Molecules **2002**, *7*, 475-486

molecules

ISSN 1420-3049

http://www.mdpi.org

Synthetic Studies on Diels-Alder Adducts: Intramolecular Interactions Between Two Functions

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Received: 17 August 2001; in revised form: 28 June 2002 / Accepted: 28 June 2002 / Published: 30 June 2002

Abstract: In this paper we describe the synthesis of a γ,δ-unsaturated aldehyde from a bicyclic Diels-Alder adduct, to be used in future electrocyclic reaction studies. A number of reactions produced undesired materials resulting from the interaction between functions, forcing the use of partial protection to accomplish a synthesis that would be otherwise straightforward. Suggestions to account for the results are given.

Keywords: Diels-Alder adducts, Intramolecular interactions, 1,4-Diols oxidation, Cyclic phosphite

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Introduction

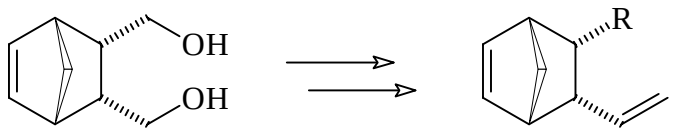
During our studies on the preparation of polycyclic compounds through the Diels-Alder reactions we have faced a circumstance of unusual recurrence of interference between two functions existing in the same molecule, resulting in changes of the properties usually associated with each function and giving rise to unexpected and rather surprising results.

In our view, it is essential to improve the systematization of knowledge about interferences between functions, thus bringing higher reliability to organic syntheses projects. The results disclosed

in this paper, for instance, confirm that some 1,4-diols cannot be easily oxidized to 1,4-dialdehydes due to a strong tendency towards formation of a lactol, which blocks further oxidation with common reagents. In these cases it is necessary to make use of partial protections, thus preventing one (protected) function to interfere in the properties of the other (unprotected) one. It is also possible to make a direct transformation through the use of special reagents [1].

Seeking the development of synthetic methods for the preparation of annulenes [2] and heliangolides [3] through the Diels-Alder reaction, our aim in this work [4] was the preparation of compound **2**, from **1,** for use in electrocyclic reactions studies (**Scheme 1**).

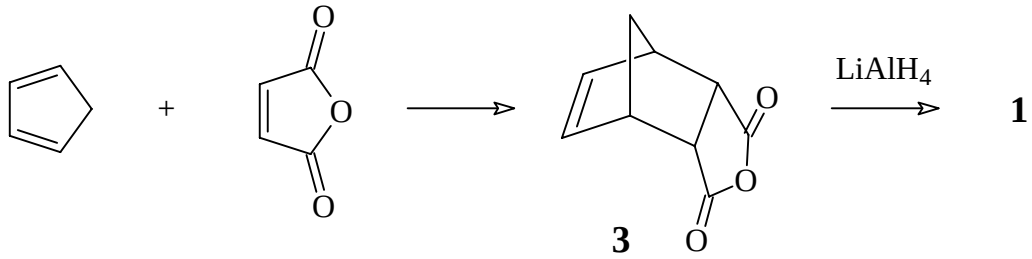
Scheme 1



1 **2a:** R = CHO
2b: R = -CH=CH_2

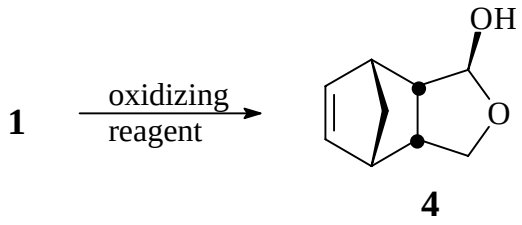
This is an apparently a very simple transformation, as it would require only the oxidation of the diol to a dialdehyde and a Wittig reaction, using $Ph_3P{=}CH_2$, with one or both aldehyde groups. The starting material **1** can be easily prepared by Diels-Alder reaction between cyclopentadiene and maleic anhydride, followed by reduction (Scheme **2**) [5].

Scheme 2



However, the oxidation of 1,4-diols to 1,4-dialdehydes is not an easily accomplishable transformation, as these diols usually give lactols or lactones [6] upon treatment with oxidizing reagents (see, however, reference [1]). The use of *o*-iodoxybenzoic acid in DMSO to oxidize 1,4-diols to lactols has recently been proposed [7], the transformation of **1** into **4** (Scheme **3**) being one of the examples used by the authors. In exploratory experiments we have confirmed that only lactol **4** is obtained when **1** is treated with a number of oxidizing reagents; two examples are mentioned in Scheme **3**.

Scheme 3



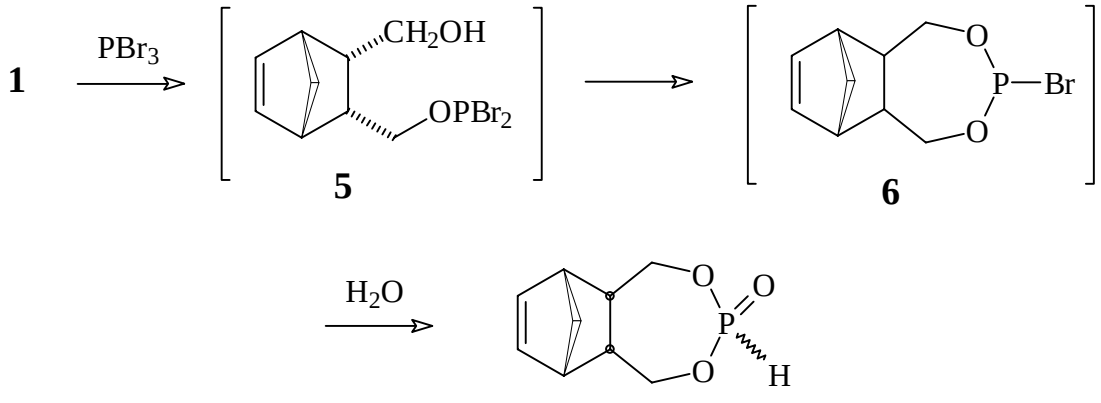
4

Reagent / solvent	Yield
o-iodoxybenzoic acid in DMSO	82 % (ref. 7)
PDC in CH_2Cl_2	60 %
Dess-Martin Periodinane in CH_2Cl_2	66 %

These results show that, as soon as one of the CH_2OH groups is oxidized (or even *during* the oxidation), the other –OH attacks the carbonyl group, forming the stable lactol **4** and preventing the oxidation of the second alcohol group. The obvious solution to this kind of problem is to protect one of the -OH groups and make the desired transformations on the other. However, before following this distended route (described ahead), we decided to try a smaller modification in the same method, just interchanging carbonyl group and phosphorane in the Wittig reaction: diol **1** could be transformed into the corresponding dibromo compound, and this into the di-Wittig reagent, which would be treated with formaldehyde.

Treatment of **1** with PBr_3, however, led to a surprising result: after hydrolysis and extraction, a phosphite of the diol was obtained as a mixture of stereoisomers that were separated by column chromatography (compounds **7a** and **7b**). The transformation of an alcohol into the corresponding bromide with PBr_3 normally involves the initial formation of phosphites [8] such as **5**, **6** (Scheme **4**) or trialkyl phosphites, that undergo a C-O bond breaking and simultaneous or successive C-Br bond formation.

Scheme 4

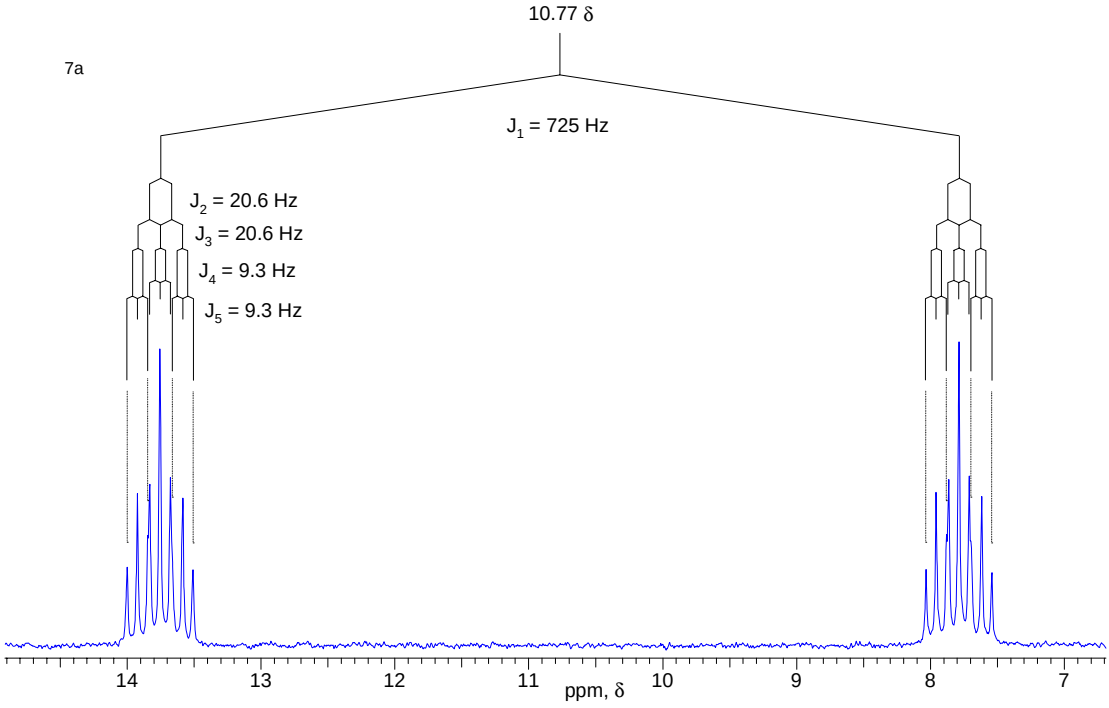


7a + **7b** (1:1)

90 %

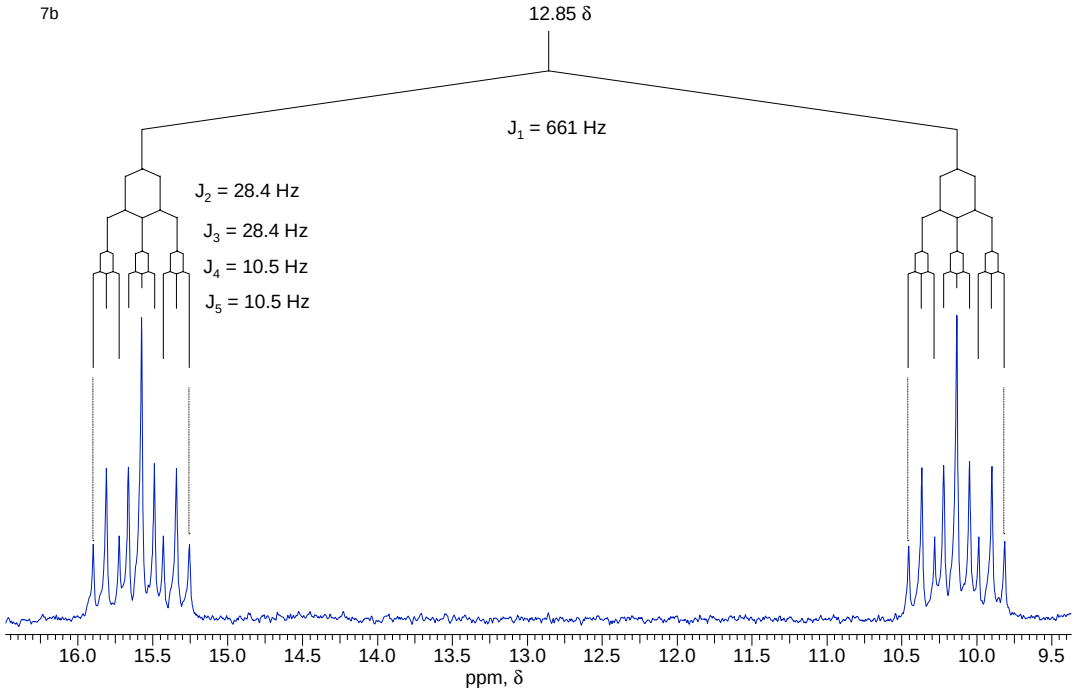
The final result of this reaction suggests that intermediate **5** has been fully transformed into intermediate **6** and no further reaction occurred; hydrolysis during extraction resulted in the formation of cyclic phosphites **7**. The unusual structures of compounds **7a** and **7b** was first suggested by the occurrence, in their ^{1}H-NMR spectra, of doublets corresponding to one hydrogen each in 6.71 δ (**7a**) and 6.73 δ (**7b**) with very large coupling constants (725 Hz for **7a** and 660 Hz for **7b**), values observed only when a P-H bond is present [9]. The ^{13}C-NMR spectra of these compounds also show doublets for the methylene carbons (CH_2O) corresponding to coupling between these methylene carbons and the phosphorus atom with normal J values [10] for this type of structure (6.9 Hz for **7a** and 5.1 Hz for **7b**). Further confirmation of these structures is given by the ^{31}P-NMR spectra. As shown in Figures **1** and **2**, each of these spectra contains a double triple triplet with the same J values found in the corresponding ^{1}H-NMR spectra. Obviously, the coupling between phosphorus and carbon cannot be seen in these spectra due to the low abundance of the ^{13}C isotope.

Figure 1. ^{31}P NMR spectrum of **7a**



It is clear, from the data we have collected until now, that compounds **7a** and **7b** are stereoisomers differing by the relative stereochemistry at the phosphorus atom; however, we could not yet assign the corresponding stereochemistry to each isomer. Further studies with this purpose are presently in course.

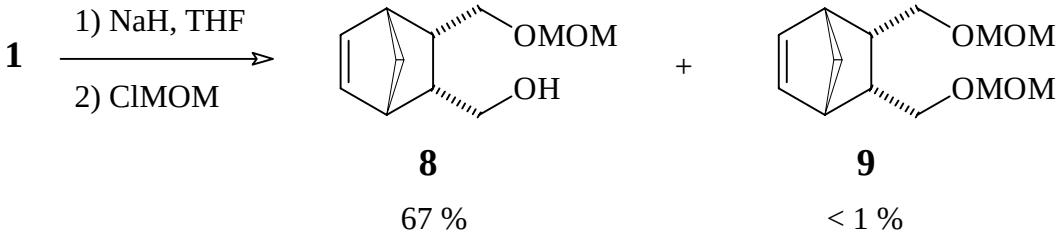
Figure 2. ^{31}P NMR spectrum of **7b**



The two cases of interactions just discussed, resulting in formation of **4** and of **7**,respectively, however similar, are not quite the same. To some extent, the formation of lactol **4** could be considered as a foreseeable result, because a 5-membered ring is formed, a transformation usually favored both kinetically and thermodynamically (entropy playing a very important role here); on the other hand, this doesn't seem to be the case of compound **7**, as 7-membered rings are not as easily formed. We should remark, however, that this is a special type of 7-membered ring: it contains two oxygen atoms (which, contrary to the usual carbon atom case, have no substituents, thus reducing transannular interactions) and two strong P-O bonds. Similar compounds, also containing 7-membered rings, have been previously reported [11].

Through the use of partial protection it was possible to realize the desired transformations. Compound **1** was converted to the monoprotected compound **8**. By using the technique of transforming the alcohol into an alcoxide before adding the electrophile, the formation of the diprotected compound **9** was reduced to a minimum, due to the low tendency towards dianion formation (Scheme **5**).

Scheme 5

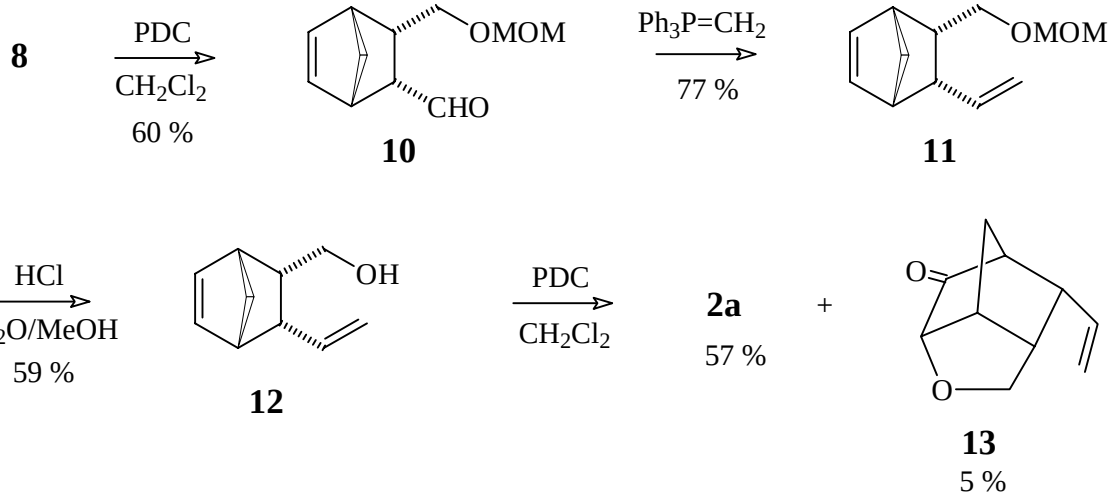


8 67 %

9 < 1 %

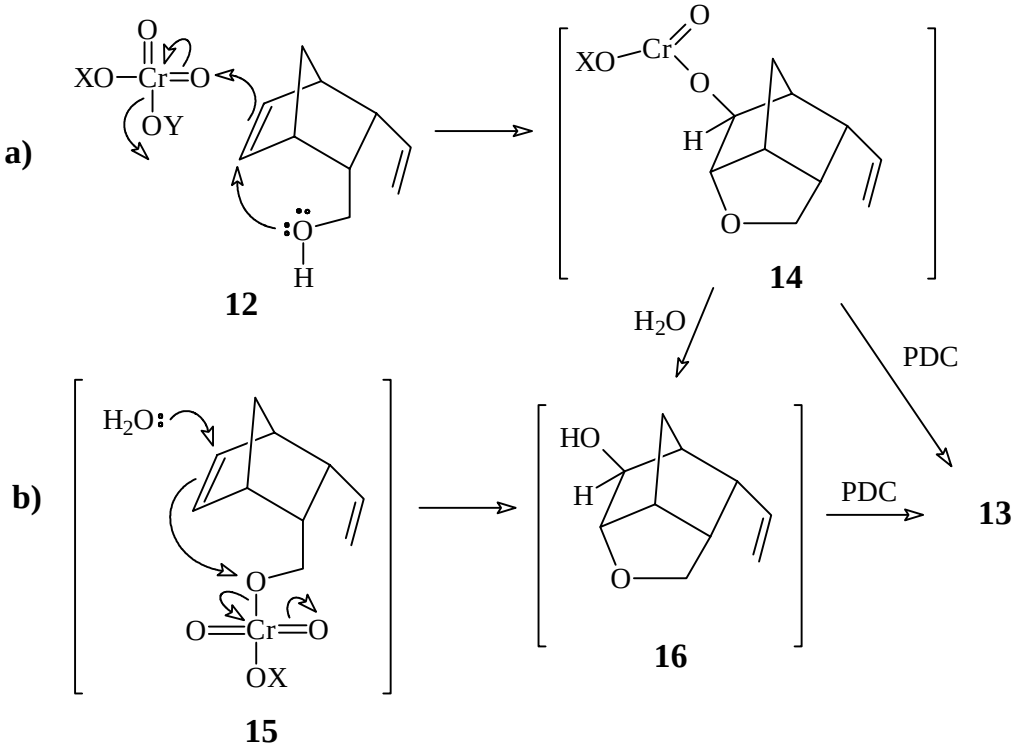
The subsequent transformations gave the expected results (Scheme **6**): oxidation of the free alcohol of **8** with PDC to produce the aldehyde in 60 % yield, a Wittig reaction giving olefin **11** (77 %) and deprotection of the alcohol (59 %). Compound **12** is rather unstable, and had to be kept in benzene solution with a small amount of hydroquinone to prevent decomposition during storage.

Scheme 6



The last step, oxidation of **12** with PDC, gave the desired product **2a** (57 % yield) together with a small amount of the by-product **13** (5 % yield), again an evidence of interference between two functions. The formation of compound **13** could be rationalized by at least two different ways, as depicted in Scheme **7**.

Scheme 7



According to hypothesis (a), the chromate reagent attacks the double bond (and not the alcohol), whose reactivity could be enhanced by influence of the –OH group, resulting in the intermediate **14;** this would be *either* hydrolyzed to **16** and then oxidized to **13**, *or* would be directly oxidized to **13**, more likely via reaction with Cr (VI). In hypothesis (b), the normal intermediate for this kind of oxidation (**15**) [8] would be formed first but, instead of the normal abstraction of the hydrogen α to the –OH group, a nucleophillic attack of the double bond (possibly assisted by water) would take place, resulting in the same intermediate **16**. In any case it is obvious that the formation of compound **13** is a result of the proximity and the resulting interactions between the double bond and the –OH group in compound **12**.

Conclusions

The relatively simple synthesis of compound **2a** here described shows the importance of taking into account the intramolecular interactions between two functions, even in simple molecules, and how valuable the use of protective groups can be to overcome this sort of problems. The ease of formation and the stability of 5-membered ring lactols is remarkable, as well as the surprising formation of the cyclic phosphite **7**. As compound **13** is formed in only 5 % yield, this reaction is obviously less important. However, it is a further evidence of how close to each other are the functions in these Diels-Alder adducts, and how important this aspect can be when designing organic syntheses.

Acknowledgments

The authors thank the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP), the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and the Coordenadoria de Aperfeiçoamento de Pessoal do Ensino Superior (CAPES) for financial support.

Experimental section

General

NMR spectra were measured using a Bruker DPX-300 (300 MHz ^{1}H-NMR and 75 MHz ^{13}C-NMR) or DRX-400 (400 MHz ^{1}H-NMR and 100 MHz ^{13}C-NMR) instruments; deuterochloroform was used as solvent and tetramethylsilane as the internal standard; ^{31}P-NMR spectra were measured with Bruker DPX-300 (121.5 MHz) using H_3PO_4/D_2O as external standard. IR spectra were measured with a Perkin-Elmer 1600-FT or Nicolet 5ZDX spectrometers. TLC was performed on precoated silica gel 60 F_{254} plates (0.25 mm thick, Merck), and for column chromatography silica gel 60 70-230 mesh (Merck) was used. Reported yields refer to samples with the same purity as the samples used in the following step.

4-Oxatricyclo[5.2.1.0^{2,6}]dec-8-en-3-ol (**4**)

a) Oxidation with PDC. To a solution of pyridinium dichromate (3.0 g, 8.0 mmol) in anhydrous CH_2Cl_2 (30 mL), maintained under N_2 atmosphere, was added a solution of compound **1** (640 mg, 4.1 mmol) in CH_2Cl_2 (10 mL). After stirring for 24 h at room temperature, the solution was filtered through a small column of $MgSO_4$. The solvent was removed under vacuum and the residue was chromatographed in a column of silica gel using a 4:6 mixture of hexane / ethyl acetate. Yield 374 mg (60 %).

b) Oxidation with Dess-Martin periodinane. To a solution of diol **1** (61 mg, 0.37 mmol) in anhydrous CH_2Cl_2 (1.2 mL), maintained under N_2 atmosphere, was added a solution of Dess-Martin periodinane [12] (351 mg, 0.80 mmol) in CH_2Cl_2 (3 mL). After stirring at room temperature for 20 min, the reaction mixture was diluted with ethyl ether (10 mL) and quenched with a 1.3 M aqueous solution of NaOH. After 10 min of vigorous stirring the organic phase was separated, washed with aqueous NaOH solution, water, and dried with $MgSO_4$. The solvent was removed under vacuum and the residue was purified by chromatography as described in (a). Yield 37 mg (66 %).

Spectroscopic data: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 6.20 (dd, 1 H, J_1 = 5.6 Hz, J_2 = 3.0 Hz), 6.09 (dd, 1 H, J_1 = 5.8 Hz, J_2 = 3.0 Hz), 4.98 (s, 1 H), 3.98 (dd, 1 H, J_1 = 7.6 Hz, J_2 = 8.8 Hz), 3.46 (dd, 1 H, J_1 = 8.8 Hz, J_2 = 2.0 Hz), 3.03 (m, 1 H), 2.95 (m, 1 H), 2.87 (m, 2 H), 2.63 (br. s, 1 H), 1.45 (dt, 1 H, J_1 = 8.3 Hz, J_2 = J_3 = 1.6 Hz), 1.36 (d, 1 H, J = 8.3 Hz); ^{13}C-NMR ($CDCl_3$, 100 MHz), 134.7 (CH), 134.6 (CH), 100.4 (CH), 69.3 (CH_2), 55.6 (CH), 51.9 (CH), 46.0 (CH), 45.9 (CH), 44.9 (CH).

4,6-Dioxa-5-phosphatricyclo[7.2.1.0^{2,8}]dodec-10-en-5-one (**7a** and **7b**).

A solution of diol **1** (50 mg, 0.32 mmol) and PBr_3 (26 mg, 0.96 mmol) in anhydrous ethyl ether (10 mL) was kept under N_2 atmosphere at 5°C for 45 h. After quenching with chopped ice and extraction with ethyl ether, the organic phase was washed with water and saturated brine, and dried with $MgSO_4$. The solvent was removed under vacuum to give 58 mg (90 %) of a mixture of isomers that were separated by chromatography in a silica gel column using a 3:7 mixture of hexane / ethyl acetate as eluent. Both isomers are white crystalline solids. Compound **7a**: yield 29 mg (45 %); ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.71 (d, 1 H, J [H-P] = 725 Hz), 6.13 (br. t, 2 H, J = 1.6 Hz), 4.16 (dt, 2 H, J_1 = J_2 = 11.7 Hz, J_3 [H-P] = 9.3 Hz), 4.05 (ddd, 2H, J_1 = 11.7 Hz, J_2 [H-P] = 20.4 Hz, J_3 = 3.6 Hz), 2.84 (m, 2 H), 2.81 (m, 2 H), 1.59 (dt, 1 H, J_1 = 8.5 Hz, J_2 = J_3 = 1.7 Hz), 1.53 (br. d, 1 H, J = 8.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 134.9 (CH), 66.0 (CH_2, d, J_{C-P} = 6.9 Hz), 51.2 (CH_2), 45.7 (CH), 44.7 (CH); ^{31}P-NMR ($CDCl_3$, 121.5 MHz) δ 10.77 (dtt, J_1 = J_2 = 9.3 Hz, J_3 = J_4 = 20.6 Hz, J_5 = 725 Hz). Compound **7b**: yield 29 mg (45 %) ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.73 (d, 1H, J [H-P] = 660 Hz), 6.13 (t, 2H, J = 1.9 Hz), 4.14 (ddd, 2H, J_1 [H-P] = 28.4 Hz, J_2 = 12.0 Hz, J_3 = 3.0 Hz), 3.68 (dt, 2H, J_1 = J_2 = 12.0 Hz, J_3 [H-P] = 10.7 Hz), 2.88 (m, 2H), 2.83 (m, 2H), 1.59 (dt, 1H, J_1 = 8.5 Hz, J_2 = J_3 = 1.7 Hz), 1.50 (br.

d, 1H, J = 8.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 135.0 (CH), 65.5 (CH_2, d, J_{C-P} = 5.1 Hz), 50.6 (CH_2), 45.7 (CH), 42.8 (CH); ^{31}P-NMR ($CDCl_3$, 121.5 MHz) δ 12.85 (dtt, $J_1 = J_2$ = 10.5 Hz, $J_3 = J_4$ = 28.4 Hz, J_5 = 660 Hz); IR (KBr) ν_{max} 2966, 2389, 1267, 1047, 797 cm^{-1}.

{3-[(Methoxymethoxy)methyl]bicyclo[2.2.1]hept-5-en-2-yl}methan-1-ol (**8**) **and (methoxymethoxy)-{3-[(methoxymethoxy)methyl]bicyclo[2.2.1]hept-5-en-2-yl}methane** (**9**).

To a suspension of NaH (29 mg of a 60 % suspension in mineral oil, corresponding to 1.2 mmol), previously washed with anhydrous hexane, in anhydrous THF (10 mL), maintained at 0°C under N_2 atmosphere, was added a solution of diol **1** (103 mg, 0.66 mmol) in THF (1 mL). After 5 min the ice bath was removed and the reaction mixture was stirred for 1 h. Chloromethyl methyl ether (80 mg, 1.0 mmol) was then added and the mixture was stirred for a further 1 h period. After quenching with chopped ice, the product was extracted with ethyl ether, the organic phase was dried with $MgSO_4$ and the solvent was removed under vacuum. The crude product was purified by column chromatography in silica gel, using a 7:3 mixture of hexane and ethyl acetate as eluent. Compound **8**: yield 88 mg (67 %); ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.10 (dd, 1H, J_1 = 5.5 Hz, J_2 = 2.6 Hz), 6.06 (dd, 1H, J_1 = 5.5 Hz, J_2 = 2.6 Hz), 4.60 (s, 2H), 3.42 (m, 4H), 3.37 (s, 3H), 2.85 (m, 2H), 2.55 (m, 2H), 1.45 (dt, 1H, J_1 = 8.3 Hz, $J_2 = J_3$ = 1.9 Hz), 1.37 (dt, 1H, J_1 = 8.3 Hz, $J_2 = J_3$ = 1.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 135.1 (CH), 134.8 (CH), 96.6 (CH_2), 68.9 (CH_2), 63.0 (CH_2), 55.6 (CH_3), 49.7 (CH_2), 46.43 (CH), 46.38 (CH), 45.4 (CH), 41.9 (CH); IR (KBr) ν_{max} 3421, 2934, 1383, 1157, 1111, 1045 cm^{-1}. Compound **9**: yield 1 mg (< 1 %); this sample was identical (by ^{1}H-NMR) to other samples obtained in higher yields by other methods, from which come some of the spectral data that follow: ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.14 (t, 2H, J = 1.9 Hz), 4.58 (d, 2H, J = 8.4 Hz), 4.56 (d, 2H, J = 8.4 Hz), 3.38 (m, 2H), 3.35 (s, 6H), 3.13 (t, 2H, J = 9.1 Hz), 2.95 (m, 2H), 2.48 (m, 2H), 1.50 (dt, 1H, J_1 = 8.3 Hz, $J_2 = J_3$ = 1.9 Hz), 1.35 (dt, 1H, J_1 = 8.3 Hz, $J_2 = J_3$ = 1.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 135.4 (CH), 96.5 (CH_2), 67.9 (CH_2), 55.2 (CH_3), 49.0 (CH_2), 45.6 (CH), 41.5 (CH); IR (KBr) ν_{max} 2991, 1158, 1111, 1055 cm^{-1}.

3-[(Methoxymethoxy)methyl]bicyclo[2.2.1]hept-5-ene-2-carbaldehyde (**10**).

To a solution of pyridinium dichromate (113 mg, 0.30 mmol) in anhydrous CH_2Cl_2 (3 mL), maintained under N_2 atmosphere, was added a solution of compound **8** (39 mg, 0.19 mmol) in CH_2Cl_2 (3 mL). After stirring for 24 h at room temperature, the product was extracted and purified as described in experiment 1a. Yield 22 mg (60 %). ^{1}H-NMR δ ($CDCl_3$, 300 MHz) 9.41 (d, 1H, J = 3.9 Hz), 6.33 (dd, 1H, J_1 = 5.7 Hz, J_2 = 2.7 Hz), 6.20 (dd, 1H, J_1 = 5.7 Hz, J_2 = 3.0 Hz), 4.54 (s, 3H), 3.38 (d, 2H, J = 7.8 Hz), 3.32 (s, 3H), 3.10 (m, 1H), 3.01 (m, 1H), 2.97 (m, 1H), 2.83 (m, 1H), 1.55 (dt, 1H, J_1 = 8.7 Hz, $J_2 = J_3$ = 2.0 Hz), 1.40 (dt, 1H, J_1 = 8.7 Hz, $J_2 = J_3$ = 1.5 Hz); ^{13}C-NMR δ ($CDCl_3$, 75 MHz) 204.6 (C=O), 135.03 (CH), 134.95 (CH), 96.1 (CH_2), 67.9 (CH_2), 54.9 (CH or CH_3), 54.3 (CH_3 or CH), 49.1 (CH_2), 45.7 (CH_2), 44.9 (CH), 44.8 (CH); IR (KBr) ν_{max} 2935, 2740, 1713, 1391 cm^{-1}.

Methoxy[(3-vinylbicyclo[2.2.1]hept-5-en-2-yl)methoxy]methane (**11**)

To a mixture of the phosphonium salt Ph_3PCH_3Br (207 mg, 0.58 mmol) and THF (5 mL), cooled to 0°C under a N_2 atmosphere, was added a solution of *n*-BuLi (0.35 mL of a 1.17 M solution in hexane, 0.67 mmol). After stirring for 15 min at 0°C, a solution of compound **10** (56 mg, 0.29 mmol) in THF (1 mL) was added. The ice bath was removed and the reaction mixture was stirred at room temperature for 22 h. After quenching with chopped ice and extracting with ethyl ether, the resulting organic solution was washed with water and saturated brine, and dried with $MgSO_4$. The solvent was removed under vacuum and the residue was purified by column chromatography (silica gel), eluting with a 7:3 mixture of hexane / ethyl acetate. Yield 43 mg (77 %). ^{1}H-NMR δ ($CDCl_3$, 300 MHz) 6.18 (t, 2H, J = 1.1 Hz), 5.30 (dt, 1H, J_1 = 16.9 Hz, J_2 = J_3 = 9.9 Hz), 5.07 (ddd, 1H, J_1 = 16.9 Hz, J_2 = 2.5 Hz, J_3 = 0.6 Hz), 4.90 (ddd, 1H, J_1 = 9.9 Hz, J_2 = 2.6 Hz, J_3 = 0.4 Hz), 4.58 (d, 1H, J = 6.4 Hz), 4.55 (d, 1H, J = 6.4 Hz), 3.34 (s, 3H), 3.29 (dd, 1H, J_1 = 9.6 Hz, J_2 = 5.6 Hz), 3.04 (dd, 1H, J_1 = 9.6 Hz, J_2 = 10.5 Hz), 2.98 (m, 1H), 2.86 (dt, 1H, J_1 = J_2 = 9.9 Hz, J_3 = 3.4 Hz), 2.79 (m, 1H), 2.46 (dddd, 1H, J_1 = 10.5 Hz, J_2 = 9.9 Hz, J_3 = 5.6 Hz, J_4 = 3.4 Hz), 1.49 (dt, 1H, J_1 = 8.1 Hz, J_2 = J_3 = 1.5 Hz), 1.35 (dt, 1H, J_1 = 8.1 Hz, J_2 = J_3 = 1.5 Hz); ^{13}C-NMR δ ($CDCl_3$, 75 MHz) 139.6 (CH), 135.8 (CH), 135.3 (CH), 115.9 (CH_2), 96.5 (CH_2), 69.0 (CH_2), 55.1 (CH_3), 49.0 (CH_2), 48.2 (CH), 46.9 (CH), 45.2 (CH), 43.6 (CH); IR (KBr) ν_{max} 2924, 1634, 1453, 1151, 1041, 912, 732 cm^{-1}.

(3-Vinylbicyclo[2.2.1]hept-5-en-2-yl)methan-1-ol (**12**).

To a solution of compound **11** (2.41 g, 12.4 mmol) in MeOH (70 mL) were added a few drops of concentrated HCl. The reaction mixture was heated to 60°C for 3 h (following the disappearance of the starting material by TLC) and then most of the MeOH was removed under vacuum. The product was extracted with ethyl ether, the organic solution was washed with $NaHCO_3$ solution and dried with $MgSO_4$. The solvent was removed under vacuum and the residue was purified by chromatography on a silica gel column, using a 7:3 mixture of hexane / ethyl acetate as eluent. Yield 1.10 g (59 %). ^{1}H-NMR δ ($CDCl_3$, 300 MHz) 6.17 (m, 2H), 5.34 (dt, 1H, J_1 = 17.0 Hz, J_2 = J_3 = 10 Hz), 5.11 (dd, 1H, J_1 = 17.0 Hz, J_2 = 2.4 Hz), 4.94 (dd, 1H, J_1 = 10 Hz, J_2 = 2.4 Hz), 3.37 (dd, 1H, J_1 = 10 Hz, J_2 = 6.6 Hz), 3.15 (dt, 1H, J_1 = J_2 = 10 Hz, J_3 = 3.5 Hz), 3.02 (br. s, 1H), 2.94 (m, 1H), 2.85 (dt, 1H, J_1 = J_2 = 10 Hz, J_3 = 3.4 Hz), 2.78 (m, 1H), 2.40 (ddt, 1H, J_1 = J_2 = 10 Hz, J_3 = 6.6 Hz, J_4 = 3.4 Hz), 1.49 (dt, 1H, J_1 = 8.4 Hz, J_2 = J_3 = 1.8 Hz), 1.35 (d, 1H, J = 8.4 Hz); ^{13}C-NMR δ ($CDCl_3$, 75 MHz) 139.9 (CH), 135.6 (CH), 135.3 (CH), 116.1 (CH_2), 63.4 (CH_2), 49.4 (CH_2), 48.9 (CH), 46.8 (CH), 46.6 (CH), 44.9 (CH); IR (KBr) ν_{max} 3329, 2966, 1636, 1451, 1342, 910, 732 cm^{-1}.

3-Vinylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde (**2a**) **and 4-Oxa-9-vinyltricyclo[4.2.1.0^{3,7}]-nonan-2-one** (**13**)

To a solution of pyridinium dichromate (230 mg, 0.59 mmol) in anhydrous CH_2Cl_2 (4 mL) maintained under N_2 atmosphere, was added a solution of compound **12** (62 mg, 0.41 mmol) in CH_2Cl_2 (2 mL). After stirring for 24 h at room temperature, the product was extracted and purified as described in experiment 1a, using a 7:3 mixture of hexane / ethyl acetate as eluent. Compound **2a**: yield 35 mg (57 %). ^{1}H-NMR δ ($CDCl_3$, 300 MHz) 9.35 (d, 1H, J = 3.4 Hz), 6.36 (dd, 1H, J_1 = 5.9 Hz, J_2 = 2.8 Hz), 6.24 (dd, 1H, J_1 = 5.9 Hz, J_2 = 2.8 Hz), 5.41 (dt, 1H, J_1 = 17.0 Hz, J_2 = J_3 = 10.0 Hz), 5.21 (ddd, 1H, J_1 = 17.0 Hz, J_2 = 2.0 Hz, J_3 = 0.6 Hz), 5.02 (ddd, 1H, J_1 = 10.0 Hz, J_2 = 2.0 Hz, J_3 = 0.6 Hz), 3.24 (dt, 1H, J_1 = J_2 = 10.0 Hz, J_3 = 3.4 Hz), 3.12 (m, 1H), 3.02 (dt, 1H, J_1 = 10.0 Hz, J_2 = J_3 = 3.4 Hz), 2.92 (m, 1H), 1.54 (dt, 1H, J_1 = 8.6 Hz, J_2 = J_3 = 1.9 Hz), 1.41 (m, 1H); ^{13}C-NMR δ ($CDCl_3$, 75 MHz) 205.5 (C=O), 138.6 (CH), 135.9 (CH), 135.5 (CH), 117.0 (CH_2), 57.4 (CH), 49.4 (CH_2), 49.0 (CH), 48.5 (CH), 45.4 (CH); IR (KBr) ν_{max} 2972, 2729, 1716, 1636, 1453, 1392, 912, 737 cm^{-1}. Compound **13**: yield 3 mg (5 %). ^{1}H-NMR δ ($CDCl_3$, 300 MHz) 5.59 (ddd, 1H, J_1 = 17.4, J_2 = 10.0 Hz, J_3 = 8.3 Hz), 5.19 (ddd, 1H, J_1 = 17.4 Hz, J_2 = 1.5 Hz, J_3 = 1.0 Hz), 5.15 (dd, 1H, J_1 = 10.0, J_2 = 1.5 Hz), 3.85 (m, 3H), 3.09 (m, 1H), 2.78 (m, 2H), 2.47 (m, 1H), 1.91 (d, 1H, J = 11.5 Hz), 1.78 (d, 1H, J = 11.5 Hz); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 211.9 (C=O), 134.9 (CH), 118.3 (CH_2), 80.8 (CH), 70.4 (CH_2), 50.7 (CH), 44.6 (CH), 44.1 (CH), 41.2 (CH), 29.1 (CH_2); IR (KBr) ν_{max} 2974, 1753, 1639, 1178, 1129, 1040 cm^{-1}.

References and Notes

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Sample availability: Samples of compounds **1** and **12** are available from MDPI.