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2,2,4,4-Tetramethyl-3-methylenebicyclo[3.2.1]oct-6-ene

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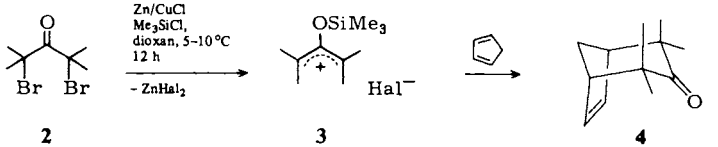
Die sterisch anspruchsvolle Titelverbindung **1** wurde in einer Eintopfreaktion aus Cyclopentadien und 2,4-Dimethyl-3-[(trimethylsilyl)methyl]-3-penten-2-ol (**5**) in Gegenwart von Titantetrachlorid/*N*-Methylanilin hergestellt. 2,2,4,4-Tetramethylbicyclo[3.2.1]oct-6-en-3-on (**4**) wurde vereinfacht im 15-g-Maßstab dargestellt.

In context with recent efforts towards the synthesis of 9,10-didehydronorzizaene[2a)] and 9,10-didehydrozizaene[2b)] we required the title bicyclic **1** as a model compound. **1** has a plane of symmetry – which simplifies NMR spectra – and also has aesthetic appeal. A simple precursor of **1** appeared to be bicyclic ketone **4**[3)], which, as we now show, can be obtained most conveniently from α,α'-dibromo ketone **2**, zinc-copper couple and cyclopentadiene in the presence of chlorotrimethylsilane[4)]. Under these conditions **4** has been isolated in 50% yield, and there is no problem in starting or scaling up the organometallic reaction, which may otherwise be sluggish. The key intermediate in this cycloaddition is siloxyallyl cation **3**[5)]. Unfortunately, various attempts to methylenate **4** to give **1** failed[6)] and we have learnt from Professor *Krief* that he has been unable to isopropylidenate ketone **4**, using organoselenium chemistry[7)].

1



2 **3** **4**

As an alternative approach to **1** we activated allylic alcohol **5** in the presence of cyclopentadiene. At the outset one could have serious doubts whether **1** would be formed at all by this approach. Since cation **6** is more crowded than cation **3**, the nonplanar conformation of **6** should be preferred further. However, the nonplanar conformation is expected to suffer ready elimination[5,8)] to **7**, because unlike **3** cation **6** lacks a nucleophilic group Y at the central allylic carbon (Y = CH_2SiMe_3 in **6** vs. $OSiMe_3$ in **3**); such a nucleophilic group helps to disperse positive charge and to suppress elimination by 1,3-interaction with an allylic terminus in the nonplanar conformation[5)]. In the event, the functionalized permethylated allylic alcohol **5** had first to be pre-

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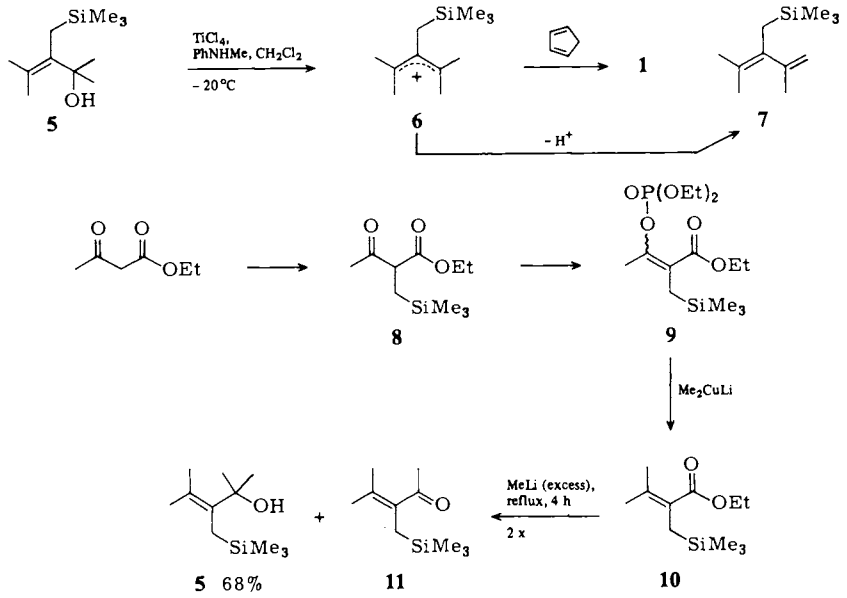
pared. After trying several plausible approaches without success we obtained **5** using the enol phosphorylation of functionalized acetoacetic ester (**8** → **9**) and reaction with dimethylcopper-lithium (**9** → **10**)[9]. This sequence seems to work well for constructing crowded tetrasubstituted olefins such as **10**. Methylation of the substituted acrylic ester **10** to give **5** required forcing conditions and even after repeating the methylation with fresh methyllithium some ketone **11** remained (**5**:**11** = 9:1).



Previously, we had activated allylic alcohols related to **5** via trifluoroacetylation and treatment with zinc halides[8]. In the present case, a still simpler procedure worked, i.e. ionization of **5** with $TiCl_4$ in the presence of *N*-methylaniline at −20 °C[10]. Under these conditions conjugated diene **7** was formed in only 12% yield and the desired bicycle **1** in a respectable 38% yield. The structure of **1** was established spectroscopically, especially by comparison with bicyclic ketone **4**.

Conclusions: Tetrasubstituted olefins **5**, **10**, and **11**, which all contain further functionality, are new and useful terpenoid building blocks. The direct electrophilic activation of alcohol **5** without previous esterification, i.e. by treatment with modified titanium tetrachloride, simplifies the desired cycloaddition. Finally, the preparation of **1** with its two crowded quaternary centres separated by the exo-methylene double bond demonstrates the considerable driving force for the formation of [3.2.1]bicyclic systems from cyclopentadiene and allylic cations, which contain a donor at the central carbon[5], even in the presence of adverse steric effects.

We thank *Ulrike Bültel* and *Kunibert Giesel* for experimental contributions and the *Deutsche Forschungsgemeinschaft* and *the Fonds der Chemischen Industrie* for support of this work.

Experimental Part

Improved Procedure for the Preparation of 2,2,4,4-Tetramethylbicyclo[3.2.1]oct-6-en-3-one (**4**): The mixture of commercial zinc dust (26.1 g, 0.4 mol) and copper(I) chloride (3.96 g, 40 mmol) in freshly distilled dioxan (80 ml) is cooled to 0 °C (ice bath) with stirring and a solution of freshly

distilled cyclopentadiene (13.2 g, 200 mmol), freshly distilled 2,4-dibromo-2,4-dimethyl-3-pentanone **2** (36.1 g, 133 mmol) and chlorotrimethylsilane (17.3 g, 20.2 ml, 160 mmol) in dioxan (45 ml) is added dropwise over 2 h. Ice cooling is maintained for 5 h, and then the reaction mixture is allowed to slowly reach room temperature, while being stirred overnight. The mixture is suction filtered through a dichloromethane moistened celite 545 pad contained in a large sintered glass funnel and washed well with dichloromethane. The filtrate is washed with water, saturated NH_4Cl solution, water, saturated NaCl solution and dried (K_2CO_3). Removal of the solvent on a rotary evaporator gives a yellow oil. Fractional distillation (short path head, 20 cm Vigreux) of the crude product furnishes **4**[3] (16.7 g, 55%), b.p. 45–50°C/ca. 1 Torr, as a low melting solid (m.p. ca. 25°C). Alternatively, flash chromatography (substance/silica gel = 1/20, ether/light petroleum = 1/10) gives a yellow oil which is recrystallized from pentane. – ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 221.0 (s, C-3), 136.5 (d, C-6, -7), 50.0 (s, C-2, -4), 49.9 (d, C-1, -5), 35.2 (t, C-8), 28.3 (q, 2 CH_3), 25.2 (q, 2 CH_3).

2,4-Dimethyl-3-[(trimethylsilyl)methyl]-3-penten-2-ol (**5**)

a) *Ethyl 3-Oxo-2-[(trimethylsilyl)methyl]butanoate* (**8**): Ethyl acetoacetate (13 g, 0.10 mol) in absol. dimethylformamide (DMF) (25 ml) was dropped slowly into a cooled (water bath) suspension of sodium hydride (3.85 g, 75%; 0.12 mol) in absol. DMF (25 ml). After complete addition a solution of (iodomethyl)trimethylsilane (24.6 g, 116 mmol) in absol. DMF (20 ml) was added slowly and the mixture was heated for 4 h to 80°C. After cooling down a dilute aqueous solution (150 ml) of NH_4Cl was added carefully, and the mixture was extracted with pentane (3 × 100 ml). The organic phase was washed with a saturated solution of NaCl and dried ($MgSO_4$). The solvent was removed to leave a residue which was fractionated over a Vigreux column to give **8** (15 g, 70%), b.p. 111–113°C. – IR (CCl_4): 2980 (m), 2958 (m), 2900 (m), 1742 (vs), 1717 (vs), 1250 (vs), 1238 (vs), 1188 (s), 1135 (s), 850 (vs), cm^{-1}. – 90 MHz ^1H NMR ($CDCl_3$, standard TMS added afterwards): δ = −0.01 (s, 9H), 1.08 (ABX system, AB part, 2H, CH_2Si), 1.14 (t, J = 7 Hz, 3H, CH_2CH_3), 2.19 (s, 3H, CH_3), 3.39 (ABX system, X part, 1H, CH), 4.16 (q, J = 7 Hz, 2H, CH_2CH_3). – MS (70 eV, room temperature): *m/e* = 216 (M^+, 2%), 201 (21), 188 (10), 173 (20), 155 (13), 143 (23), 129 (22), 127 (14), 113 (12), 103 (12), 97 (11), 75 (100), 73 (84), 60 (39), 55 (18), 53 (27).

b) *Ethyl-3-(Diethoxyphosphinyloxy)-2-[(trimethylsilyl)methyl]-2-butenoate* (**9**): Silylated ester **8** (5.4 g, 25 mmol) in absol. ether (20 ml) was stirred at 0°C into a suspension of sodium hydride (0.88 g, 75%; 27 mmol) in absol. ether (30 ml) under argon. After the mixture had reached room temperature (15 min) diethyl chlorophosphate (4.75 g, 27.5 mmol) was added and the resulting mixture was stirred for 2 h at room temperature. After addition of a dilute solution of aqueous NH_4Cl the organic phase was washed with aqueous $NaHCO_3$ and dried (Na_2SO_4). Removal of the solvent in vacuo yielded spectroscopically pure **9** (8.45 g, 96%) as a light yellow oil. – IR (CCl_4): 2980 (m), 2960 (m), 2930 (m), 2910 (m), 1722 (vs), 1650 (w), 1300 (vs), 1280 (vs), 1250 (m), 1200 (m), 1165 (s), 1135 (m), 1035 (vs), 972 (vs), 850 (vs), cm^{-1}. – 90 MHz ^1H NMR ($CDCl_3$, benzene standard): δ = −0.03 (s, 9H), 1.22 (t, J = 7 Hz, 3H, $CO_2CH_2CH_3$), 1.24, 1.26 [2 × t, J = 7 Hz, 6H), $P(OCH_2CH_3)_2$], 1.62 (m, 2H, CH_2Si), 1.98 [m, 3H, $CH_3C(OP\langle)$], 4.06 (q, J = 7 Hz, 2H, $CO_2CH_2CH_3$), 4.12, 4.15 [2 × q, J = 7 Hz, 4H, $P(OCH_2CH_3)$]. – MS (70 eV, room temperature): *m/e* = 352 (M^+, 3%), 307 (12), 235 (12), 227 (15), 199 (38), 183 (27), 178 (13), 171 (25), 155 (100), 154 (18), 153 (12), 150 (22), 127 (19), 126 (17), 111 (13), 99 (37), 97 (17), 75 (58), 73 (87), 55 (14).

c) *Ethyl 3-Methyl-2-[(trimethylsilyl)methyl]-2-butenoate* (**10**): Methyllithium (40 mmol, 25 ml of a 1.6 M solution in ether) was added to a suspension of copper(I) iodide (3.81 g, 20 mmol) in absol. ether at 0°C. The resulting dimethylcopperlithium was used immediately: it was cooled to

– 78 °C and a solution of enol phosphate **9** (3.52 g, 10 mmol) in absol. ether (10 ml) was added slowly. After stirring at – 78 °C for 4 h a saturated solution of NH_4Cl was added and the product was extracted several times with ether. The combined organic phase was washed with a solution made up from a saturated solution of NaCl and conc. NH_3 and then with a saturated solution of NaCl alone. The solvent was dried (Na_2SO_4) and removed in vacuo to leave a light yellow oil, which was distilled in a Kugelrohr apparatus to give **10** (1.85 g, 87%), b.p. 90 °C/0.5 Torr. – IR (CCl_4): 2980 (m), 2958 (m), 2930 (m), 1710 (vs), 1625 (m), 1295 (m), 1278 (s), 1248 (s), 1218 (m), 1152 (vs), 1120 (m), 1050 (vs), 850 (vs), cm^{-1}. – 90 MHz ^1H NMR ($CDCl_3$, benzene standard): δ = – 0.08 (s, 9H), 1.20 (t, J = 7 Hz, 3H, CH_2CH_3), 1.64 (s, 3H, Z-CH_3), 1.74 (s, 2H, CH_2Si), 1.89 (s, 3H, E-CH_3), 4.09 (q, J = 7 Hz, 2H, CH_2CH_3). – ^{13}C NMR ($CDCl_3$): δ = 169.5 (s, C-1), 137.2 (s, C-3), 125.1 (s, C-2), 59.6 (t, CH_2CH_3), 22.4 (q, CH_3), 22.3 (q, CH_3), 20.0 (t, CH_2Si), 14.0 (q, CH_2CH_3), – 1.4 (q, $SiMe_3$). – MS (70 eV, room temperature): m/e = 214 (M^+, 3%), 198 (39), 171 (26), 170 (10), 169 (17), 155 (12), 103 (11), 96 (31), 75 (71), 73 (100), 68 (48), 67 (39), 59 (11), 50 (27).

HRMS: $C_{11}H_{22}O_2Si$ Calcd. 214.13891 Found 214.13872

2,4-Dimethyl-3-[(trimethylsilyl)methyl]-3-penten-2-ol (**5**): Silylated ester **10** (2.14 g, 10 mmol) in absol. ether (20 ml) was mixed with a 1.6 M solution (20 ml) of methyllithium (32 mmol) in ether under argon at room temperature and refluxed for 4 h. After addition of aqueous NH_4Cl the organic phase was separated and dried (Na_2SO_4). The solvent was removed to leave a mixture (65:35) of allylic alcohol **5** and ketone **11**, which was again refluxed with methyllithium (10 ml, 16 mmol) for 4 h. Chromatography with aluminium oxide (activity III; eluant light petroleum/ether = 9:1) gave **5** (1.35 g, 68%) and **11** (0.12 g). – IR (CCl_4): 3552 (m), 2940 (m), 2910 (m), 2850 (m), 1240 (s), 844 (vs), cm^{-1}. – 90 MHz ^1H NMR ($CDCl_3$, benzene standard) of **5**: δ = – 0.03 (s, 9H, $SiMe_3$), 1.32 [s, 6H, $C(OH)(CH_3)_2$], 1.35 (s, 1H, OH), 1.53 (s, 3H, Z-CH_3), 1.57 (s, 2H, CH_2), 1.80 (s, 3H, E-CH_3). – ^{13}C NMR ($CDCl_3$): δ = 137.4 [s, $C(CH_3)_2$], 122.5 [s, $C=C(CH_3)_2$], 73.6 [s, $C(OH)(CH_3)_2$], 30.6 [q, $C(OH)(CH_3)_2$], 24.1 (q, CH_3), 22.6 (q, CH_3), 20.2 (t, CH_2), – 0.06 [q, $Si(CH_3)_3$]. – MS (70 eV, room temperature): m/e = 200 (M^+, 0%), 182 (10), 110 (21), 95 (42), 75 (26), 73 (100), 67 (10), 45 (11).

4-Methyl-3-[(trimethylsilyl)methyl]-3-penten-2-one (**11**): IR (CCl_4): 2940 (m), 2900 (m), 2840 (m), 1680 (vs), 1615 (m), 1240 (s), 868 (s), 848 (s), 830 (s), cm^{-1}. – 90 MHz ^1H NMR ($CDCl_3$, benzene standard): δ = – 0.08 (s, 9H), 1.59 (s, 3H, Z-CH_3), 1.67 (s, 2H, CH_2), 1.72 (s, 3H, E-CH_3), 2.14 (s, 3H, CH_3CO). – ^{13}C NMR ($CDCl_3$): δ = 206.4 (s, C=O), 135.4 [s, $C(CH_3)_2$], 131.9 [s, $C=C(CH_3)_2$], 30.4 (q, CH_3CO), 22.5 (q, CH_3), 22.0 (q, CH_3), 20.4 (t, CH_2), – 0.83 (q, $SiMe_3$). – MS (70 eV, room temperature): m/e = 184 (M^+, 11%), 169 (82), 115 (12), 79 (12), 75 (50), 73 (100), 45 (15).

2,2,4,4-Tetramethyl-3-methylenebicyclo[3.2.1]oct-6-ene (**1**): A solution of titanium tetrachloride (5.6 ml of a 2 M solution in CH_2Cl_2, 11.3 mmol) in absol. CH_2Cl_2 (20 ml) was dropped into a solution of freshly distilled *N*-methylaniline (1.2 g, 11.3 mmol) in absol. CH_2Cl_2 (10 ml) at – 20 °C[10]. The resulting red-brown solution was stirred for 15 min and a solution of **5** (1.5 g, 7.5 mmol) and cyclopentadiene (1.0 g, 15 mmol) in absol. CH_2Cl_2 (30 ml) was added dropwise at – 20 °C, the color changing to clay-brown. After a further 3 h at – 20 °C the solution was treated with ether (200 ml) and washed with water (3 × 100 ml). The organic phase was dried (Na_2SO_4) and the solvent was removed in the cold at reduced pressure to give a yellow liquid containing **1** and **7** in a ratio of 2:1 (GLC). Chromatography over silica gel (eluant pentane) gave **1** (500 mg, 38%) and diene **7** (170 mg, 12%). – IR (CCl_4) of **1**: 3060 (w), 2980 (s), 2910 (s), 2875 (m), 1622 (w), 1462 (m), 1380 (m), 1362 (m), 908 (m), 892 (m), cm^{-1}. – 90 MHz ^1H NMR ($CDCl_3$): δ = 1.07 (s, 6H, 2 × α-CH_3), 1.25 (s, 6H, 2 × β-CH_3), 1.59 – 1.79 (m; 1H, H_{anti}), 2.02 – 2.29 (m, 3H, 1-, 5-H, H_{syn}), 4.95 (s, 2H, CH_2=), 6.06 (br s, 2H, CH=CH). – ^{13}C NMR ($CDCl_3$): δ =

164.9 (s, C-3), 136.4 (d, C-6, -7), 111.4 (t, CH_2=), 52.4 (d, C-1, -5), 40.0 (s, C-2, -4), 35.8 (t, C-8), 33.6 (q, 2 CH_3), 30.9 (q, 2 CH_3). – MS (70 eV, room temperature): *m/e* = 176 (M^+, 9%), 161 (14), 160 (72), 133 (59), 120 (63), 119 (95), 110 (29), 106 (34), 105 (100), 95 (70), 93 (40), 92 (56), 91 (74), 79 (34), 77 (42), 69 (76), 67 (44), 60 (45), 41 (46).

HRMS: $C_{13}H_{20}$ Calcd. 176.15650 Found 176.15650

2,4-Dimethyl-3-[(trimethylsilyl)methyl]-1,3-pentadiene (7): 90 MHz ^{1}H NMR ($CDCl_3$): δ = 0.00 (s, 9H, $SiMe_3$), 1.60 (s, 5H, CH_3, CH_2Si), 1.68 (s, 3H, *E*-CH_3), 1.76 [t, *J* = 1.5 Hz, 3H, $CH_3C(=CH_2)$], 4.52 – 4.62 (m, 1H, C=CH), 4.84 – 4.93 (m, 1H, C=CH).

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[2] [2a] *H. M. R. Hoffmann* and *R. Henning*, Helv. Chim. Acta **66**, 828 (1983). – [2b] *J. Rabe* and *H. M. R. Hoffmann*, Angew. Chem. **95**, 796 (1983); Angew. Chem., Int. Ed. Engl. **22**, 796 (1983).

[3] *H. M. R. Hoffmann, K. E. Clemens*, and *R. H. Smithers*, J. Am. Chem. Soc. **94**, 3940 (1972).

[4] Cf. *R. J. Giguere, D. I. Rawson*, and *H. M. R. Hoffmann*, Synthesis **1978**, 902.

[5] Review: *H. M. R. Hoffmann*, Angew. Chem. **96**, 29 (1984); Angew. Chem., Int. Ed. Engl. **23**, 1 (1984).

[6] Cf. also *H. M. R. Hoffmann* and *H. Vathke*, Chem. Ber. **113**, 3416 (1980).

[7] *A. Kief*, personal communication. Cf. *D. Labor* and *A. Kief*, J. Chem. Soc., Chem. Commun. **1982**, 564.

[8] *R. Henning* and *H. M. R. Hoffmann*, Tetrahedron Lett. **23**, 2305 (1982). Preparation of parent 2-[(trimethylsilyl)methyl]-2-propen-1-ol: *B. M. Trost, D. M. T. Chan*, and *T. N. Nanninga*, Org. Synth., checked procedure No. 2216.

[9] *F. W. Sum* and *L. Weiler*, Can. J. Chem. **57**, 1431 (1979); corrigenda ibid. **57**, 2895 (1979).

[10] *T. Saito, A. Itoh, K. Oshima*, and *H. Nozaki*, Tetrahedron Lett. **1979**, 3519.

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