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3,3-Dimethyl-7-methylenecycloocta-1,5-dione, a Versatile Building Block for the Preparation of Substituted Cyclooctadienones and δ-Valerolactones

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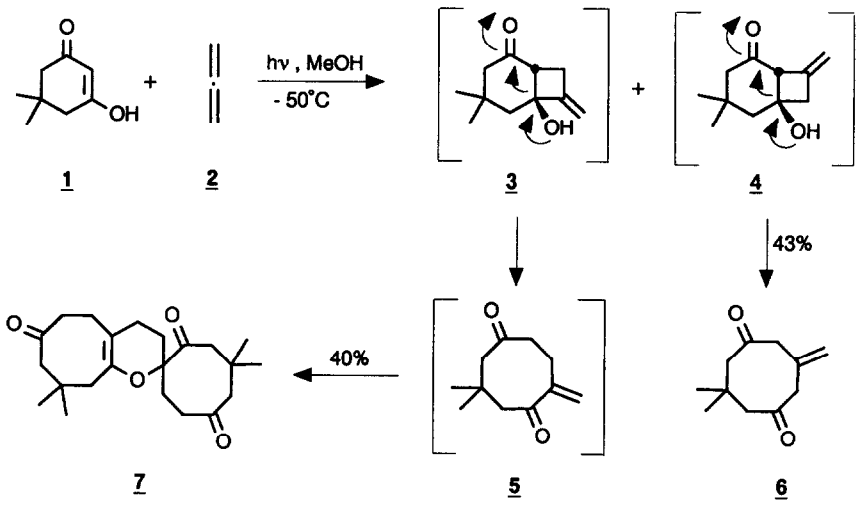
Abstract: De Mayo reaction of dimedone with allene results in the formation of 3,3-dimethyl-7-methylenecycloocta-1,5-dione **6** together with the corresponding head-to-tail adduct **5**, which spontaneously dimerizes to the hetero Diels-Alder adduct **7**. Reduction of **6** with sodium borohydride or Grignard reagents affords the transannular hemiketals **9**, which can easily be isomerized (DBU) to their conjugated analogues **10**. Depending on the substrate chosen (**9** or **10**), the substituent R and the applied reaction conditions, an acid-catalyzed rearrangement of these hemiketals leads to the cyclooctadienones **12** in either pure form or in admixture with δ-valerolactones **11** or substituted cyclohexenones.

In connection with one of our fragrance related projects we have recently thoroughly reanalyzed Kephalis[R], an old Givaudan-Roure speciality, which is characterized by a warm ambery note[1]. Among the newly identified constituents of this perfumery material, 3,5,7,7-tetramethylcycloocta-2,4-dien-1-one (**12b**) turned out to be of particular interest, as it was found to contribute significantly to the overall odour of Kephalis[R], despite its low percentage occurrence (0.5%). Both the need for larger quantities for further evaluation and our general interest in structure-odour relationships initialized a synthetic program[2], focussing on **12b** and related eight-membered ring systems, a class of raw materials hitherto hardly represented in the perfumers palette.

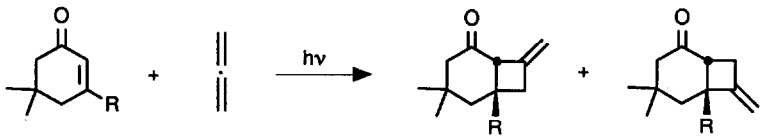
In spite of the relatively simple structure of cyclooctadienone **12b**, we could not prepare it easily either from commercially available eight membered ring precursors or by the usual synthetic ways leading to such systems[3]. The most straightforward approach we found is based on a de Mayo reaction between allene and dimedone, which is followed by a spontaneous retroaldol opening of the initially formed cyclobutane adduct **4** (Scheme 1)[4].



Scheme 1. [2+2] - Photoaddition of Dimedone to Allene

Such [2+2]-photocycloadditions of substituted cyclohexenones to allene usually proceed with some regiochemical discrimination (Table 1).

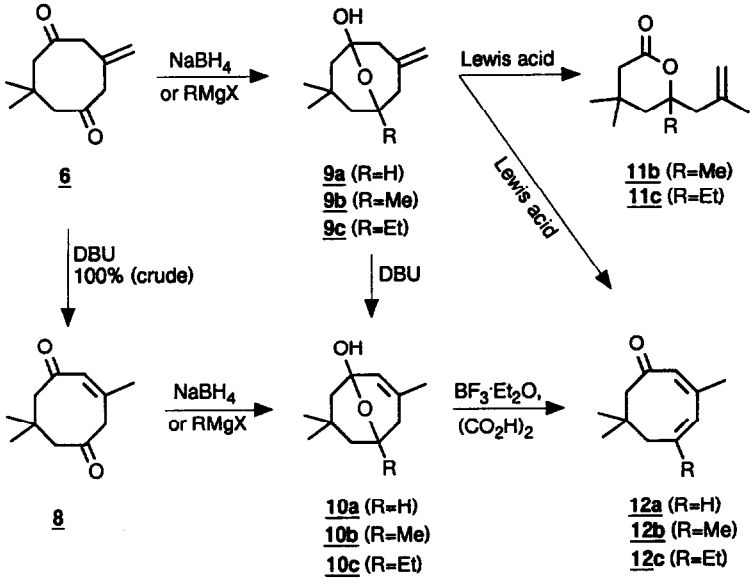
Table 1. Observed Regioselectivities of [2+2]-Photoadditions between Allene and 5,5-Dimethylcyclohex-2-en-1-ones



R	Solvent	HH : HT	Isolated Yield (%)	Reference
CH_3	CH_2Cl_2	13 : 1	not reported	5
CH_3	dry silica gel	1,4 : 1	69	5
$OCO_2CH_2CH{=}CH_2$	not reported	1 : 0	90	6
$OCOCH_3$	CH_2Cl_2	2,3 : 1	87	7
OCH_3	CH_2Cl_2	1 : 4	67	7
OH	MeOH	1 : 1	83	this work

However, no selectivity was observed in our case, as both the desired head-to-head adduct **6** and its head-to-tail counterpart **5** were formed in approximately equal amounts (40%). The latter compound could not be isolated as such, as it underwent spontaneously a hetero Diels-Alder dimerization to generate **7**, whose structure was unambiguously determined by an X-ray crystallographic analysis (Scheme 1).

Owing to the proximity effect of functional groups in medium sized ring systems[8], both the methylenic dione **6** and its more rigid conjugated isomer **8**, which can easily be obtained by isomerization of **6** with 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU), revealed a particular behaviour upon reduction (Scheme 2).[9]



Scheme 2. Synthesis of δ-Valerolactones **11** and Cyclooctadienones **12**

Thus, their treatment with Grignard reagents or simply with $NaBH_4$ resulted in the formation of the transannular hemiketals **9** and **10** respectively, i.e. compounds which after formal loss of water should easily be convertible to the target cyclooctadienones **12**. In practice, this proved true for hemiketals **10a-c**, which under acid catalysis rearranged in good yields to the target cyclooctadienones **12** (entries 15-18 in Table 2). Among the numerous Lewis acids ($BF_3{\cdot}Et_2O$, $SnCl_4$, $AlCl_3$, $ZnBr_2$, $FeCl_3$, $TiCl_4$) and Brönsted acids ($(COOH)_2$, CH_3COOH, $HClO_4$, PTSA, PPTS, H_2SO_4) tested, the couple $BF_3{\cdot}Et_2O/(COOH)_2$ gave the best

results in terms of isolated yields[10]. All attempts, however, to effect a similar tandem ring opening/double bond migration/dehydration reaction sequence with the exo-methylene counterparts **9**, succeeded only fully in the case of the 5-unsubstituted hemiketal **9a** (R=H) (entries 6 and 7 in Table 2), whereas for the 5-substituted hemiketals **9b** and **9c** isolated yields of **12b** or **12c**, respectively, did not exceed 46%.

Table 2. Preparation and Rearrangement of Transannular Hemiketals **9** and **10**

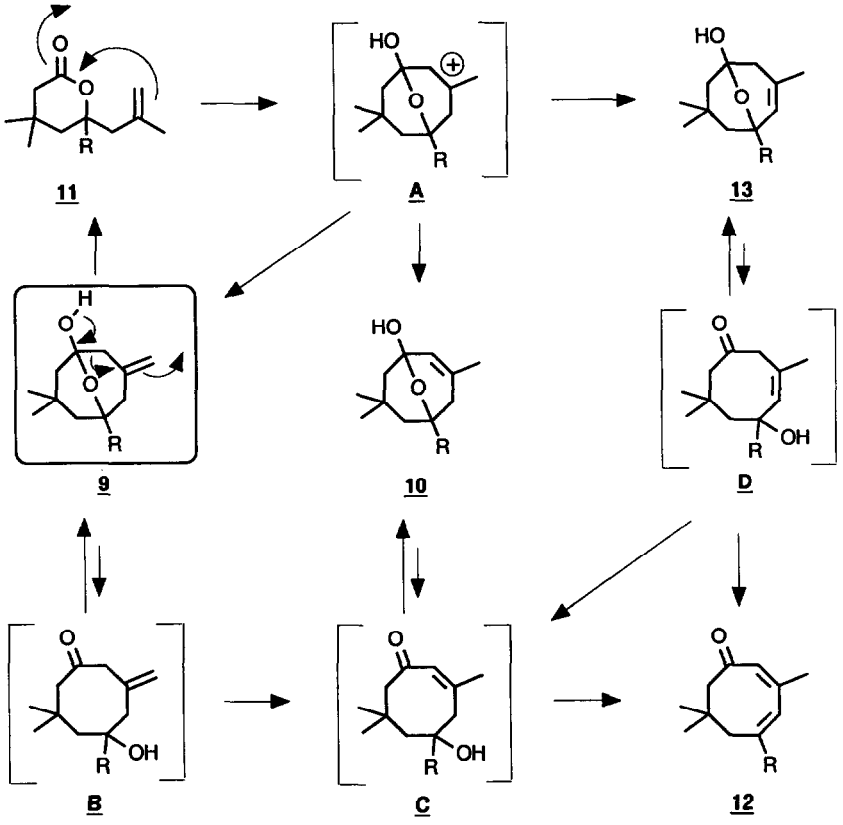
Entry	Substrat	Reagent	Conditions	Isolated Yields (%)			
				9	**10**	**11**	**12**
1	**6**	$NaBH_4$	EtOH/0°→22°C/2h	66 (**9a**)	30 (**10a**)		
2	**6**	MeMgI	Et_2O/0°→22°C/5h	72 (**9b**)			
3	**6**	EtMgBr	Et_2O/0°C/2.3h	62 (**9c**)			
4	**8**	$NaBH_4$	EtOH/0°→22°C/3h		> 88 (**10a**)		
5	**8**	MeMgI	Et_2O/0°→22°C/16h	16 (**9b**)	24 (**10b**)		
6	**9a**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/22°C/2h				75 (**12a**)
7	**9a**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/80°C/0.5h				78 (**12a**)
8	**9b**	DBU	CH_2Cl_2/reflux/72h		77 (**10b**)		
9	**9b**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/22°C/6h			24 (**11b**)	33 (**12b**)
10	**9b**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/80°C/0.5h				46 (**12b**)[a]
11	**9c**	DBU	CH_2Cl_2/reflux/9h		92 (**10c**)		
12	**9c**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/22°C/1.5h			43 (**11c**)	23 (**12c**)
13	**9c**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/22°C/6h			21 (**11c**)	27 (**12c**)
14	**9c**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/80°C/0.5h				33 (**12c**)[b]
15	**10a**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/80°C/0.5h				85 (**12a**)
16	**10b**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/22°C/6h				81 (**12b**)
17	**10c**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/22°C/50h				> 67 (**12c**)
18	**10c**	$BF_3{\cdot}Et_2O$ / $(COOH)_2$	C_6H_6/80°C/0.3h				61 (**12c**)

a) In addition 10% of 5,5-dimethyl-3-(isobut-1-enyl)cyclohex-2-en-1-one was isolated

b) In addition 28% of 5,5-dimethyl-2-methyl-3-(isobut-1-enyl)cyclohex-2-en-1-one was isolated

These modest yields were found to have their origin in the concomitant formation of δ-valerolactones **11b/11c** or isobutenyl substituted cyclohexenones (entries 9,10,12-14 in Table 2), the proportion of which could be varied by modifying the reaction conditions (temperature/time). A kinetic GC-MS study then showed that under mild conditions the lactones **11** may be obtained as the main

products of this transformation (entry 12 in Table 2), but they slowly disappear if reaction time or temperature is increased. Furthermore, this same study also revealed that irrespective of the substrate chosen, i.e. pure hemiketals **9** or δ-lactones **11**, isomeric hemiketals **10** and **13** appear as intermediates during this reaction (Scheme 3).



Scheme 3. Postulated Reaction Mechanism for the Rearrangement of Hemiketals **9** and **10**

All the above observations, together with the fact, that hemiketals **10** rearrange smoothly and with no trace of lactone formation to cyclooctadienones **12**, led us to postulate the reaction mechanism indicated in Scheme 3. Accordingly, hemiketals **9** might, besides undergoing ring opening/double bond migration/dehydration reactions, also rearrange via a retro-Prins type reaction to the lactones **11**, which themselves can undergo a Prins type reaction to lead, via carbocation **A**, to all three isomeric hemiketals **9**, **10** and **13**. The latter are certainly in equilibrium with the ring-opened δ-hydroxy ketones **B**, **C** and **D**, of which only **C** and **D** would be able to loose water spontaneously, thereby affording cyclooctadienones **12**

in an irreversible way. The proposed reaction scheme would finally also explain why the initially formed lactones **11** slowly fade away as the reaction progresses and therefore cannot be obtained in high yields.

From an olfactory point of view the new cyclooctadienones **12a-c** cover a broad spectrum of odour descriptors such as camphoraceous, earthy, woody, anisic, amber, fruity, spicy, tobacco or saffron. We believe that these rich multifaceted odour profiles are due to the conformational flexibility of the eight-membered carbocyclic ring systems, which allows them to address various olfactory receptors simultaneously.

In conclusion, by starting from methylenecyclooctadione **4** and passing through hemiketals **10**, the cyclooctadienones **12** have been prepared in good preparative yields. These hitherto unknown compounds exhibit interesting and complex olfactory notes. If, on the other hand, the isomeric hemiketals **9** are subjected to a similar acid catalyzed rearrangement, δ-lactones **11** are formed competitively via a retro-Prins type reaction. These, due to their lability under the reaction conditions, could only be isolated in low to moderate yields.

Experimental

General

Melting points were obtained with an Electrothermal apparatus by using open capillary tubes and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AC 200 spectrometer, at 200 MHz and 50.3 MHz respectively. The chemical shifts are reported on the δ scale (ppm) downfield from TMS. Coupling constants (J) are reported in Hz . Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; dd, doublet of doublet; dt, doublet of triplet; etc. IR spectra were obtained with a Nicolet 510 or Beckman Aculab 3 spectrophotometer. GC/MS spectra were recorded on a Finnigan Incos or Finnigan 4500 instrument (EI, 70eV). TLC was performed on glass plates precoated with 0.25 mm Kieselgel 60 F_{254} (Merck). Flash chromatograhy columns were packed with 35 - 70 μm Amicon silica gel. Commercial starting materials were used without further purification. Solvents were dried by standard procedures. Unless otherwise stated, extractive workup consisted of extraction with the indicated solvent followed by drying with anhydrous $MgSO_4$, filtering, and removal of the solvents at reduced pressure (12 mm Hg).

Photoaddition of dimedone (1) to allene (2)

A photoreaction vessel equipped with a 125 W high pressure Philips HPK lamp was charged with a solution of 19.6 g (0.14 mol) of **1** in 800 ml of methanol and 112 g (2.8 mol) of **2** (condensed at -40°C). The stirred reaction mixture, kept under argon and at -50°C, was irradiated during 7 h, while monitoring consumption

of dimedone by GC. Excess of allene was then evaporated carefully by slowly warming up to room temperature and the solvent removed *in vacuo*. Flash chromatography of the residual oil (Et_2O/ petroleum ether, 2:1), afforded 10.7 g (42.5% with respect to **1**[11]) of **3,3-dimethyl-7-methylenecycloocta-1,5-dione (6)** and 10.1g (40%) of **4,4,9',9'-tetramethyl-3',4',5',6',7',8',9',10'-octahydrospiro[cyclooctane-1,2'-cycloocta[b]= pyrane]-2,6,7'-trione (7)**.

6: white crystals, mp 67.5-68.8°C; R_F (Et_2O/petroleum ether 4:1): 0.48; ^1H NMR δ 1.06(s,6H), 2.41(s,4H), 3.14(s,4H) 5.26(s,2H); ^{13}C NMR δ 208.1(s), 136.2(s), 121.8(t), 55.4(t), 51.2(t), 33.7(s), 29.3(q); IR (KBr) 2960, 2920, 1696, 1646, 1464, 1394, 1371, 1334, 1229, 1183, 1106, 959, 926, 628 cm^{-1}; MS (m/z) 180(M^+,11), 165(14), 137(10), 112(8), 109(29), 96(21), 83(100), 82(65), 69(13), 55(36), 54(97), 53(24), 41(32), 39(66).

7: white crystals, mp 134°C; R_F (Et_2O/petroleum ether 4:1): 0.30; ^1H NMR δ 1.02(s,3H), 1.07(s,3H), 1.075(s,3H), 1.13(s,3H), 1.42(m,1H), 1.5-2.6(m,17H), 2.86(m,2H); ^{13}C NMR δ 212.7(s), 211.7(s), 211.4(s), 147.3(s), 108.2(s), 82.9(s), 53.1(t), 51.7(t), 46.2(t), 45.5(t), 44.3(t), 39.2(t), 36.2(s), 35.0(s), 34.3(t), 31.3(q), 29.1(t), 28.5(q), 27.1(2q), 26.5(t), 21.6(t); IR (KBr) 2959, 2902, 1704, 1688, 1464, 1304, 1229, 1173, 1110, 1076, 923 cm^{-1}; MS (m/z) 360(M^+,4), 220(3), 218(7), 205(3), 181(5), 180(26), 137(5), 136(6), 125(6), 97(9), 96(100), 95(13), 91(7), 83(14), 79(8), 55(14), 41(7).

3,7,7-Trimethylcyclooct-2-ene-1,5-dione (8)

1.67 g (11 mmol) of DBU were added to a solution of 4.0 g (22 mmol) of **6** in 400 ml of CH_2Cl_2. After stirring for 2 h at room temperature the reaction mixture was quenched with 100 ml of 10% HCl. Extractive workup furnished quantitatively enone **8** as a partly crystallized oil, which was used in the following without further purification. An analytical sample was purified by flash chromatography (Et_2O/petroleum ether 2:1): R_F (Et_2O/petroleum ether 4:1): 0.45; ^1H NMR δ 1.02 (s,6H), 2.02(d,3H,J=1.5), 2.53(s,2H), 2.68(s,2H), 3.50 (s,2H), 6.20(br s,1H); ^{13}C NMR δ 200.7(s), 198.7(s), 150.2(s), 132.6(d), 53.2(t), 51.5(t), 50.9(t), 33.1(s), 29.6(2q), 29.5(q); IR (neat) 2962, 2930, 1701, 1632, 1560, 1434, 1312, 1292, 1273, 1239, 1095 cm^{-1}.

3,3-Dimethyl-7-methylene-9-oxabicyclo[3.3.1]nonan-1-ol (9a)

A slurry of 170 mg (4.4 mmol) of $NaBH_4$ in 5 ml of ethanol was added to a solution of 300 mg (1.66 mmol) of **6** in 8 ml of the same solvent at 0°C. Stirring was continued for 1 h at 0°C and 1 h at room temperature, before 1 ml of acetic acid was added carefully. The resulting mixture was evaporated to dryness at reduced pressure and then worked up as usual using CH_2Cl_2 as the extraction solvent. Repeated flash chromatography (CH_2Cl_2 then petroleum ether/Et_2O 11:7) of the residue gave 90 mg (30%) of **10a** and 200 mg (66%) of **9a** as a colourless oil.

9a: R_F (CH_2Cl_2/methanol 97:3): 0.34; ^1H NMR δ 0.86(s,3H), 1.01(m,1H), 1.15 (s,3H), 1.54(br s,2H), 1.60(m,1H), 1.84 (d,1H,J=13), 2.10(br d,1H,J=12.5), 2.32(d,1H,J=12.5), 2.49 (ddq,1H,J= 13.5;6.5;2), 2.59(br s,1H,exch), 4.45(m,1H), 4.83 (m,1H), 4.88(m,1H); ^{13}C NMR δ 140,8(s), 113.5(t), 95.7(s), 68.5(d), 49.8(t),

46.7(t), 40.5(t), 37.7(t), 32.1(q), 29.4(q), 28.8(s); IR (neat) 3374, 2955, 2927, 2862, 1412, 1350, 1319, 1181, 1031, 887, 693, 654 cm^{-1}; MS (m/z) 183(2), 182(M^+,22), 167(3), 139(5), 127(51), 123(37), 122(74), 111(12), 109(14), 107(100), 95(33), 93(16), 85(44), 83(58), 82(74), 81(77), 79(32), 67(47), 59(85), 55(59), 43(87), 41(90).

10a: see below.

7-Methylene-3,3,5-trimethyl-9-oxabicyclo[3.3.1]nonan-1-ol (9b)

8 ml (24 mmol) of a 3.0 M solution of methylmagnesium iodide in Et_2O were added dropwise during 0.5 h to a stirred solution of 4.0 g (22 mmol) of **6** in 150 ml of Et_2O kept at 0°C. After stirring for 0.5 h at 0°C and 4 h at room temperature, the yellow reaction mixture was poured onto 350 ml of 10% aqueous NH_4Cl solution. Extractive workup with 3x150 ml of Et_2O, and purification of the residue by flash chromatography (Et_2O/petroleum ether 1:1) afforded 3.1 g (72%) of **9b** as white crystals: mp 47°C; R_F (Et_2O/petroleum ether 4:1): 0.57; ^1H NMR δ 0.83(s,3H), 1.12(s,3H), 1.22(m,2H), 1.32(s,3H), 1.88(d,1H,J=12.5), 2.05(m,2H), 2.29(d,1H,J=12.5), 2.91(s,1H,exch), 4.79-4.84 (m,2H); ^{13}C NMR δ 142.0(s), 112.7(t), 96.8(s), 73.1(s), 49.3(t), 47.9(t), 45.7(t), 43.7(t), 32.0(q), 31.6(q), 29.6(s), 28.9(q); IR (KBr) 3364, 3071, 2954, 2865, 1652, 1451, 1340, 1229, 1091, 1028, 898, 802, 678 cm^{-1}; MS (m/z) 196(M^+,6), 181(3), 141(38), 137(25), 125(11), 121(22), 113(8), 109(6), 99(7), 96(24), 95(25), 83(45), 81(29), 79(10), 67(13), 59(48), 55(24), 43(100), 41(36), 39(23).

5-Ethyl-3,3-dimethyl-7-methylene-9-oxabicyclo[3.3.1]nonan-1-ol (9c)

1.6 ml (4.8 mmol) of a 3.0 M solution of ethylmagnesium bromide in Et_2O were added dropwise during 45 min, to a stirred solution of 0.66g (3.66 mmol) of **6** in 13 ml of Et_2O kept at 0°C. After 1 h at 0°C another 0.3 ml (0.9 mmol) of Grignard reagent were added and stirring was continued for 0.5 h before the reaction mixture was poured onto 50 ml of 10% aqueous NH_4Cl. Extractive workup with 3x150 ml of Et_2O and flash chromatography (petroleum ether/Et_2O 9:1) of the residue gave 0.47 g (62%) of **9c** as white crystals: mp 88.5-89.5°C; R_F (Et_2O/petroleum ether 1:1): 0.37; ^1H NMR δ 0.85(s,3H), 0.91(t,3H, J=7), 1.07(d,1H,J=12.5), 1.10(s,3H), 1.33(d,1H,J=12.5), 1.50(br s,2H,), 1.61(q,2H,J=7), 1.85(d,1H,J=12), 2.03(m,2H), 2.30(d,1H, J=12), 2.63(s,1H,exch), 4.82(m,2H); ^{13}C NMR δ 142.1(s), 112.8(t), 96.7(s), 75.7(s), 49.7(t), 45.9(t), 45.1(t), 41.5(t), 36.7(t), 32.2(q), 29.3(q), 7.7(q); IR (KBr) 3349, 3078, 2963, 2933, 1650, 1450, 1327, 1218, 1089, 999, 899, 798, 675 cm^{-1}; MS (m/z) 210(M^+,3), 195(3), 181(5), 155(73), 151(14), 135(18), 127(13), 121(12), 110(28), 109(29), 95(61), 83(87), 81(29), 67(21), 59(67), 57(100), 55(43), 43(50), 41(42).

3,7,7-Trimethyl-9-oxabicyclo[3.3.1]non-2-en-1-ol (10a)

A slurry of 1.0 g (26.5 mmol) of $NaBH_4$ in 80 ml of ethanol was added during 1 h to a solution of crude **8**, prepared from 4.0 g (22 mmol) of **6**, in 120 ml of Et_2O kept at 0°C. Stirring was continued for 1h at 0°C, and 1 h at room temperature before the reaction mixture was poured carefully onto 40 ml of cold acetic acid.

After careful evaporation of solvents (55°C, 20 mm Hg), the residue was taken up in 400 ml of CH_2Cl_2 and worked up as usual. Purification of the residual oil by flash chromatography (CH_2Cl_2/methanol 97:3) gave 3.5 g (88%) of **10a** as a slightly yellowish liquid: R_F (CH_2Cl_2/methanol 97:3): 0.30; ^1H NMR δ 0.96(s,3H), 0.98(s,3H), 1.30(dd,1H,J=14,2.5), 1.50(d,1H,J=13), 1.62(d,1H,J=13), 1.63(d,1H,J=18), 1.66(br s,3H), 1.74(dd,1H,J=14,7), 2.34(br s,1H,exch), 2.52(dd,1H,J=18,7), 4.48(td,1H,J=7.5,3), 5.48(m,1H); ^{13}C NMR δ 135.3(s), 127.4(d), 93.0(s), 69.5(d), 47.1(t), 42.0(t), 35.3(q), 34.5(t), 30.1(s), 29.2(q), 22.5(q); IR (neat) 3385, 3003, 2952, 2925, 1687, 1637, 1434, 1329, 1212, 1109, 1078, 1039, 831 cm^{-1}; MS (m/z) 182(M^+,8), 127(5), 126(61), 112(10), 111(100), 83(24), 81(86), 80(19), 79(20), 57(69), 55(44), 43(34), 41(75), 39(46).

3,5,7,7-Tetramethyl-9-oxabicyclo[3.3.1]non-2-en-1-ol (10b)

310 mg (2.04 mmol) of DBU were added portionwise (31 mg at the beginning, 124 mg after 3 h and 155 mg after 72 h) to a solution of 200 mg (1.02 mmol) of **9b** in 18 ml of CH_2Cl_2 kept at reflux. After stirring a total of 78 h the reaction mixture was quenched with 15 ml of 10% HCl, extracted with 3x10 ml of CH_2Cl_2 and worked up as usual. The resulting residue was purified by flash chromatography (petroleum ether/Et_2O 4:1) affording 154 mg (77%) of **10b** as a colourless liquid: R_F (Et_2O/petroleum ether 1:1): 0.32; ^1H NMR δ 0.94(s,3H), 0.97(s,3H), 1.30 (s,3H), 1.37(br s,2H), 1.44(d,1H,J=13.5), 1.61(d,1H,J=13.5), 1.63(br s,3H), 1.73(br d,1H,J=17.5), 2.13(br d,1H, J=17.5), 2.78(s,1H,exch), 5.47(m,1H); ^{13}C NMR δ 135.6(s), 126.8(d), 94.8(s), 73.3(s), 48.7(t), 46.4(t), 41.4(t), 35.7(q), 32.0(q), 29.7(s), 28.9(q), 22.2(q); IR (neat) 3352, 3007, 2963, 2901, 1690, 1436, 1366, 1330, 1227, 1122, 1041, 830 cm^{-1}; MS (m/z) 196(M^+,3), 181(6), 140(5), 126(5), 125(100), 123(7), 97(8), 95(29), 79(12), 57(21), 43(46), 41(28).

5-Ethyl-3,7,7-trimethyl-9-oxabicyclo[3.3.1]non-2-en-1-ol (10c)

A solution of 1.2 g (5.7 mmol) of **9c** and 0.43 g (2.82 mmol) of DBU in 1.2 ml of CH_2Cl_2 was stirred at reflux for 9 h. After addition of 5 ml of Et_2O and 4 ml of 10% HCl, an extractive workup with 3x10 ml of Et_2O followed by purification of the residue by flash chromatography (petroleum ether/Et_2O 17:3) furnished 1.1 g (92%) of **10c** as a colourless liquid: R_F (Et_2O/petroleum ether 1:1): 0.32; ^1H NMR δ 0.89(t,3H,J=7), 0.93(s,3H), 0.94(s,3H), 1.33(br s,2H), 1.44(d,1H,J=13.9), 1.53(d,1H,J=13.9), 1.54(q,2H, J=7), 1.60(br s,3H), 1.65(d,1H,J=18), 2.07(d,1H,J=18), 5.47(m,1H); ^{13}C NMR δ 134.7(s), 127.3(d), 91.6(s), 75.7(s), 46.6(t), 46.4(t), 38.7(t), 37.7(t), 36.1(q), 30.1(s), 28.9(q), 22.3(q), 7.4(q): IR (neat) 3396, 2950, 1695, 1364, 1335, 1217, 1104, 1046, 831 cm^{-1}; MS (m/z) 210(M^+,1), 195(5), 182(7), 181(64), 150(6), 139(47), 135(9), 125(100), 109(28), 93(12), 83(13), 57(42), 55(13), 41(14).

Rearrangement of transannular hemiketals 9a-c and 10a-c

General procedure:

An equimolar mixture of **9** (**10**), BF_3 etherate and oxalic acid in benzene (100 ml/18 mmol) was stirred either at room temperature or at reflux (with a Dean Stark trap) for the time indicated in Table 2. After total disappearance of the substrate (TLC), the reaction mixture was diluted with Et_20, washed with 10% aqueous $NaHCO_3$ and brine, dried ($MgSO_4$) and evaporated *in vacuo*. The resulting residue was purified by flash chromatography (petroleum ether/Et_2O 4-20:1) to afford **11** and/or **12**, as colourless liquids. According to this procedure the following δ-valerolactones (**11**) and cyclooctadienones (**12**) have been obtained in the yields indicated in Table 2:

6-(2-Methylprop-2-enyl)-4,4,6-trimethyltetrahydropyran-2-one (11b)

R_F (CH_2Cl_2/methanol 97:3): 0.68; ^{1}H NMR δ 1.04(s,3H), 1.08(s,3H), 1.41(s,3H), 1.60(dd,1H,J= 14,1.5), 1.80(br s, 3H), 1.90(d,1H,J=14), 2.17(d,1H,J=16), 2.30(dd,1H,J=16.5, 1.5), 2.33(br s,2H), 4.74 (m,1H), 4.94(m,1H); ^{13}C NMR δ 171.6 (s), 141.2(s), 116.6(t), 83.2(s), 52.0(t), 45.3(t), 43.5(t), 30.8(q), 30.5(s), 29.4(q), 29.2(q), 24.5(q); IR (neat) 3076, 2960, 2939, 1735, 1644, 1378, 1351, 1269, 1071, 993, 896 cm^{-1}; MS (m/z) 181(M^+-CH_3,0.5), 142(5), 141(63), 113(15), 83(78), 55(11), 43(100), 41(13).

4,4-Dimethyl-6-ethyl-6-(2-methylprop-2-enyl)tetrahydropyran-2-one (11c)

R_F (Et_2O/petroleum ether 1:1): 0.42; ^{1}H NMR δ 0.92(t,3H, J=7), 1.06(s,6H), 1.69(q,2H,J=7), 1.70(m,2H), 1.81(br s,3H), 2.24(s,2H), 2.35(br s,2H), 4.75(m,1H), 4.94(m,1H); ^{13}C NMR δ 171.8(s), 141.2(s), 116.5(t), 85.6(s), 48.5(t), 43.6 (t), 42.2(t), 34.1(t), 30.5(s), 30.3(2q), 24.6(q), 8.2(q); IR (neat) 3045, 2959, 2882, 1735, 1640, 1464, 1372, 1353, 1268, 1010, 984, 895 cm^{-1}; MS (m/z) 181(M^+-C_2H_5,7), 156(9), 155(90), 127(23), 84(6), 83(100), 57(80), 55(22), 41(15).

3,7,7-Trimethylcycloocta-2,4-dien-1-one (12a)

R_F (Et_2O/petroleum ether 1:1): 0.56; ^{1}H NMR δ 1.01(s,6H), 1.94(d,3H,J=1.5), 2.0(m,4H), 5.93(br s,1H), 6.10-6.35(m, 2H); ^{13}C NMR δ 202.4(s), 147.4(s), 136.8(d), 132.0(d), 130.8(d), 51.6(t), 43.8(s), 40.5(t), 28.4(2q); IR (neat) 3018, 2960, 2927, 1643, 1601, 1466, 1434, 1371, 1325, 1307, 1281, 1222, 900, 812, 729 cm^{-1}; MS (m/z) 164(M^+,16), 149(4), 122(31), 121(10), 108(31), 107(58), 93(8), 91(15), 81(8), 80(100), 79(78), 77(24), 65(13), 53(14), 51(12), 41(30), 39(46).

3,5,7,7-Tetramethylcycloocta-2,4-dien-1-one (12b)

R_F (Et_2O/petroleum ether 4:1): 0.60; ^{1}H NMR δ 1.02(s,6H), 1.92(d,3H,J=1.5), 2.02(d,3H,J=1.5), 1.7-2.4(m,4H), 5.90(br s,1H), 6.02(br s,1H); ^{13}C NMR δ 202.2(s), 149.2(s), 147.0 (s), 129.4(d), 128.3(d), 51.6(t), 45.8(t), 43.2(s), 29.6(br q), 28.1(q), 27.0(q); IR (neat) 3016, 2963, 2922, 1644, 1597, 1434, 1373, 1285, 1235 cm^{-1}; MS (m/z) 178(M^+,28), 163(9), 136(6), 135(7), 122(33), 121(100), 107(8), 94(42), 91(10),

79(70), 77(20).

5-Ethyl-3,7,7-trimethylcycloocta-2,4-dien-1-one (12c)

R_F (CH_2Cl_2/methanol 97:3): 0.60; ^1H NMR δ 1.0(s,6H), 1.09(t,3H,J=7), 1.93(d,3H,J=1.5), 2.02(br m,4H), 2.26(m,2H), 5.92(br s,1H), 5.97(br s,1H); ^{13}C NMR δ 202.2(s), 152.5(s), 149.6(s), 129.3(d), 126.4(d), 51.5(t), 44.2(t), 43.2(s), 33.4(t), 29.5(2q), 21.1(q), 12.8(q); IR (neat) 2963, 2928, 1644, 1598, 1371, 1285, 1233, 870 cm^{-1}; MS (m/z) 192(M^+,55), 177(22), 163(28), 155(23), 136(59), 135 (95), 121(73), 107(45), 108(35), 93(100), 91(37), 83(36), 41(35).

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