found to be *cis-trans* by NOE experiments (*cis* for the cyclopentane ring; *trans* for the furan ring). This stereochemistry would correspond to the most favoured arrangement of the cyclooctene ring allowing coordination of the metal ion by the *re* face. This coordination would dispose the ring in a pseudoaxial configuration near the metal centre and a pseudoequatorial one at the α-oxy tertiary centre. The substantially higher degree of planarity in the cyclohexene ring when **2m** was used as the substrate would, therefore, not be expected to allow a stable coordination of the double bond with the metal ion and, again, **5m** and **12m** were produced instead in variable amounts.

As expected, under noncarbonylative conditions, **2f** yielded **8f** (among other products),[11] while neither **2g** or **2i** (Entries 10, 12) proved able similarly to undergo the "ene-type" reaction, giving, as usual, linear methanolysis products.

Finally, we also attempted the formation of a cyclopentanone ring fused to a six-membered ring, using the substrates **2j** and **2k**. No cycloaddition products were ever detected, pointing to a high entropy barrier, probably adding to the conformational restrictions, for these cases.

Conclusions

$Ni(COD)_2$ efficiently promotes intramolecular carbonylative cycloaddition with 2,7-dienals to give diquinane-like systems. In the absence of CO, or in the presence of protic acids, "ene-type" reactions are also promoted, which can be considered to constitute the initiation of the carbonylative cycloaddition. Both classes of reactions are stereoselective and are blocked by the presence of highly coordinating heteroatoms and/or the presence of substituents that may interact sterically with the initially formed π-allyl complex when the double bond approaches to coordinate the metal centre. Surprisingly, the pseudoaxial arrangement of these

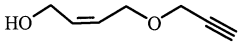
substituents in the putative intermediate [from (*Z*)-olefins] would be more favoured than that in the pseudoequatorial ones [from (*E*)-olefins]. A possible explanation for these results could be found in the known distortion of the π-allyl plane from orthogonality.

Experimental Section

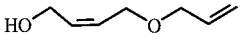
General Remarks: IR spectra were recorded with a Bomem MB-120 instrument with Fourier transform capability and are reported in cm^{-1}. ^1H and ^{13}C NMR spectra were obtained in $CDCl_3$ solutions (unless otherwise indicated) and were recorded with Gemini 200 Varian and Unity 300 Varian machines, operating at 200 and 300 MHz for ^1H and 50 and 75 MHz for ^{13}C, respectively. Chemical shifts are reported in δ units (ppm) downfield from Me_4Si, or relative to the singlet at δ = 7.26 for $CDCl_3$ for ^1H and relative to the centre line of a triplet at δ = 77.0 of $CDCl_3$ for ^{13}C. Splitting patterns are designated as: s, singlet; d, doublet; t, triplet; q, quadruplet; quint, quintuplet; *, apparent multiplicity; m, multiplet; br, broad. Elemental analyses were performed with a Carlo Erba apparatus (1106 and 1108 Models). GC-MS data were determined with a Fisons MD800 mass spectrometer coupled to a gas chromatograph equipped with an SPB-5 (30 m × 0.32 mm i.d.) fused silica capillary column. High resolution MS (EI) spectra (70 eV) were obtained with an Auto Spec-Q instrument. TLC was performed on Merck 60 F_{254} silica gel plates. Flash chromatography was performed on 230−400 mesh Merck 60 silica gel. Commercial analytical grade reagents were obtained from commercial suppliers and were used directly without further purification. Solvents were distilled under Ar prior to use and dried by standard methods.

Syntheses of 1a−i, 1l, 1m: Under Ar, NaH (6 g, 0.25 mol) and anhydrous THF (50 mL) were introduced into a three-necked, 250-mL flask. (*Z*)-But-2-ene-1,4-diol (44 g, 500 mmol) was slowly added, while keeping the temperature at 0 °C, at which point a white slurry appeared. When the H_2 evolution ceased, the mixture was allowed to come to room temperature and the corresponding allyl bromide (or allyl chloride for **1d**, **1e** and **1h**) (500 mmol) was added dropwise with vigorous stirring. The mixture warmed up while the sodium halide separated. After the addition was complete, the contents of the flask were refluxed for 4 h. The solvent was evaporated to dryness and a saturated solution of NaCl was added. The organic material was extracted three times with diethyl ether. The combined organic layers were dried with Na_2SO_4 and purified by passing through a flash chromatography column (eluent: ethyl acetate/hexane, 1:1).

(2*Z*)-4-(Prop-2-ynyloxy)but-2-en-1-ol (1a): 45%. − ^1H NMR (300 MHz, $CDCl_3$): δ = 2.45 (t, *J* = 2.4 Hz, 1 H), 2.71 (br. s, 1 H), 4.13 (m, 4 H), 4.21 (d, *J* = 6.3 Hz, 2 H), 5.60 (m, 1 H), 5.80 (m, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 57.1 (CH_2), 58.2 (CH_2), 64.8 (CH_2), 74.7 (CH), 79.3 (C), 126.9 (CH), 133.1 (CH).

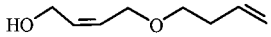


(2*Z*)-4-(Allyloxy)but-2-en-1-ol (1b): 55%. − IR (film): $\tilde{\nu}$ = 3383, 3022, 1645 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 2.70 (br. s, 1 H), 3.94 (d, *J* = 8.7 Hz, 2 H), 4.03 (d, *J* = 8.4 Hz, 2 H), 4.16 (br. s, 2 H), 5.20 (m, 2 H), 5.74 (m, 3 H). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 58.4 (CH_2), 65.5 (CH_2), 71.2 (CH_2), 117.3 (CH), 127.8 (CH_2), 132.2 (CH), 134.2 (CH).

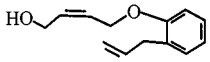


Syntheses of 1j, 1k, 1n: Under Ar, NaH (0.6 g, 25 mmol) and THF (30 mL) were introduced into a three-necked, 100-mL flask. The alcohol (**1j**, **1k**) or ester (**1n**) (25 mmol) was added dropwise at 0 °C. Once the H_2 evolution had ceased, (2*Z*)-4-bromobut-2-enyl acetate (4.82 g, 25 mmol) was added dropwise at room temperature. The contents were then heated to reflux for 4 h, monitoring (by TLC) the completion of the reaction by the disappearance of the allyl halide. The crude product was extracted as above and the residue, without purification, hydrolysed[12] for deprotection.

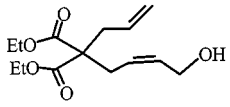
(2*Z*)-4-(But-3-enyloxy)but-2-en-1-ol (1j): 73%. − ^1H NMR (300 MHz, $CDCl_3$): δ = 2.34 (tq, *J* = 1.2, 6.6 Hz, 3 H), 3.49 (t, *J* = 6.6 Hz, 2 H), 4.05 (d, *J* = 6.0 Hz, 2 H), 4.18 (d, *J* = 6.3 Hz, 2 H), 5.06 (m, 2 H), 5.70 (m, 1 H), 5.80 (m, 2 H). − ^{13}C NMR (75 MHz): δ = 34.1 (CH_2), 58.7 (CH_2), 66.4 (CH_2), 69.8 (CH_2), 116.6 (CH_2), 128.3 (CH), 132.21 (CH), 134.9 (CH).



(2*Z*)-4-(2-Allylphenoxy)but-2-en-1-ol (1k): 47%. − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.50 (br. s, 1 H), 3.39 (d, *J* = 6.4 Hz, 2 H), 4.29 (br. s, 2 H), 4.63 (d, *J* = 3.6 Hz, 2 H), 5.05 (dd, *J* = 15.8, 4.4 Hz, 2 H), 5.85 (t, *J* = 3.8 Hz, 2 H), 6.00 (m, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.93 (d, *J* = 7.4 Hz, 1 H), 7.17 (d, *J* = 7.4 Hz, 2 H). − ^{13}C NMR (75 MHz): δ = 34.3 (CH_2), 59.0 (CH_2), 64.1 (CH_2), 111.7 (CH), 115.4 (CH_2), 120.9 (CH), 127.3 (CH), 127.6 (CH), 129.9 (CH), 132.1 (CH), 136.9 (CH), 156.0 (C).

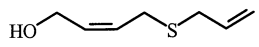


Diethyl 2-Allyl-2-[(2*Z*)-4-hydroxybut-2-enyl]malonate (1n): 82%. − IR (film): $\tilde{\nu}$ = 3448, 1735, 1641 cm^{-1}. − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.0 Hz, 6 H), 2.65 (d, *J* = 7.6 Hz, 4 H), 4.15 (m, 4 H), 5.10 (m, 2 H), 5.40 (m, 1 H), 5.66 (m, 2 H). − ^{13}C NMR (50 MHz): δ = 13.9 (CH_3), 30.3 (CH_2), 37.0 (CH_2), 57.2 (C), 58.2 (CH_2), 61.3 (CH_2), 119.1 (CH_2), 125.6 (CH), 132.1 (CH), 132.2 (CH), 170.7 (C).

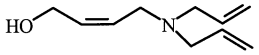


Syntheses of 1o, 1p: Solid K_2CO_3 (4.5 g, 105 mmol) was added to a solution of diallylamine (5.09 g, 52.5 mmol) (or prop-2-ene-1-thiol) in 25 mL of THF. The mixture was vigorously stirred while 2-{[(2*Z*)-4-chlorobut-2-enyl]oxy}tetrahydro-2*H*-pyran (10.00 g, 52.5 mmol) was added dropwise, and then left to stir for 24 h. The precipitate was filtered off and the solution concentrated to dryness. Saturated NaCl solution was then added to the residue, and the mixture was extracted a few times with diethyl ether until a drop did not show a residue after solvent evaporation. The combined organic phases were concentrated and the product treated with an excess of MeOH and *p*-toluenesulfonic acid for deprotection.[13] After concentration, the residue was found pure enough to be used in the case of **1o**, while **1p** was purified by passing it through a chromatography column (silica gel; EtOAc/hexane, 1:1).

(2*Z*)-4-(Allylsulfanyl)but-2-en-1-ol (1o): 77%. − ^1H NMR (200 MHz, $CDCl_3$): δ = 1.43 (br. s, 1 H), 3.11 (d, *J* = 5.8 Hz, 2 H), 3.14 (d, *J* = 5.4 Hz, 2 H), 4.21 (d, *J* = 6.0 Hz, 2 H), 5.11 (m, 2 H), 5.74 (m, 3 H). − ^{13}C NMR (50 MHz): δ = 27.0 (CH_2), 34.0 (CH_2), 58.2 (CH_2), 117.1 (CH_2), 128.2 (CH), 131.1 (CH), 134.2 (CH).

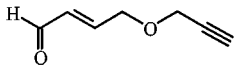


(2*Z*)-4-(Diallylamino)but-2-en-1-ol (1p): 46%. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.08 (dq, *J* = 1.5, 6.0 Hz, 2 H), 3.13 (tt, *J* = 1.5, 6.6 Hz, 4 H), 4.15 (dq, *J* = 1.5, 6.0 Hz, 2 H), 5.18 (m, 2 H), 5.22 (m, 2 H), 5.68 (dtt, *J* = 1.5, 6.0, 11.7 Hz, 1 H), 5.80−5.96 (m, 3 H).

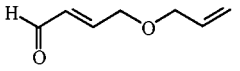


Syntheses of 2a−o: A slight excess of pyridinium chlorochromate (5.05 g, 23.4 mmol) in CH_2Cl_2 (1 mL) was added to a solution of **1b** (2 g, 15.6 mmol) (or **1a−o**) in CH_2Cl_2 (5 mL) at room temperature. After stirring for 30−45 min, the reaction was complete (TLC monitoring) and anhydrous diethyl ether (20 mL) was added. The crude product was filtered through silica gel and the filtrate was concentrated to dryness to afford the aldehydes **2a−o**.

(2*E*)-4-(Prop-2-ynyloxy)but-2-enal (2a): 45%. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.47 (t, *J* = 2.1 Hz, 1 H)4.19 (d, *J* = 2.1 Hz, 2 H), 4.31 (dd, *J* = 1.8, 4.2 Hz, 2 H), 6.30 (ddt, *J* = 1.8, 8.1, 15.6 Hz, 1 H), 6.80 (dt, *J* = 4.2, 15.6 Hz, 1 H), 9.60 (d, *J* = 8.1 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 58.1 (CH_2), 68.0 (CH_2), 75.3 (CH), 78.8 (C), 132.0 (CH), 152.0 (CH), 193.1 (CH);

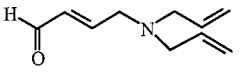


(2*E*)-4-(Allyloxy)but-2-enal (2b): 67%. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.05 (dt, *J* = 1.8, 5.7 Hz, 2 H), 4.26 (dd, *J* = 1.8, 3.9 Hz, 2 H), 5.22 (dq, *J* = 1.8, 10.5 Hz, 1 H), 5.30 (dq, *J* = 1.8, 17.4 Hz, 1 H), 5.90 (ddt, *J* = 5.7, 10.5, 17.4 Hz, 1 H), 6.38 (ddt, *J* = 1.8, 7.8, 15.6 Hz, 1 H), 6.84 (dt, *J* = 3.9, 15.6 Hz, 1 H), 9.58 (d, *J* = 7.8 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 65.6 (CH_2), 71.1 (CH_2), 117.5 (CH_2), 130.9 (CH), 131.7 (CH), 153.1 (CH), 193.2 (CH);

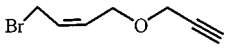


Synthesis of 2p: The oxidation with PCC gave a mixture of products. For this particular dienal, MnO_2 was preferred, in a molar excess of 40:1. The aldehyde was obtained as the crude product in 60% yield (corresponding by ^{1}H NMR to an estimated 50% actual yield) and used as such.

(2*E*)-4-(Diallylamino)but-2-enal (2p): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.10 (dt, *J* = 1.2, 6.3 Hz, 4 H), 3.33 (dd, *J* = 1.6, 5.6 Hz, 2 H), 5.19 (m, 4 H), 5.80 (m, 2 H), 6.26 (ddt, *J* = 1.6, 8.0, 15.6 Hz, 1 H), 6.83 (dt, *J* = 5.6, 15.6 Hz, 1 H), 9.58 (d, *J* = 8.0 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 54.3 (CH_2), 56.9 (CH_2), 118.0 (CH_2), 133.6 (CH), 134.9 (CH), 155.7 (CH), 193.6 (CH).

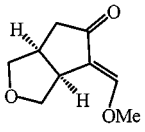


(2*E*)-4-Bromobut-2-enyl Prop-2-ynyl Ether): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.48 (t, *J* = 2.4 Hz, 1 H), 4.05 (d, *J* = 8.4 Hz, 2 H), 4.18 (d, *J* = 2.4 Hz, 2 H), 4.22 (dd, *J* = 1.5, 6.6 Hz, 2 H), 5.71 (m, 1 H), 5.93 (m, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 26.2 (CH_2), 57.3 (CH_2), 64.1 (CH_2), 74.8 (CH), 79.3 (C), 129.3 (CH), 130.0 (CH).

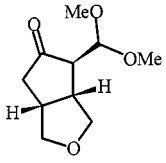


General Procedure for the Cyclization: $Ni(COD)_2$ (1.12 g, 4.07 mmol) and anhydrous toluene (or acetonitrile) (20 mL) were introduced under Ar into a 100-mL Schlenk flask and kept at − 20 °C while the dienal **2** (0.51 g, 4.07 mmol for **2b**) was added dropwise. Soon a red precipitate or solution was formed. The temperature was allowed to increase until it reached −10 °C. At this point, Me_3SiCl (0.88 g, 8.14 mmol) was added dropwise. After 1 h, the oxidative addition was complete. The temperature was lowered once more to −78 °C (−50 °C for acetonitrile) and the Ar was replaced by CO, by bubbling under atmospheric pressure. The temperature was again allowed to rise to room temperature. An excess of methanol (2 mL) was added (quenching). The reaction was allowed to proceed for a further 4 h. The solvent was completely evaporated in vacuo. The residue was treated with water and extracted several times with diethyl ether. The combined organic phases were dried with Na_2SO_4 and concentrated to dryness. The crude oil was chromatographed on silica gel (eluent: hexane/EtOAc, 6:1) and dried to obtain the expected adducts. For the reaction in acetonitrile, a 55% yield of **3b** and an 18% yield of **4b** were isolated.

(4*E*)-4-(Methoxymethylene)tetrahydro-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (3b): Colourless solid, m.p 58 °C. − IR (film): $\tilde{\nu}$ = 1706, 1625 cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (dd, *J* = 4.8, 18.9 Hz, 1 H), 2.61 (dd, *J* = 9.6, 18.9 Hz, 1 H), 2.88 (m, 1 H), 3.52 (m, 1 H), 3.53 (dd, *J* = 4.8, 9.0 Hz, 1 H), 3.73 (dd, *J* = 4.2, 9.0 Hz, 1 H), 3.86 (s, 3 H), 3.92 (dd, *J* = 6.6, 9.0 Hz, 1 H), 4.01 (dd, *J* = 7.8, 9.0 Hz, 1 H), 7.21 (d, *J* = 2.1 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 37.1 (CH_2), 43.0 (CH), 43.4 (CH), 62.0 (CH_3), 73.8 (CH_2), 74.7 (CH_2), 118.6 (C), 156.3 (CH), 206.5 (C). − MS (40 eV, EI); *m*/*z* (%): 168 (76) $[M]^+$, 138 (29), 126 (33), 109 (100). − HR MS for $C_9H_{12}O_3$: calcd: 168.078644; found 168.078640.

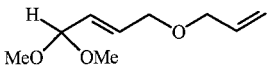


4-(Dimethoxymethyl)tetrahydro-1*H*-cyclopenta[*c*]furan-5(3*H*)-one (4b): Diastereomeric mixture (93:7), colourless oil. − IR (film): $\tilde{\nu}$ = 1741 cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.21 (dd, *J* = 4.2, 18.9 Hz, 1 H), 2.45 (dd, *J* = 3.3, 6.3 Hz, 1 H), 2.56 (dd, *J* = 9.0, 18.9 Hz, 1 H), 2.92 (m, 1 H), 3.14 (m, 1 H), 3.40 (s, 3 H), 3.41 (s, 3 H), 3.53 (dd, *J* = 5.1, 9.0 Hz, 1 H), 3.70 (dd, *J* = 3.3, 9.0 Hz, 1 H), 3.92 (dd, *J* = 3.3, 9.0 Hz, 1 H), 3.96 (dd, *J* = 4.2, 9.0 Hz, 1 H), 4.56 (d, *J* = 3.3 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 38.4 (CH), 40.8 (CH), 43.5 (CH_2), 55.7 (CH_3), 56.8 (CH), 57.1 (CH_3), 74.3 (CH_2), 74.6 (CH_2), 105.5 (CH), 217.3 (C).



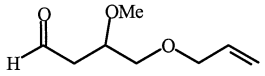
(2*E*)-4-(Allyloxy)-1,1-dimethoxybut-2-ene (5b): As a result of applying the general procedure, from **2b** (0.28 g, 2.20 mmol), $Ni(COD)_2$ (0.61 g, 2.20 mmol) and trimethylsilyl chloride (0.24 g, 2.20 mmol) in toluene (20 mL), **5b** was obtained after flash chromatography (hexane/EtOAc, 9:1) as a yellow oil (0.152 g, 40%). − ^{1}H NMR

(300 MHz, $CDCl_3$): δ = 3.31 (s, 6 H), 3.98 (dt, *J* = 1.5, 5.4 Hz, 2 H), 4.01 (d, *J* = 5.4 Hz, 2 H), 4.78 (d, *J* = 4.8 Hz, 1 H), 5.17 (dd, *J* = 1.5, 10.2 Hz, 1 H), 5.27 (dq, *J* = 1.5, 17.1 Hz, 1 H), 5.70 (ddt, *J* = 1.5, 4.8, 15.9 Hz, 1 H), 5.90 (m, 2 H). − ^{13}C NMR (75 MHz): δ = 52.7 (CH_3), 69.5 (CH_2), 71.2 (CH_2), 102.4 (CH), 117.0 (CH_2), 128.6 (CH), 131.2 (CH), 134.5 (CH). − MS (40 eV, EI); *m*/*z* (%): 141 (30) $[M - OCH_3]^+$, 115 (28), 101 (100), 81 (43), 75 (73), 71 (60).

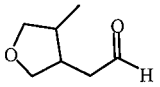


4-(Allyloxy)-3-methoxybutanal (7b) and (4-Methyltetrahydrofuran-3-yl)acetaldehyde (8b): As a result of applying the general procedure, from **2b** (0.44 g, 3.53 mmol), $Ni(COD)_2$ (0.97 g, 3.53 mmol) and trifluoroacetic acid (0.40 g, 3.80 mmol) in MeOH (20 mL), **7b** (15%) and **8b** (25%) were obtained after flash chromatography (hexane/EtOAc, 9:1).

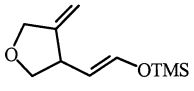
Compound 7b: Yellow oil (0.083 g, 15%). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.64 (dd, *J* = 2.1, 6.3 Hz, 2 H), 3.41 (s, 3 H), 3.50 (dd, *J* = 1.2, 4.8 Hz, 2 H), 3.86 (m, 1 H), 4.00 (dq, *J* = 1.5, 5.7 Hz, 2 H), 5.17 (dd, *J* = 1.2, 9.0 Hz, 1 H), 5.25 (dq, *J* = 1.5, 17.1 Hz, 1 H), 5.78 (m, 1 H), 9.80 (t, *J* = 1.8 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 45.9 (CH_2), 57.6 (CH_3), 70.7 (CH_2), 72.3 (CH_2), 75.2 (CH), 117.2 (CH_2), 134.2 (CH), 200.7 (CH).



Compound 8b: Colourless oil (0.113 g, 25%). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.91 (d, *J* = 7.2 Hz, 3 H), 2.40 (m, 1 H), 2.45 (dd, *J* = 1.5, 8.4 Hz, 1 H), 2.56 (dd, *J* = 1.5, 6.0 Hz, 1 H), 2.67 (m, 1 H), 3.41 (dd, *J* = 3.3, 8.4 Hz, 1 H), 3.44 (dd, *J* = 6.6, 8.4 Hz, 1 H), 3.93 (dd, *J* = 6.6, 8.4 Hz, 1 H), 3.99 (dd, *J* = 7.2, 8.4 Hz, 1 H), 9.81 (t, *J* = 1.5 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 14.0 (CH_3), 35.2 (CH), 36.15 (CH), 42.4 (CH_2), 72.0 (CH_2), 74.5 (CH_2), 201.0 (CH).

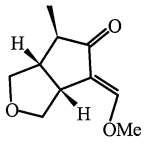


3-[(*E*)-2-Trimethylsilyloxyethenyl]-4-methylenetetrahydrofuran (10b): As a result of applying the general procedure, from **2b** (0.41 g, 3.23 mmol), $Ni(COD)_2$ (0.89 g, 3.23 mmol) and trimethylsilyl chloride (0.38 g, 3.56 mmol), **10b** (0.26 g 40%) was obtained after flash chromatography (hexane/EtOAc, 9:1). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.2 (s, 9 H), 3.20 (m, 1 H), 3.40 (dd, *J* = 8.4, 9.6 Hz, 1 H), 4.06 (t, *J* = 8.4 Hz, 1 H), 4.30 (dq, *J* = 2.4, 13.2 Hz, 1 H), 4.45 (dq, *J* = 2.4, 13.2 Hz, 1 H), 4.80 (dd, *J* = 9.4, 12.0 Hz, 1 H), 4.92 (q, *J* = 2.4 Hz, 1 H), 4.96 (q, *J* = 2.4 Hz, 1 H), 6.31 (d, *J* = 12.0 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = −0.52 (CH_3), 43.6 (CH), 71.3 (CH_2), 74.1 (CH_2), 104.7 (CH_2), 109.4 (CH), 142.1 (CH), 151.7 (C). − MS (40 eV, EI); *m*/*z* (%): 198 (9) $[M]^+$, 168 (70), 75 (79), 73 (100). − Product **9b** could only be tentatively identified in the mixture since, being the minor product, some signals were overlapped by those of the major. Any attempt to separate them resulted in isolation of **8b**.

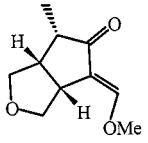


(4*E*)-4-(Methoxymethylene)-6-methyltetrahydro-1*H*-cyclopenta[*c*]-furan-5(3*H*)-one (3c): As a result of applying the general procedure, from **2c** (0.46 g, 3.23 mmol), $Ni(COD)_2$ (0.89 g, 3.23 mmol) and trimethylsilyl chloride (0.35 g, 3.23 mmol), **3c** was obtained after flash chromatography (hexane/EtOAc, 6:1) as a 3:1 diastereomeric mixture, yellow oil (0.306 g, 52%).

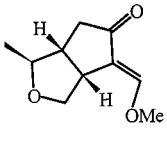
Compound 3c (Major Isomer): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.15 (d, *J* = 7.2 Hz, 3 H), 2.19 (q, *J* = 7.2 Hz, 1 H), 2.43 (m, 1 H), 3.43 (m, 1 H), 3.69 (dd, *J* = 3.0, 9.0 Hz, 1 H), 3.82 (dd, *J* = 3.6, 7.2 Hz, 1 H), 3.84 (s, 3 H), 3.85 (dd, *J* = 3.9, 9.0 Hz, 1 H), 3.95 (t, *J* = 8.4 Hz, 1 H), 7.22 (d, *J* = 2.1 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 15.7 (CH_3), 41.0 (CH), 47.0 (CH), 48.8 (CH), 61.9 (CH_3), 73.5 (CH_2), 73.6 (CH_2), 118.3 (C), 156.0 (CH), 208.7 (C). − For the mixture of both isomers: HR MS for $C_{10}H_{14}O_3$: calcd. 182.094294; found 182.093965.



Minor Isomer: Data deduced from the mixture by signal subtraction. − ^{1}H NMR (300 MHz, $CDCl_3$; main visible signals): δ = 1.09 (d, *J* = 7.2 Hz, 3 H), 2.57 (dq, *J* = 7.2, 8.4 Hz, 1 H), 2.92 (q, *J* = 8.1 Hz, 1 H), 4.06 (dd, *J* = 7.2, 9.0 Hz, 1 H), 7.25 (d, *J* = 2.1 Hz, 1 H). − ^{13}C NMR (75 MHz): δ = 11.1 (CH_3), 41.3 (CH), 42.8 (CH), 45.1 (CH), 62.0 (CH_3), 69.1 (CH_2), 73.4 (CH_2), 117.6 (C), 156.5 (CH), 207.2 (C).



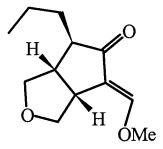
(4*E*)-4-(Methoxymethylene)-1-methyltetrahydro-1*H*-cyclopenta[*c*]-furan-5(3*H*)-one (3e): As a result of applying the general procedure, from **2e** (0.46 g, 3.23 mmol), $Ni(COD)_2$ (0.89 g, 3.23 mmol) and trimethylsilyl chloride (0.35 g, 3.23 mmol), **3e** was obtained after flash chromatography (hexane/EtOAc, 6:1) as a 95:5 diastereomeric mixture, colourless oil (0.353 g, 65%). − IR (film): $\tilde{\nu}$ = 1708, 1631, 1456 cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.24 (d, *J* = 6.0 Hz, 3 H), 2.10 (dd, *J* = 3.0, 18.6 Hz, 1 H), 2.34 (m, 1 H), 2.54 (dd, *J* = 9.3, 18.6 Hz, 1 H), 3.45 (dq, *J* = 6.0, 7.8 Hz, 1 H), 3.51 (m, 2 H), 3.86 (s, 3 H), 4.30 (tt, *J* = 3.3, 7.8 Hz, 1 H), 7.23 (d, *J* = 2.1 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.7 (CH_3), 40.9 (CH_2), 43.4 (CH), 44.3 (CH), 61.9 (CH_3), 73.1 (CH_2), 81.2 (CH), 118.4 (C), 156.6 (CH), 206.2 (C). − MS (40 eV, EI); *m*/*z* (%): 182 (32) $[M]^+$, 137 (100), 123 (42), 109 (93), 93 (44). − Data for the mixture of isomers: HR MS for $C_{10}H_{14}O_3$: calcd. 182.094294; found 182.094516.



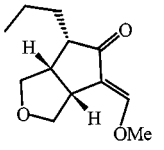
(4*E*)-4-(Methoxymethylene)-6-propyltetrahydro-1*H*-cyclopenta[*c*]-furan-5(3*H*)-one (3f): As a result of applying the general procedure, from **2f** (0.40 g, 2.40 mmol), $Ni(COD)_2$ (0.66 g, 2.40 mmol) and trimethylsilyl chloride (0.26 g, 2.40 mmol), **3f** was obtained after flash chromatography (hexane/EtOAc, 9:1) as a 3:1 diastereomeric mix-

ture, colourless oil (0.35 g, 69%). − Data for the mixture: IR (film): $\tilde{\nu}$ = 1706, 1633, 1463 cm^{-1}.

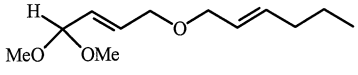
Major Isomer: ^1H NMR (300 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 6.6 Hz, 3 H), 1.37 (m, 4 H), 2.17 (m, 1 H), 2.53 (m, 1 H), 3.44 (m, 1 H), 3.60 (dd, *J* = 3.6, 9.0 Hz, 1 H), 3.68 (dd, *J* = 4.5, 8.7 Hz, 1 H), 3.85 (s, 3 H), 3.89 (dd, *J* = 6.6, 9.0 Hz, 1 H), 3.98 (t, *J* = 8.4 Hz, 1 H), 7.20 (d, *J* = 2.1 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 20.3 (CH_2), 33.6 (CH_2), 41.3 (CH), 44.7 (CH), 53.9 (CH), 61.8 (CH_3), 73.6 (CH_2), 74.3 (CH_2), 118.5 (C), 155.9 (CH), 208.4 (C). − MS (40 eV, EI); *m*/*z* (%): 181 (5), 168 (100), 137 (34), 106 (41). −Data for the mixture: HR MS for $C_{12}H_{18}O_3$: calcd. 210.125595; found 210.123947.



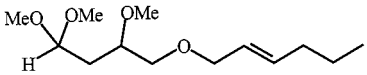
Minor Isomer: Data deduced from the mixture by signal subtraction. − ^1H NMR (300 MHz, $CDCl_3$; main visible signals): δ = 1.17 (d, *J* = 6.3 Hz, 3 H), 2.10 (dd, *J* = 3.0, 18.6 Hz, 1 H), 2.29 (m, 1 H), 2.50 (dd, *J* = 9.3, 18.6 Hz, 1 H), 3.39 (dq, *J* = 6.3, 7.8 Hz, 1 H), 3.51 (m, 2 H), 3.81 (s, 3 H), 4.30 (tt, *J* = 3.3, 7.8 Hz, 1 H), 7.13 (d, *J* = 2.1 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 15.7, 20.9 (CH_2), 38.3 (CH), 41.2 (CH), 60.3, 61.8 (CH_3), 73.0 (CH_2), 81.2 (CH), 118.4 (C), 155.2 (CH), 206.2 (C). − MS (40 eV, EI); *m*/*z* (%): 181 (8), 168 (100), 137 (35), 106 (26).



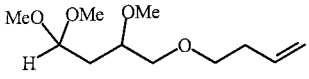
(2*E*)-1-{[(2*E*)-4,4-Dimethoxybut-2-enyl]oxy}hex-2-ene (5g): As a result of applying the general procedure, from **2g** (0.36 g, 2.14 mmol), $Ni(COD)_2$ (0.59 g, 2.14 mmol) and trimethylsilyl chloride (0.23 g, 2.14 mmol), **5g** was obtained after flash chromatography (hexane/EtOAc, 9:1) as a 3:1 diastereomeric mixture, colourless oil (0.183 g, 40%). − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.90 (t, *J* = 7.2 Hz, 3 H), 1.40 (quint*, *J* = 7.2 Hz, 2 H), 2.04 (q, *J* = 7.2 Hz, 2 H), 3.33 (s, 6 H), 3.93 (d, *J* = 6.0 Hz, 2 H), 4.01 (d, *J* = 6.3 Hz, 2 H), 4.80 (d, *J* = 4.8 Hz, 1 H), 5.56 (m, 2 H), 5.70 (m, 2 H). − ^{13}C NMR (75 MHz): δ = 13.6 (CH_3), 22.1 (CH_2), 34.3 (CH_2), 52.7 (CH_3), 69.2 (CH_2), 71.0 (CH_2), 102.4 (CH), 126.1 (CH), 128.5 (CH), 131.4 (CH), 134.8 (CH);



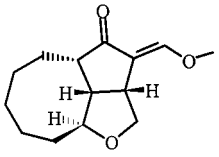
(2*E*)-1-(2,4,4-Trimethoxybutoxy)hex-2-ene (12g): As a result of applying the general procedure (without CO) for **2g** (0.76 g, 4.54 mmol), $Ni(COD)_2$ (1.25 g, 4.54 mmol) and trimethylsilyl chloride (0.99 g, 9.09 mmol) in toluene (25 mL), **12g** was obtained after flash chromatography (hexane/EtOAc, 9:1) as a yellow oil (0.168 g, 15%). − ^1H NMR (300 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 7.2 Hz, 3 H), 1.40 (m, 2 H), 1.79 (t, *J* = 6.0 Hz, 2 H), 2.02 (q, *J* = 7.2 Hz, 2 H), 3.31 (s, 3 H), 3.32 (s, 3 H), 3.39 (s, 3 H), 3.42 (m, 2 H), 3.93 (d, *J* = 6.0 Hz, 2 H), 4.03 (m, 1 H), 4.54 (t, *J* = 6.0 Hz, 1 H), 5.52 (m, 2 H). − ^{13}C NMR (75 MHz): δ = 13.6 (CH_3), 22.1 (CH_2), 34.2 (CH_2), 34.9 (CH_2), 52.7 (CH_3), 52.9 (CH_3), 57.6 (CH_3), 71.2 (CH_2), 72.0 (CH_2), 77.4 (CH), 102.0 (CH), 126.3 (CH), 134.5 (CH).



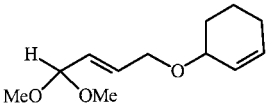
4-(2,4,4-Trimethoxybutoxy)but-1-ene (12j): As a result of applying the general procedure, from **2j** (0.22 g, 1.53 mmol), $Ni(COD)_2$ (0.42 g, 1.53 mmol) and trimethylsilyl chloride (0.33 g, 3.05 mmol), **12j** was obtained after flash chromatography (hexane/EtOAc, 9:1) as a colourless oil (0.123 g, 27%). − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.79 (t, *J* = 6.0 Hz, 2 H)2.43 (tq, *J* = 1.2, 6.6 Hz, 2 H), 3.32 (s, 3 H), 3.33 (s, 3 H), 3.44 (s, 3 H), 3.50 (m, 5 H), 4.54 (t, *J* = 6.0 Hz, 1 H), 5.06 (m, 2 H), 5.80 (m, 1 H).



(3*E*)-3-(Methoxymethylene)decahydro-1-oxacycloocta[*cd*]pentalen-4(2*H*)-one (3l): As a result of applying the general procedure, from **2l** (0.41 g, 2.11 mmol), $Ni(COD)_2$ (0.58 g, 2.11 mmol) and trimethylsilyl chloride (0.23 g, 2.11 mmol), **3l** was obtained after flash chromatography (hexane/EtOAc, 9:1) as a single diastereomer, yellow oil (0.42 g, 85%), m.p. 107 ° C. − IR (film): $\tilde{\nu}$ = 1706, 1631 cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.2−1.6 (m, 6 H), 1.87 (m, 2 H), 2.11 (m, 1 H), 2.21 (m, 1 H), 2.36 (m, 1 H), 2.66 (q, *J* = 9.9 Hz, 1 H), 3.39 (dd, *J* = 6.3, 8.7 Hz, 1 H), 3.48 (dt, *J* = 3.3, 10.2 Hz, 1 H), 3.58 (m, 1 H), 3.86(s, 3 H), 4.36 (t, *J* = 8.4 Hz, 1 H), 7.26 (d, *J* = 2.4 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.5 (CH_2), 22.9 (CH_2), 25.4 (CH_2), 27.9 (CH_2), 35.7 (CH_2), 43.0 (CH), 47.9 (CH), 50.4 (CH), 61.9 (CH_3), 72.4 (CH_2), 81.0 (CH), 117.8 (C), 156.5 (CH), 207.5 (C). − MS (40 eV, EI); *m*/*z* (%): 236 (30) $[M]^+$, 208 (35), 178 (33), 137 (50), 84 (100). − $C_{14}H_{20}O_3$ (236.31): calcd. C 71.18, H 8.47; found C 70.97, H 8.64



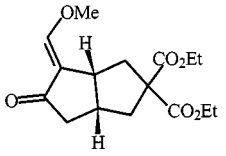
3-{[(2*E*)-4,4-Dimethoxybut-2-enyl]oxy}cyclohex-1-ene (5m): As a result of applying the general procedure, from **2m** (0.25 g, 1.53 mmol), $Ni(COD)_2$ (0.42 g, 1.53 mmol) and trimethylsilyl chloride (0.16 g, 1.53 mmol), **5m** was obtained after flash chromatography (hexane/EtOAc, 6:1) as a yellow oil (0.136 g, 42%). − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.48−2.11 (m, 6 H), 3.32 (s, 6 H), 3.93 (m, 1 H), 4.05 (m, 2 H), 4.80 (d, *J* = 4.5 Hz, 1 H), 5.78 (m, 4 H).



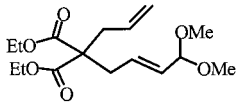
Diethyl (4*E*)-4-(Methoxymethylene)-5-oxohexahydropentalene-2,2(1*H*)-dicarboxylate (3n): As a result of applying the general procedure, from **2n** (1.05 g, 3.93 mmol), $Ni(COD)_2$ (1.08 g, 3.93 mmol) and trimethylsilyl chloride (0.85 g, 7.85 mmol), **3n** was obtained after flash chromatography (hexane/EtOAc, 9:1) as a yellow oil (0.791 g, 65%), together with **5n** (8%).

Compound 3n: IR (film): $\tilde{\nu}$ = 1706, 1633, 1463 cm^{-1}. − ^1H NMR (300 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 7.2 Hz, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 1.90 (dd, *J* = 9.0, 13.5 Hz, 1 H), 2.12 (dd, *J* = 6.6, 13.5 Hz, 1 H), 2.21 (dd, *J* = 3.6, 18.9 Hz, 1 H), 2.55 (dd, *J* = 9.0,

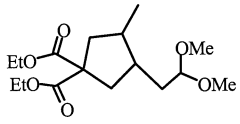
18.9 Hz, 1 H), 2.58 (ddd, J = 1.5, 7.8, 13.2 Hz, 1 H), 2.77 (m, 1 H), 2.81 (ddd, J = 1.5, 8.4, 13.8 Hz, 1 H), 3.43 (m, 1 H), 3.86 (s, 3 H), 4.15 (q, J = 7.2 Hz, 2 H), 4.21 (q, J = 7.2 Hz, 2 H), 7.20 (d, J = 2.4 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.9 (CH_3), 36.0 (CH_2), 39.7 (CH_2), 41.1 (CH), 41.6 (CH_2), 44.4 (CH), 61.4 (CH_2), 61.9 (CH_3), 62.0 (CH_2), 119.7 (C), 156.5 (CH), 171.4 (C), 171.8 (C), 206.9 (C).



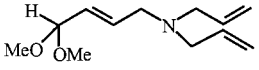
Diethyl 2-Allyl-2-[(2*E*)-4,4-dimethoxybut-2-enyl]malonate (5n): 98 mg, 8%. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.23 (t, J = 6.8 Hz, 6 H), 2.64 (m, 4 H), 3.27 (s, 6 H), 4.21 (q, J = 6.8 Hz, 4 H), 4.68 (d, J = 4.8 Hz, 1 H), 5.13 (m, 2 H), 5.66 (m, 3 H). − ^{13}C NMR (75 MHz): δ = 13.8 (CH_3), 13.9 (CH_3), 34.9 (CH_2), 36.7 (CH_2), 52.5 (CH_3), 57.1 (C), 61.3 (CH_2), 61.2 (CH_2), 102.4 (CH), 119.2 (CH_2), 128.6 (CH), 131.0 (CH), 131.9 (CH), 170.4 (C).



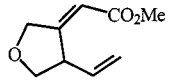
Diethyl 3-(2,2-Dimethoxyethyl)-4-methylcyclopentane-1,1-dicarboxylate (11n): As a result of applying the general procedure, from **2n** (0.51 g, 1.89 mmol), $Ni(COD)_2$ (0.52 g, 1.89 mmol) and trifluoroacetic acid (0.22 g, 1.89 mmol), **11n** was obtained after flash chromatography (hexane/EtOAc, 9:1) as a yellow oil (0.311 g, 52%). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.98 (d, J = 5.7 Hz, 3 H), 1.22 (t, J = 7.2 Hz, 6 H), 1.53 (m, 2 H), 1.72 (d, J = 13.2 Hz, 1 H), 1.80 (dd, J = 4.2, 13.5 Hz, 1 H), 1.85 (m, 1 H), 1.90 (dd, J = 3.0, 7.2 Hz, 1 H), 2.44 (dd, J = 6.0, 13.2 Hz, 1 H), 2.55 (dd, J = 6.9, 13.5 Hz, 1 H), 3.31 (s, 3 H), 3.33 (s, 3 H), 4.17 (q, J = 7.2 Hz, 4 H), 4.40 (dd, J = 4.5, 7.2 Hz, 1 H). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.0 (CH_3), 17.5 (CH_3), 36.3 (CH_2), 40.2 (CH_2), 40.5 (CH_2), 42.2 (CH), 42.7 (CH), 53.0 (CH_3), 56.9 (C), 61.2 (CH_2), 61.3 (CH_2), 103.7 (CH), 177.7 (C), 177.8 (C). − MS (40 eV, EI); m/z (%): 285 (7) $[M - OCH_3]^+$, 239 (26), 165 (12), 137 (15), 107 (14), 75 (100).



(2*E*)-*N*,*N*-Diallyl-4,4-dimethoxybut-2-en-1-ylamine (5p): As a result of applying the general procedure, from a 1:1 mixture of **1p**/**2p** (0.624 g, 1.89 mmol), $Ni(COD)_2$ (0.52 g, 1.89 mmol) and trimethylsilyl chloride (0.23 g, 2.08 mmol), **5p** was isolated after flash chromatography (hexane/EtOAc, 5:1) as a yellow oil (40 mg, 10%). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.10 (m, 6 H), 3.32 (s, 3 H), 3.38 (s, 3 H), 4.16 (d, J = 5.4 Hz, 1 H), 5.18 (m, 4 H), 5.80 (m, 4 H). − ^{13}C NMR (75 MHz): δ = 52.8 (CH_2), 56.2(CH_2), 57.6(CH_2), 102.3 (CH), 118.7(CH_2), 127.7(CH), 130.0 (CH), 134.2 (CH).



Methyl (2*E*)-[4-Vinyldihydrofuran-3(2*H*)-ylidene]acetate: See footnote [a] in Table 1. As a result of applying the general procedure, from (2*E*)-4-bromobut-2-enyl prop-2-ynyl ether (0.41 g, 2.18 mmol), $Ni(COD)_2$ (0.60 g, 2.18 mmol) in toluene (20 mL), this compound was isolated after flash chromatography (hexane/EtOAc, 5:1) as a yellow oil (0.307 g, 84%). − IR (film): $\tilde{\nu}$ = 1720, 1672, 1434 cm^{-1}. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.71 (s, 3 H, CH_3), 3.90 (dd, J = 5.7, 9.0 Hz, 1 H, CH_2O), 4.01 (dd, J = 2.1 9.0 Hz, 1 H, CH_2O), 4.18 (m, 1 H, CH), 4.32 (dt, J = 1.5, 15.3 Hz, 1 H, CH_2O), 4.55 (dt, J = 1.5, 15.3 Hz, 1 H, CH_2O), 5.09 (dt, J = 1.5, 10.2 Hz, 1 H, =CH), 5.17 (dt, J = 1.5, 17.1 Hz, 1 H, =CH), 5.83 (q, J = 1.8 Hz, 1 H, =CH), 5.89 (ddd, J = 6.9, 10.2, 17.1 Hz, 1 H, =CH). − ^{13}C NMR (75 MHz, $CDCl_3$): δ = 46.2 (CH), 51.2 (CH_3), 71.7 (CH_2), 74.0 (CH_2), 111.2 (CH_2), 115.4 (CH_2), 136.1 (CH), 162.7 (C), 165.8 (C).



Acknowledgments

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[6] Ni^0 complexes are active alkyne polymerisation catalysts; see: P. W. Jolly, G. Wilke, *The Organic Chemistry of Nickel Academic Press*, New York, **1975**, vol. II, chapter II.

[7] Additional evidence for the stereochemistry of the enol ethers **3** reported here was provided by the X-ray crystal diffractometry resolution of cycloadduct **3l**.

[8] We think that under the present conditions these kinds of products actually arise from a methoxy group attack onto the π-allyl ligand.

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[10] The dihedral angle formed between the π-allyl plane and the equatorial is found always to be larger than 90° (usually around 106° and even attaining values of 120° in particular cases). See ref.[6], vol. I, chapter VI.

[11] Although **8f** was produced as the major product in the crude product, its isolation after purification turned out to be im-

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