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THE USE OF A COMBINED ANNULATION - RING CLEAVAGE STRATEGY FOR THE NOVEL SYNTHESIS OF SEVEN , EIGHT AND NINE - MEMBERED RINGS

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Summary:- *A new method for the synthesis of seven, eight and nine-membered rings carbocycles is described. Reaction of the allylsilane* ***4*** *with a range of enediols gives, in a single-step, bicyclic diols which are oxidatively cleaved to form a medium ring product.*

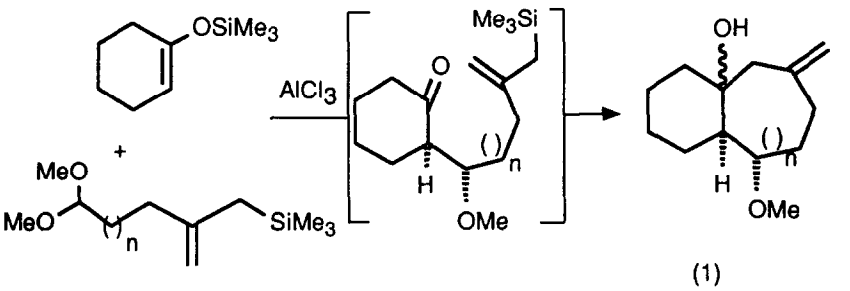
Introduction

Achieving the facile synthesis of medium sized carbocyclic rings is still a major challenge in organic chemistry [1]. The classic acyloin and Dieckmann reactions are still amongst the more useful methods available, with intramolecular alkylation on conformationally restricted precursors also being of value [2]. Amongst the more recently introduced methods are some interesting [4 + 4] cycloadditions for eight membered ring synthesis [3], and of more general utility, intramolecular Claisen rearrangements [4] and intramolecular McMurry coupling of dicarbonyl compounds [5]. However access to these compounds *via* a direct annulation strategy is currently limited, which is restrictive if one considers the large number of fused bi- and tricyclic medium sized ring compounds which are known.

In addition to the above methods a further route to these compounds are ring expansion reactions, with the ring cleavage of bicyclic bridgehead diols [6] being one of the more widely applicable examples of this strategy. However this protocol is often limited because of a lack of simple routes to the required diols. This paper addresses this problem by describing a new synthesis of seven, eight and nine-membered rings which combines a direct annulation strategy with a ring cleavage of a bicyclic diol. The result of this is an improved access to medium sized rings possessing a wide variety of additionally useful functionality, of value in achieving the synthesis of a range of complex target molecules.

This paper is warmly dedicated to Professor Jake MacMillan FRS, to mark the occasion of his retirement.

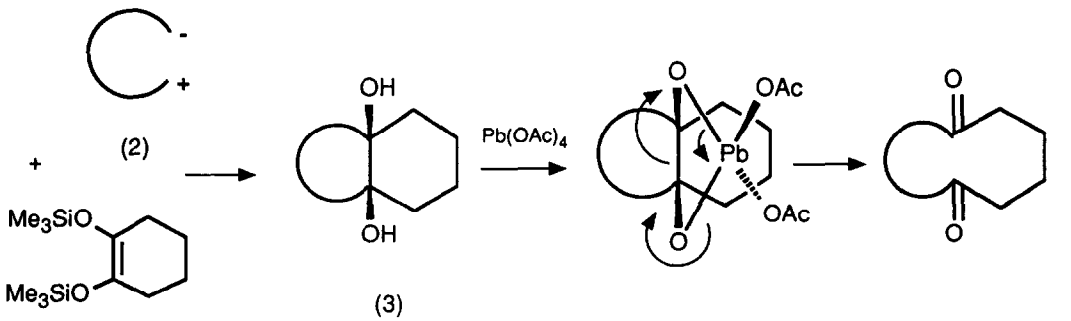
The annulation strategy employed utilises multi-functional compounds, which are becoming increasingly important in organic synthesis, especially because of the opportunities they offer for performing efficient single-step multi-bond forming reactions. A good example of this is the novel bifunctional annulation strategy, for the direct synthesis of carbocyclic compounds, that we have recently introduced [7]. This involves the selective *intermolecular* reaction of the acetal function of a bifunctional



(1)

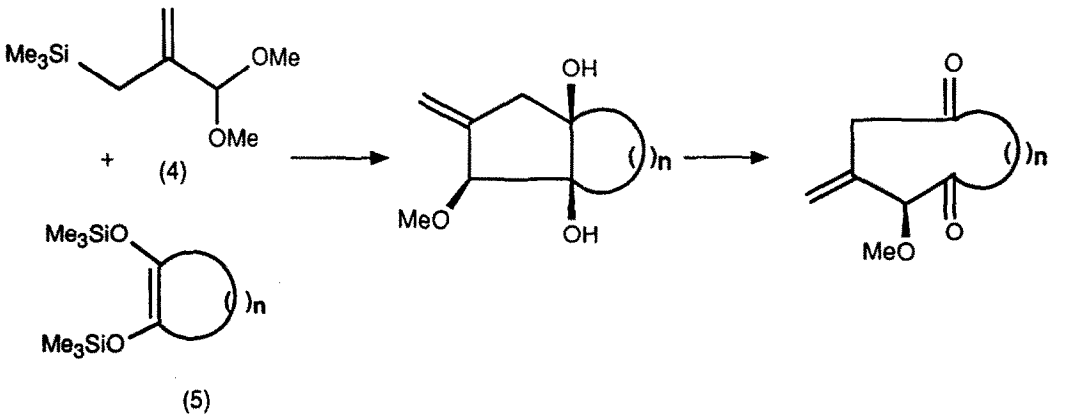
allylsilane with an enolsilane to form after sequential *intramolecular* ring closure an annulated product **1**. This arises because the alternative "self destructive" pathway, of the allylsilane attacking the acetal, is a kinetically disfavoured process which allows intermolecular attack to be the favoured pathway [8].

It is apparent that the ease with which these acetals allow the preparation of carbocyclic compounds in a single-step process, could provide considerable advantages in addressing the problems of medium sized ring synthesis. Thus reaction of such bifunctional reagents, whose reactivity pattern can be represented by the formalism **2**, with silylated enediol derivatives, should form a diol **3** in one pot. This would then be susceptible to ring cleavage with an oxidant such as lead tetraacetate, leading to a ring expanded product.



(3)

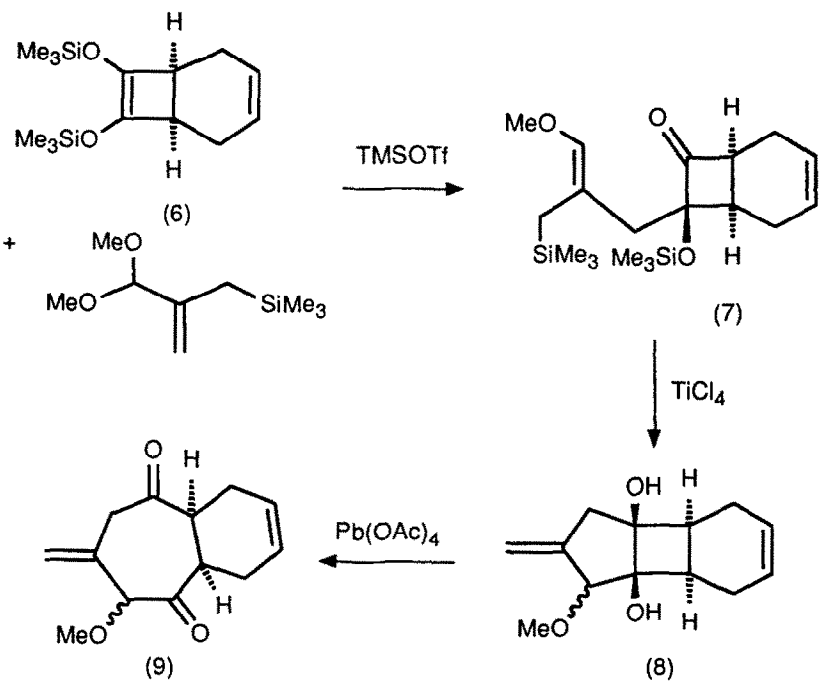
Since such ring expansions are more facile when the diol to be cleaved is of the *cis* configuration, an ideal bifunctional reagent for such a process would be **4** which is an excellent precursor to exclusively *cis*-fused cyclopentanes. Therefore to achieve the preparation of a range of ring cleaved products by using **4**, it is the size of the silylated ene-diol derivative **5** that should be varied. Since, as described below, these compounds are genuinely readily available, this overall process should be very facile.



Discussion

The required acyloin reaction derived silylated enediols are obtained in high yields by quenching of the traditional acyloin reaction conditions of sodium sand in toluene with chlorotrimethylsilane[10], and so are readily available for study with these bifunctional annulating reagents.

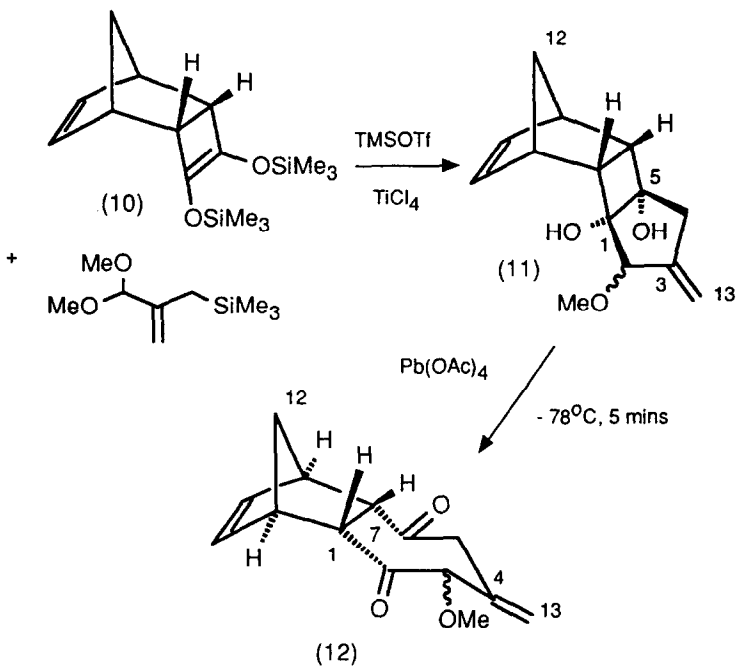
The initial study focused upon the four-membered ring enediol **6** to give access to seven-membered systems. Upon reaction of the enediol **6** with the allylsilane **4** [11], using a catalytic amount of TMSOTf, the



intermediate ketone **7** was isolated in 94% yield [12]. In previous studies of **4** it was shown that the initial bond forming reaction, which occurs by nucleophilic attack at an unsymmetrical carbocation, displays a dependence upon the structure of the enol ether, with S_N1' attack being highly favoured in most cases [13]. The present example indicates that a similar mode of reaction has occurred to form an intermediate which cyclizes to the diol **8**, whose symmetry masks any indication of the inherent initial regioselectivity of this process.

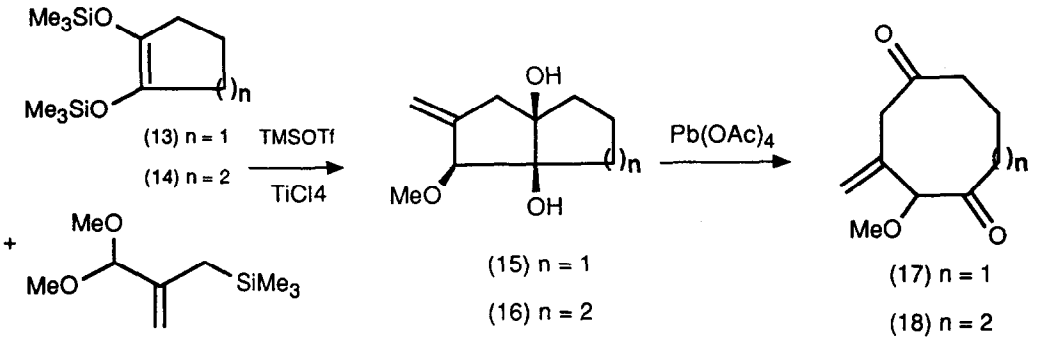
Routes to bridgehead diols normally involve a multi-step procedure and the ability of the acetal-allylsilane **4** to undergo this single-step annulation reaction offers appreciable promise, especially when considered with the fact that **8** possesses additional synthetically useful functionality. Ring expansion of the diol **8**, by treatment with lead tetraacetate at -78°C for 5 minutes [14], afforded 51% of the diketone **9**, based on the enediol. This overall strategy thus provides an alternative and efficient way of preparing highly functionalised fused seven-membered rings.

A second example of this reaction is the use of the readily available enediol **10**, which in a similar reaction sequence to the above gave 50% of the diketone **12**, via the diol **11**. This example demonstrates how the conformational rigidity of the enediol can allow the diastereoselective formation of the bicyclic alcohol, which can be ring expanded without epimerisation.



This new strategy also permits the preparation of eight-membered rings. Thus reaction of **4** with the silylated enediol **13** led, *via* the diol **15**, to a new synthesis of the eight-membered ring **17** in an overall yield of 35%. The lower yield in this overall process reflect a slower reaction in the first two bond forming process, during which some decomposition of the acetal occurs. However since there is no necessity to

purify the intermediate diol the new chemistry does constitute a reasonably efficient way to synthesise eight-membered rings.



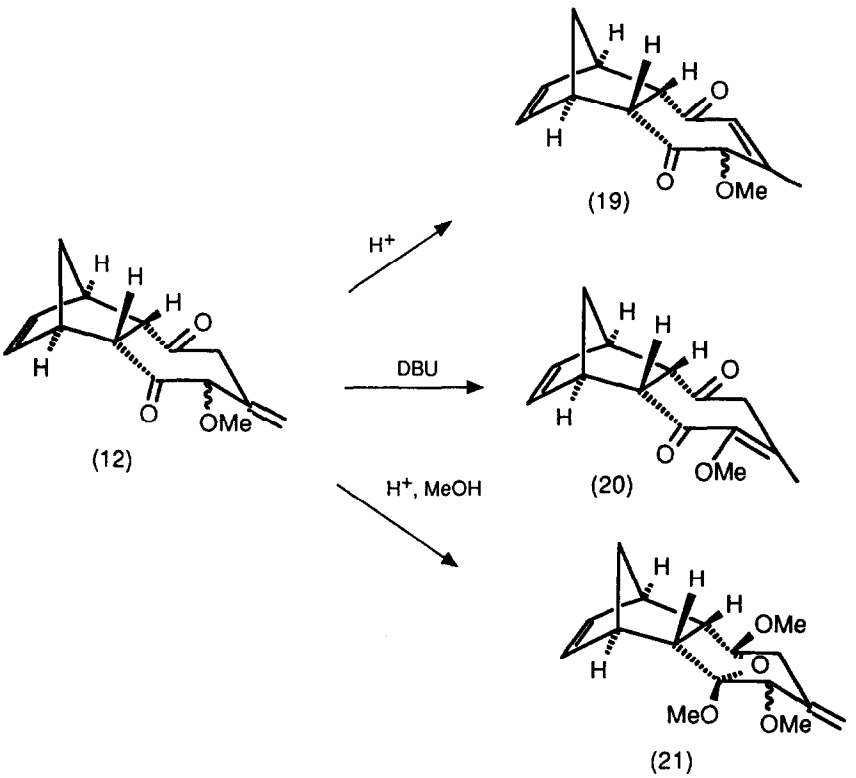
More notably nine-membered rings, which are the most difficult to synthesise via an annulation strategy, can also be accessed in this manner. Reaction of the enediol **14** with **4** gave 67% isolated yield of the corresponding diol **16**. Once obtained **16** reacted with $Pb(OAc)_4$ in a ring cleavage process to form the nine-membered ring diketone **18** in essentially quantitative yield. In both cases the direct conversion of crude mixtures of the initially formed diols gives greater overall yields e.g. 75% for **18**.

The fact that the two ketones in these two products can be chemodifferentiated is an important additional feature of this chemistry which enhances and contrasts it with other similar ring cleavages, for which the two ketones are often chemically indistinguishable. An example of this is seen in some transformations of the dione **12** (Scheme), which, because of its scope for oxidative cleavage of the norbornene, is of obvious use as a precursor to a variety of naturally occurring fused five-seven ring systems. For instance, mild acid treatment converts **12** to the keto-enone **19**, whereas base treatment (DBU) moves the exocyclic alkene into the ring in the opposite sense, giving the enol ether **20**. In both **19** and **20** the ketone functions will thus have very different chemoselectivities. Additionally, both ketone functions in this dione can be simultaneously protected as the cyclic acetal **21**, so permitting transformations of the remaining functionality to be undertaken.

The combination of a direct annulation strategy and a ring cleavage strategy does therefore offer real advantages in accessibility and yield for the synthesis of ring sizes of this type. The method will be especially useful in reactions with bicyclic enediols such as **10** to give access to fused medium sized rings. Furthermore the demonstration of using substrate control to achieve diastereoselectivity in these reactions provides an additional advantage. Combining all of this with the wealth of useful functionality readily introduced in this process offers considerable scope for the ready synthesis of complex synthetic targets, which we are in the process of demonstrating.

Acknowledgements: *We thank SERC (Grant GR/D/83019) and a studentship (to FSR), and the University of Bristol Research Committee, for support of this work, and Dr. Chris Willis for helpful discussions.*

Scheme



Experimental

All organic solvents were distilled prior to use as listed (tetrahydrofuran and ether, which refers to diethyl ether, from sodium/benzophenone; dichloromethane and triethylamine from calcium hydride; methanol from dimethoxy magnesium; trimethylorthoformate and carbon tetrachloride from potassium hydroxide). Infra-red spectra were recorded on a Perkin-Elmer 881 spectrophotometer, nmr on JEOL PMX 60, GX 270 and GX 400 spectrometers using TMS or CH_2Cl_2 as an internal standard, and mass spectra were obtained on a VG9090 mass spectrometer. Reactions involving air and/or moisture sensitive intermediates were performed under a nitrogen atmosphere and magnesium sulphate was used for drying solutions of organic compounds.

The enediols were prepared according to reference 10, with the example below being representative:-

Enediol **10** :- A 3-necked 1l round bottomed flask, fitted with a nitrogen line, pressure equalised dropping funnel and mechanical stirrer was flame dried under a flow of nitrogen. The flask was charged with dry toluene (300 ml), freshly cut sodium (9.60 g; 0.4 g atom) was added and the mixture was vigorously stirred under gentle reflux for 1h to form sodium sand. A solution of dimethyl bicyclo[2.2.1]hept-5-ene-2,3-di-carboxylate (21.0 g: 100 mmoles) and freshly distilled chlorotrimethylsilane (60.0 ml; 400 mmoles) in toluene (100 ml) was added dropwise over 2 h and the resulting grey-purple mixture refluxed for 20 h under

nitrogen. The reaction mixture was cooled to room temperature and filtered through a sinter under nitrogen. The residue was washed with ether and the solvent evaporated *in vacuo* to give an orange oil (26.3 g; 89%). Vacuum distillation afforded the enediol **10** as a colourless oil (21.2 g; 72%). b.p. 90-100°C/0.5 mmHg. Found: C, 60.70; H, 9.13, $C_{15}H_{26}O_2Si_2$ requires C, 61.17, H, 8.90%. ν_{max}, 1 745 (C=C), 1 712 (C=C), 1 250 (Si-Me_3) cm^{-1}. ^1H nmr, 6.25-6.24 (2H, m, C=CH_2), 2.71-2.68 (2H, m, -CHCOTMS), 2.56-2.52 (2H, m, -CHCHCOTMS), 1.92-1.88 (1H, m, -CH_2), 1.55-1.51 (1H, brd, -CH_2), 0.16 (18H, s, -$SiMe_3$). ^{13}C nmr, 131.5 (CH), 125.9 (C), 54.2 (CH_2), 42.3 (CH), 41.1 (CH), 0.4 (CH_3). m/z, 294 (M^+, 27.0%), 282, 228, 147, 73 (100%).

General Procedure for the Reaction of Enediols with Allylsilanes

The enediol (1.0 mmol) and allylsilane (1.0 mmol) in dry CH_2Cl_2 (15 ml), under nitrogen at -78°C, were treated with TMSOTf (0.01 mmol). After 1h, $TiCl_4$ (2.0 mmol) in CH_2Cl_2 (2 ml) was added at -78°C and the resulting reddish brown solution was stirred for 1.5h. Addition of water (7 ml) at -78°C and warming to room temperature was followed by washing with CH_2Cl_2 (4 x 5 ml). The combined organic layers were washed with water (10 ml), saturated aqueous sodium hydrogen carbonate (10 ml), dried ($MgSO_4$) and evaporated *in vacuo* to give an oil, which can either be used directly or purified by chromatography on silica gel (eluting with diethyl ether-petrol 1:1) to afford the diol.

Example of the isolation of the intermediate hydroxy ketone:-
2-Trimethylsilyloxy-3-oxo-2-(3'-methoxy-2'-trimethylsilylmethyl-2'-propenyl)-bicyclo[4.2.0]oct-6-ene **7**:
2,3-Bis(trimethylsilyloxy)bicyclo[4.2.0]oct-2,6-diene (0.15 g; 0.53 mmol) and 3,3-dimethoxy-2-trimethylsilylmethylprop-1-ene (0.10 g; 0.53 mmol) were reacted with TMSOTf (0.010 ml; 0.053 mmol). Column chromatography, using ether-petrol (1:1), afforded the ketone 7 as a colourless oil (0.192 g; 96%). ^1H nmr, 5.78 (1H, s, $H_{1'}$), 5.68 (2H, d, J=3Hz, H_6,H_7), 3.51 (3H, s, -OMe), 3.07 (1H, m, H_4), 2.57-1.92 (9H, m, -CH, -CH_2), 0.12 (9H, s, -$OSiMe_3$), -0.02 (9H, s, -$SiMe_3$). ^{13}C nmr, 213.2 (C_3), 143.1 ($C_{2'}$), 126.8 ($C_{6/7}$), 125.6 ($C_{6/7}$), 110.6 ($C_{1'}$), 90.9 (C_2), 59.0 (OCH_3), 48.7, 42.5, 33.0, 20.4, 19.6, 19.0, 1.6 ($SiCH_3$), -0.9 ($SiCH_3$). m/z, 366 (M^+, 4.3%), 351 (M^+-Me), 73 (100%).

Diol **8**: 2,3-Bis(trimethylsilyloxy)bicyclo[4.2.0]oct-2,6-diene (0.284 g; 1.00 mmol) and 3,3-dimethoxy-2-trimethylsilylmethylprop-1-ene (0.188 g; 1.00 mmol) were reacted with TMSOTf (0.019 ml; 0.01 mmol), followed by $TiCl_4$ (0.219 ml; 2.00 mmol). Chromatography afforded the diol **8** as a colourless oil (0.11 g; 51%). Found: M^+ 222.1247, $C_{13}H_{18}O_3$ requires M^+ 222.1256. $\nu_{max}(CCl_4)$, 3 420 (OH), 1 719 (C=C), 1 673 (C=C), cm^{-1}. ^1H nmr, 6.11 (2H, brt, J=3.5Hz, -CH=CH), 5.18 (1H, m, C=CH_2), 5.05 (1H, m, C=CH_2), 4.06 (1H, s, -CHOMe), 3.47 (3H, s, -OMe), 2.64-1.86 (10H, m, 2 x OH, CH, CH_2). ^{13}C nmr, 144.3, 130.3, 129.65, 108.3, 87.75, 80.7, 76.5, 58.2, 43.4, 39.6, 31.6, 20.9, 20.7. m/z, 223 (M^++1, 2.4%), 222 (M^+, 14%), 204 (M^+-H_2O, 57%), 190 (M^+-MeOH, 45%), 110 (100%).

Diol **11**: Enediol **10** (2.86g; 9.71mmol) and 3,3-dimethoxy-2-trimethylsilylmethylprop-1-ene (1.66g; 8.83mmol) were reacted with TMSOTf (0.17 ml; 0.88 mmol), followed by $TiCl_4$ (1.94 ml; 17.66 mmol). Chromatography afforded the diol **11** as a colourless oil (1.65 g; 80%). Found: C, 72.13; H, 8.05, $C_{14}H_{18}O_3$ requires C, 71.77; H, 7.74%. ν_{max}, 3 426 (OH), 2 967 (CH), 1 673 (C=C), 1 165-1 123 (O-Me) cm^{-1}. ^1H nmr, 6.41 (2H, m, H_8,H_9), 5.11 (1H, m, H_{13}), 4.98-4.97 (1H, m, H_{13}), 3.95 (1H, brt, J=2.4Hz, H_2) 3.50 (3H,

s, -OMe), 3.01-2.96 (2H, m, H_7,H_{10}), 2.66-2.61 (1H, dd, J=8.0, 8.3Hz, H_{11}), 2.46-2.29 (5H, m, -OH, H_6, H_4), 1.50-1.46 (1H, brd, J=8.0Hz, H_{12}), 1.19-1.08 (1H, brd, J=8.0Hz, H_{12}). ^{13}C nmr, 143.7 (C_3), 137.4 ($C_{8/9}$), 136.9 ($C_{8/9}$), 107.7 (C_{13}), 88.2 (C_2), 81.2 ($C_{1/5}$), 77.4 ($C_{1/5}$), 58.3 (OCH_3), 53.4 (CH_2), 49.4 (CH), 44.7 (CH), 44.3 (CH), 43.9 (CH_2), 41.2 (CH). m/z, 234 (M^+, 24.9%), 219 (M^+-Me, 14.0%), 216 (M^+-H_2O, 5.6%), 202 (M^+-MeOH, 67.0%).

1,5-Dihydroxy-2-methoxy-3-methylene-bicyclo[3.3.0]octane **15**: 1,2-Bis(trimethylsilyloxy)cyclopentene (0.21 g; 0.89 mmol) and 3,3-dimethoxy-2-trimethylsilylmethyl- prop-1-ene (0.21 g; 0.89 mmol) were reacted with TMSOTf (0.015 ml; 0.085 mmol), followed by $TiCl_4$ (0.20 ml; 1.85 mmol). Chromatography, using ether-petrol (3:1) as eluent, afforded 1,5-dihydroxy-2-methoxy-3-methylene-bicyclo[3.3.0]octane as a colourless oil (0.040 g; 25%). ^1H nmr, (CCl_4) 5.05-4.70 (2H, m, C=CH_2), 3.80-3.75 (1H, m, -CHOMe), 3.40 (2H, br s, -OH), 3.25 (3H, s, -OMe), 2.40 (2H, m, allylic CH_2), 1.75-1.40 (6H, m, -CH_2). ^{13}C nmr, ($CDCl_3$) 145.0 (C), 107.3 (CH_2), 89.1 (CH), 86.4 (C), 83.0 (C), 58.5 (CH_3), 43.3 (CH_2), 41.0 (CH_2), 33.6 (CH_2), 21.7 (CH_2). m/z, 166 (M^+-H_2O, 1.1%), 85 (100%).

1,5-Dihydroxy-2-methoxy-3-methylene-bicyclo[4.3.0]nonane **16**: 1,2-Bis(trimethylsilyloxy)cylclohexene (0.68g; 2.66mmol) and 3,3-dimethoxy-2-trimethylsilylmethyl-prop-1-ene (0.50 g; 2.66 mmol) were reacted with TMSOTf (0.051 ml; 0.266 mmol), followed by $TiCl_4$ (0.58 ml; 5.32 mmol). Chromatography afforded the diol **16** as a colourless oil (0.34g: 65%). ^1H nmr, 5.19 (1H m, C=CH_2), 4.99 (1H, m, C=CH_2), 4.26 (1H, d, J=0.9Hz, -CHOMe), 3.59 (3H, s, -OMe), 2.46 (4H, m, -OH, allylic CH_2), 1.81-1.13 (8H, m, -CH_2). ^{13}C nmr, 145.3 (C), 110.1 (CH_2), 89.3 (CH), 79.7 (C), 76.4 (C), 59.6 (OCH_3), 38.0 (CH_2), 33.2 (CH_2), 28.1 (CH_2), 23.2 (CH_2), 19.8 (CH_2). m/z, 180 (M^+-H_2O, 0.88%), 166, 85.

General Procedure for the Ring Cleavage of Diols to Diones

A solution of the diol formed above (0.23 mmol) in benzene (3 ml) was treated with anhydrous lead tetraacetate (0.26 mmol) and stirred at room temperature under nitrogen. The pale yellow suspension was filtered, washed with benzene and the filtrate evaporated *in vacuo* to afford an oil, which after chromatography, using ether-petrol as eluent, gave the dione.

3-Methoxy-4-methylenebicyclo[5.4.0]undec-9-ene-2,6-dione **9**: Diol **8** (0.052 g; 0.23 mmol) was reacted with lead tetraacetate (0.114 g; 0.26 mmol) for 18 h, to afford after chromatography, using ether-petrol (1:1) as eluent, 3-methoxy-4-methylenebicyclo[5.4.0]undec-9-ene- 2,6-dione **9** as a colourless oil (0.049 g; 98%). Found: M^+ 220.1089, $C_{13}H_{16}O_3$ requires M^+ 220.1099. ν_{max}, 1 707, 1 231 cm^{-1}. ^1H nmr, 5.67 (2H, m, -CH=CH), 5.41 (1H, m, C=CH_2), 5.27 (1H, m, C=CH_2), 4.25 (1H, s, -CHOMe), 3.55 (2H, m, -CH_2), 3.34 (3H, s, -OMe), 3.21 (1H, dd, J=0.7, 16.3Hz, -CH), 3.05 (1H, m, -CH), 2.42-2.04 (4H, m, -CH_2). ^{13}C nmr, 208.5, 206.4, 137.1, 125.1, 124.1, 120.45, 91.05, 56.8, 48.8, 46.1, 42.3, 25.4, 24.9. m/z, 221 (M^++1, 1.4%), 220 (M^+, 24.0%), 192 (M^+-CO, 18%), 84 (100%).

Dione **12**: Diol **11** (1.65 g; 7.05 mmol) was reacted with lead tetraacetate (3.75 g; 8.50 mmol) for 5 min, to afford after chromatography, using ether-petrol (35:65) as eluent, the dione **12** as white crystals (0.97 g; 60%). m.p. 49.8-51.2 °C. Found: C, 72.78; H, 7.28 $C_{14}H_{16}O_3$ requires C, 72.39; H, 6.94%. ν_{max}, 1 715-1 685 (C=O), 1 656 (C=C), 1 642 (C=C) cm^{-1}. ^1H nmr, 6.14 (2H, m, H_9,H_{10}), 5.16 (2H, m, H_{13}), 3.90 (1H, s,

H_3), 3.76 (1H, dd, J=2.8, 11.6Hz, H_1), 3.50 (1H, dd, J=2.8, 11.6Hz, H_7), 3.32 (1H, d, J=13.7Hz, H_5), 3.27 (3H, s, -OMe), 2.99 (2H, m, H_8,H_{11}), 2.83 (1H, d, J=13.7Hz, H_5), 1.39 (1H, m, H_{12}), 1.25 (1H, m, H_{12}). ^{13}C nmr, 207.5 (C_2), 206.1 (C_6), 136.4 (C_4), 135.9 ($C_{8/9}$), 135.0 ($C_{8/9}$), 119.0 (C_{13}), 90.2 (C_3), 57.4 (C_{14}), 56.5 (CH), 52.2 (CH), 47.6 (CH_2), 47.3 (CH_2), 45.2 (CH), 43.8 (CH). m/z, 232 (M^+, 5.9%), 200 (M^+-MeOH, 4.3%), 166 (100%).

2-Methoxy-3-methylene-cyclonona-1,5-dione **18**: Diol **16** (0.15 g; 0.76 mmol) was reacted with lead tetraacetate (0.37 g; 0.80 mmol) for 18 h to afford, after chromatography, using ether petrol (1:1) as eluent, 2-methoxy-3-methylene-cyclonona-1,5-dione **18** as a colourless oil (0.096 g; 65%). ν_{max}, 1 700 (C=O), 1 670 (C=C), cm^{-1}. ^1H nmr, 5.41 (1H, m, C=CH_2), 5.37 (1H, s, C=CH_2), 4.11 (1H, s, -CHOMe), 3.23 (1H, d, J=14Hz, allylic CH_2), 3.23 (3H, s, -OMe), 2.90 (1H, d, J=14Hz, allylic CH_2), 2.55-2.13 (4H, m, -CH_2CO), 1.97-1.60 (4H, m, -CH_2). ^{13}C nmr, 210.0 (C), 210.9 (C), 137.8 (C), 122.3 (CH_2), 90.7 (CH), 56.7 (CH_3), 46.8 (CH_2), 39.7 (CH_2), 36,3 (CH_2), 24.6 (CH_2), 23.6 (CH_2). m/z, 196 (M^+, 39%), 178 (M^+-H_2O, 14%), 168 (M^+-CO, 70%), 164 (M^+-MeOH, 21%), 85 (100%).

Dione **19**: Dione **12** (0.102 g; 0.440 mmol) was dissolved in CH_2Cl_2 (5 ml), under nitrogen, and para-toluenesulphonic acid (8.0 mg; 10 mol%) was added. The reaction was stirred for 48 h, water (2 ml) added and the CH_2Cl_2 layers separated. The aqueous layer was extracted with CH_2Cl_2 (2 x 2 ml) and the combined organic layers washed with saturated aqueous sodium hydrogen carbonate (5 ml), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow oil (69 mg; 68%), which was further purified by chromatography, using ether-petrol (35:65) as eluent, to afford the dione **19** as a colourless oil (20 mg; 20%). ν_{max}, 1 712 (C=O), 1 652 (C=O), 1 600 (C=C) cm^{-1}. ^1H nmr, 6.15-6.11 (1H, m, $H_{9/10}$), 5.98-5.94 (1H, m, $H_{9/10}$), 5.80 (1H, s, H_5), 3.93 (1H, d, J=1.1Hz, H_3), 3.63-3.14 (7H, m, -OMe, H_1,H_7,H_8,H_{11}), 1.88 (3H, d, J=1.5Hz, -CH_3), 1.48-1.36 (2H, m, H_{12}). ^{13}C nmr, 204.5 (C_2), 202.3 (C_6), 144.7 (C_4), 136.8 ($C_{9/10}$), 133.5 ($C_{9/10}$), 129.6 (C_5), 88.4 (C_3), 56.2, 53.9, 52.6, 48.9, 47.3 (C_{12}), 44.0, 23.4. m/z, 232 (M^+, 1.2%), 218, 204, 166 (100%).

Dione **20**: Dione **12** (0.100g; 0.431 mmol) was dissolved in dry THF (5 ml), under nitrogen, and 1,8-diazabicyclo[5.4.0]undec-7-ene (0.070 ml; 0.468 mmol) was added. The resulting bright yellow solution was stirred for 4 h. Hexane (10 ml) was added and the reaction mixture washed with 1% hydrochloric acid (5 ml), saturated aqueous sodium hydrogen carbonate (5 ml), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow oil (60 mg; 60%). Chromatography, using ether-petrol (1:1) as eluent, afforded dione **20** as white crystals (50 mg; 50%). m.p. 110.9-112.5 °C. ν_{max}, 1 715 (C=O), 1 682 (C=O), 1 603 (C=C) cm^{-1}. ^1H nmr, 6.27-6.16 (2H, $H_{9/10}$), 3.86-3.04 (7H, m, -OMe, H_1,H_7,H_8,H_{11}), 2.96 (1H, dd, J=2.9, 9.0Hz, H_5), 2.36 (1H, dd, J=1.7, 9.0Hz, H_5), 1.99 (3H, d, J=1.3Hz, -CH_3), 1.61-1.32 (2H, m, H_{12}). ^{13}C nmr, 206.0 (C), 194.3 (C), 150.0 (C), 137.6 (CH), 136.0 (C), 135.9 (CH), 59.7, 55.7, 54.8, 49.1, 47.8, 43.1, 40.3, 21.6. m/z, 232 (M^+, 38.8%), 204, 166 (100%).

Acetal **21**: Dione **12** (0.102 g; 0.440 mmol) was dissolved in dry methanol (5 ml), under nitrogen, and para-toluenesulphonic acid (8.0 mg; 10 mol%) was added. The resulting yellow solution was stirred for 7 h. Ether (5 ml) and water (3 ml) were added and the layers were separated. The aqueous layer was extracted with ether (2 x 3 ml) and the combined organic layers washed with saturated aqueous sodium hydrogen

carbonate (5 ml), dried ($MgSO_4$) and evaporated *in vacuo* to give a yellow oil (0.095 g; 77%). Chromatography, using ether-petrol (1:4) as eluent, afforded the acetal **21** as white crystals (81 mg; 66%). ^1H nmr, 6.06-6.01 (2H, m, H_9,H_{10}), 5.20-5.17 (1H, m, H_{13}), 5.01-4.99 (1H, m, H_{13}), 3.73 (1H, s, H_3), 3.54 (3H, s, -OMe), 3.37 (3H, s, -OMe), 3.34 (3H, s, -OMe), 2.82 (2H, m), 2.61 (1H, m), 2.43 (1H, m), 2.19 (1H, m), 2.14 (1H,m), 1.25 (1H, m, H_{12}), 1.11 (1H, m, H_{12}). ^{13}C nmr, 141.0, 134.2, 133.5, 111.1, 105.0, 104.9, 79.7, 59.3, 52.4, 51.5, 51.1, 49.9, 48.5, 44.4, 44.2, 42.4. m/z, 278 (M^+, 28.5%), 246 (M^+-MeOH, 23.0%), 121 (100%).

References and Notes

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