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Dialkylation of β and γ-Diketone Monoethyleneketals by 1,8-Bis(trimethylsilyl)-2,6-octadiene.

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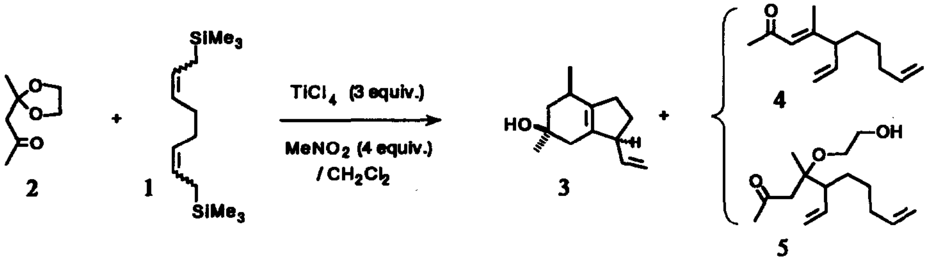
Abstract: Dialkylation of β-diketone monoethyleneketals by 1,8-bis(trimethylsilyl)-2,6-octadiene leads to bi- or tricyclic alcohols (one stereoisomer) **3** or **7a** resulting from a participation reaction. On the other hand, dialkylation of 2,5-hexanedione monoethyleneketal gives a divinylbicyclic ether **10**.

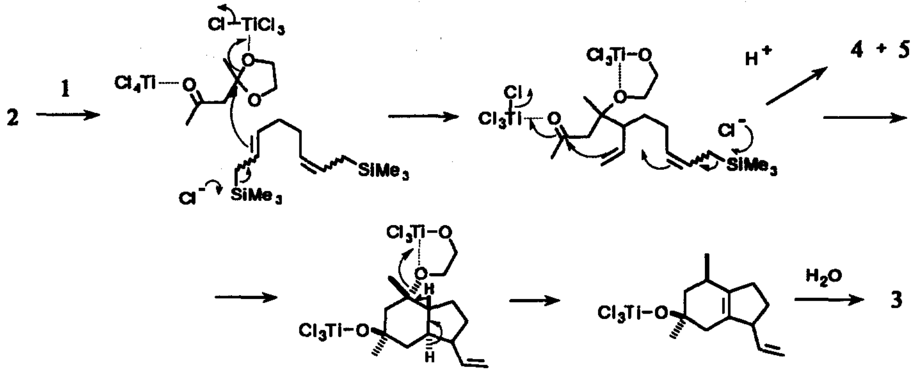
Tremendous advances have been made over the last decade in the development of new methods for the C-C bond elaboration using alkylation of electrophilic centers with allylsilanes.[1] In particular, alkylation of ethyleneketals has been extensively used.[2] We recently reported the one-step dialkylation of ethyleneketals by 1,8-bis(trimethylsilyl)-2,6-octadiene **1** leading to 1,1-dialkyl-2,5-divinylcyclopentanes.[3] We herein report the efficient one-pot synthesis of bi- or tricyclic compounds by dialkylation of β- or γ-diketone monoethyleneketals by 1,8-bis(trimethylsilyl)-2,6-octadiene.[4,5]

$TiCl_4$ mediated dialkylation of 2,4-pentanedione monoethyleneketal **2** by 1,8-bis(trimethylsilyl)-2,6-octadiene **1** gave rise to a bicyclic alcohol **3** (one isomer, 30 % yield). By-products were the unsaturated ketone **4** (8 % yield) and the alcohol **5** (one major stereomer, 30 % yield) resulting from a monoalkylation process.[6,7] In the absence of nitromethane as a co-solvent, the yield of **3** was reduced to 10-15 %.[8]

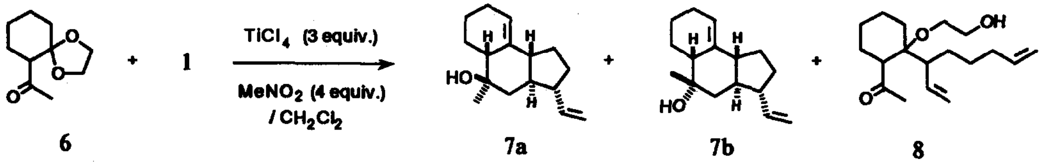


An experiment with **2**-d_5 showed that methyl group bearing by carbinol atom comes from the ketone.[9]

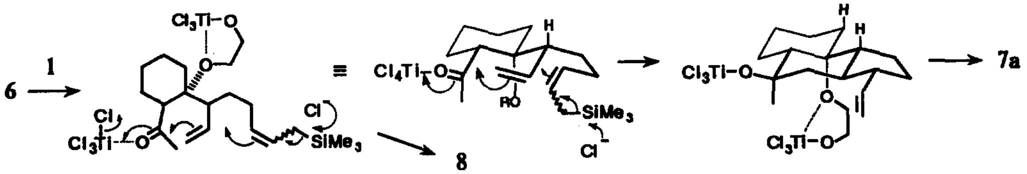
The formation of bicyclic alcohol **3** could result from the following complex process beginning by alkylation of the ethyleneketal. The bicyclization comes from a participation reaction and alkylation of the ketone group. An elimination reaction implying an hydride shift occurred: [10]



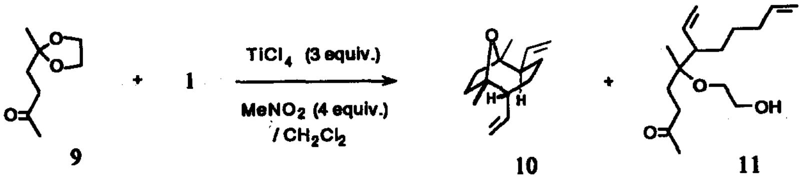
A similar result was observed with 2-acetylcyclohexanone monoethyleneketal **6**. At low temperature (-90 °C), only one tricyclic alcohol **7a** was obtained (**7a** c.a. 20 % yield, **8** : 25-35 % yield)), but when the reaction temperature was -60 °C, an isomeric bicyclic alcohol **7b** was also isolated (**7a** / **7b** : 1 / 3). The structures of these alcohols are determined by NMR spectroscopy.[11]



The following mechanism can be involved with a specific arrangement of the different groups implied in the bicyclization:



The addition of the diallylsilane **1** to 2,5-hexanedione monoethyleneketal **9** occurs via an other pathway :



the only product of dialkylation was the bicyclic ether **10** (*d,l*-pair, c.a. 20 % yield) resulting from a dehydration of the 1,4-diol intermediate.[13]

This dialkylation constitutes a total and stereoselective synthesis of bi- or tricyclic alcohols in two steps from 1,3-butadiene. Furthermore, it presents a number of interesting aspects of the allylsilane chemistry.

References and Notes

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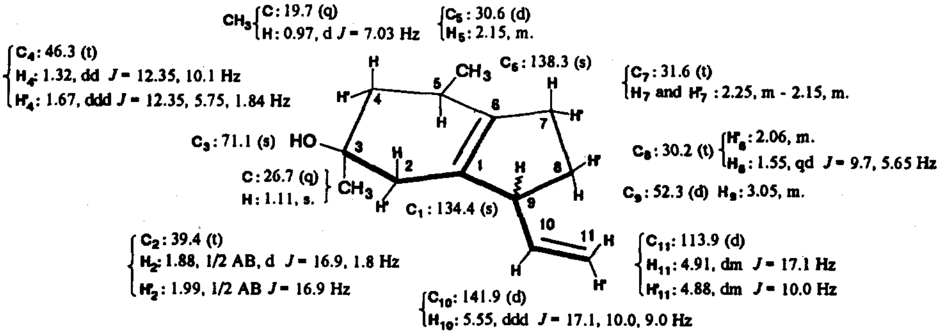
2. (a) Hosomi, A.; Endo, M.; Sakurai, H. *Chem. Lett.* **1976**, 941. (b) Sakurai, H.; Sasaki, K. Hosomi, A. *Tetrahedron Lett.* **1981**, *22*, 745. (c) Hosomi, A.; Ando, M.; Sakurai, H. *Chem. Lett.* **1986**, 365. For a review, see : (d) Mukaiyama, T.; Murakami, M. *Synthesis*, **1987**, 1043. For allylation of chiral acetals, see : (e) Bartlett, P.A.; Johnson, W.S.; Elliott, J.D. *J. Amer. Chem. Soc.* **1983**, *105*, 2088. (f) Johnson, W.S.; Crackett, P.H.; Elliott, J.D.; Jagodzinski, J.J.; Lindell, S.D.; Natarajan, S. *Tetrahedron Lett.* **1984**, *25*, 3951. (g) Kiyoka, S.; Sasaoka, H.; Fujiyama, R.; Heathcock, C.H. *Tetrahedron Lett.* **1984**, *25*, 5331. (h) Yamamoto, Y.; Nishii, S.; Yamada, J.-i *J. Amer. Chem. Soc.* **1986**, *108*, 7116 and ref. therein (i) Seebach, D.; Imwinkelried, R.; Stucky, G. *Helv. Chim. Acta* **1987**, *70*, 448. (j) Denmark, S.E.; Willson, T.M. *Selectivities in Lewis Acid Promoted Reactions*, D. Schinzer (ed.), Kluwer Academic Publ.: Dordrecht, 1989, p. 247. (k) Denmark, S.E.; Almstead, N.G. *J. Org. Chem.* **1991**, *56*, 6458 and 6485. (l) Denmark, S.E.; Almstead, N.G. *J. Amer. Chem. Soc.* **1991**, *113*, 8089 and ref. therein. (m) Panek, J.S.; Yang, M. *J. Org. Chem.* **1991**, *56*, 5755. For a review, see: (n) Alexakis, A.; Mangeney, P. *Tetrahedron: Asymmetry*, **1990**, *1*, 477.
3. Ouvrard, Ph.; Tubul, A.; Santelli, M. *Tetrahedron Lett.* **1992**, *33*, 000.
4. (a) Tubul, A.; Santelli, M. *Tetrahedron*, **1988**, *44*, 3975. (b) Tubul, A.; Ouvrard, Ph.; Santelli, M. *Synthesis*, **1991**, 173.
5. Bis(trimethylsilyl)-2,6-octadiene is a mixture of (*Z,Z*)-isomer (*ca.* 50 %), (*Z,E*)-isomer (*ca.* 40 %) and (*E,E*)-isomer (4 %) contaminated with *ca.* 4 % of (2*Z*)-1,6-bis(trimethylsilyl)-2,7-octadiene and *ca.* 2% of (2*E*)-1,6-bis(trimethylsilyl)-2,7-octadiene (this mixture is very difficult to separate by preparative gas chromatography).
6. General Procedure for dialkylation of ethyleneketals: to a solution containing 0.34 mL (30 mmol) of $TiCl_4$, anhydrous CH_2Cl_2 (50 mL) and dry nitromethane (2.2 mL) stirred at -60 °C was added ethyleneketal (10 mmol) in CH_2Cl_2 (5 mL). The mixture was cooled to -90 °C and 1,8-bis(trimethylsilyl)-2,6-octadiene (3.05 g, 12 mmol) in CH_2Cl_2 (5 mL) was slowly added. The solution was stirred at -90 °C for 5 h and then at -60 °C for 16 h. The reaction was quenched by addition of aqueous saturated NH_4Cl solution (30 mL) and extracted with CH_2Cl_2 (3 x 25 mL). The extracts were stirred with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and concentrated under vacuum. The residue was chromatographed on silica gel.
7. Dialkylation of the 2,4-pentanedione monoethyleneketal (**2**). 3,5-Dimethyl-9-vinylbicyclo[4.3.0]non-1(6)-en-3-ol (**3**, 30 %): Structure was determined by NMR (400 MHz) using concerted application of two dimensional methods: direct and long range heteronuclear and homonuclear chemical shift correlation techniques.



IR (film) 3400, 3080, 1640, 1620, 915 cm^{-1}; HRMS calcd for $C_{13}H_{20}O$ 192.1514, found 192.1510.4-Methyl-5-vinyldeca-3,9-dien-2-one (**4**, 8 %): IR (film) 3080, 1690, 1620, 920 cm^{-1};^{1}H NMR δ 6.10 (1, br. s), 5.85-5.63 (2, m), 5.10-4.93 (4, m), 2.69 (1, q, J = 7.2 Hz), 2.19 (3, s), 2.07 (3, br. s); ^{13}C NMR δ 198.2 (s), 159.0 (s), 139.2 (d), 138.5 (d), 123.9 (d), 116.0 (t), 114.8 (t), 54.1 (d), 33.7 (t), 32.0 (q), 31.7 (t), 29.8 (t), 26.7 (q).

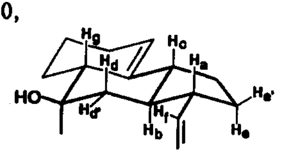
4-Methyl-4-(2-hydroxyethoxy)-5-vinyldec-9-en-2-one (**5**, 30 %): IR (film) 3450, 3080, 1710, 1645, 1100-1060, 920 cm^{-1}; ^{1}H NMR δ 5.90-5.40 (2, m), 5.15-4.85 (4, m), 3.60 (4, m), 2.55 (3, m), 2.20 (3, s), 2.05 (2, m), 1.30 (4, m), 1.20 (3, s); ^{13}C NMR (major isomer) δ 208.4 (s), 138.6 (d), 138.2 (d), 117.6 (t), 114.3 (t), 77.7 (t), 62.6 (t), 61.8 (t)(2C), 51.8 (d), 49.2 (t), 33.6 (t), 32.4 (q), 26.9 (t), 21.4 (q).

8. The influence of the nitro group during the addition of **1** to various electrophilic compounds was previously discussed, see : Tubul, A.; Ouvrard, Ph.; Santelli, M. *Bull. Soc. Chim. Fr* 1992, *129*, 265.

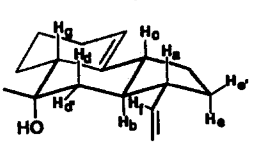
9. 4,4-Dideutero-5-methyl-3-trideuteromethyl-9-vinylbicyclo[4.3.0]non-1(6)-en-3-ol: ^{1}H NMR the signal at 1.11 is missing and the intensity of the multiplet between 1.8-1.3 was reduced.

10. Cyclization with hydride migrations and final proton loss is a known process, see, for example in biosynthesis of triterpenoids, van Tamelen, E.E. *Acc. Chem. Res.* 1975, *8*, 152.

11. Dialkylation of the 2-acetylcyclohexanone monoethyleneketal (**6**). (1*S**, 2*R**, 4*R**, 5*R**, 8*R**)-2-Methyl-5-vinyltricyclo[7.4.0.0^{4,8}]tridec-9-en-2-ol (**7a**, c.a. 20 %): IR (film) 3400, 3080, 1640, 1130, 915 cm^{-1}; ^{1}H NMR δ 5.71 (H$_f$, ddd, J = 17.7, 9.2, 8.3 Hz), 5.45 (1, br. s), 4.95 (2, m), 2.64 (H$_a$, qd, J_{ab} = J_{ae} = J_{af} = 8.3 Hz, $J_{ae'}$ = 2.7 Hz), 1.99 (H$_b$, dddd, J_{bd} = 13.2 Hz, J_{bc} = 12.2 Hz, J_{ba} = 8.3 Hz, $J_{bd'}$ = 2.4 Hz), 1.92 (H$_g$, m), 1.60 (14H, m), 1.10 (3H, s);



^{13}C NMR δ 140.8 (s), 139.1 (d), 119.4 (d), 113.7 (t), 75.8 (s), 47.59 (d), 47.58 (d), 46.3 (d), 45.0 (t), 44.5 (d), 29.4 (t), 26.0 (t), 25.0 (t), 23.3 (q), 23.0 (t), 21.7 (t); HRMS calcd for $C_{16}H_{24}O$ 232.1827, found 232.1822. When the reaction was directly monitored at -60 °C, a second isomer was obtained : (1*S**, 2*S**, 4*R**, 5*R**, 8*R**)-2-Methyl-5-vinyltricyclo[7.4.0.0^{4,8}]tridec-9-en-2-ol (**7b**)(**7a** / **7b** : 1 / 3): : ^{1}H NMR δ 5.71 (H$_f$, ddd J = 17.7, 9.2, 8.1 Hz); 5.58 (1, br s), 4.90 (2, m), 2.63 (H$_a$, qd J_{ab} = J_{ae} = J_{af} = 8.4 Hz, $J_{ae'}$ = 2.7 Hz), 1.98 (H$_g$, m), 1.70 (10H, m), 1.67 (H$_{d'}$, dd $J_{dd'}$ = 13.0 Hz, $J_{d'b}$ = 3.4 Hz), 1.57 (H$_b$, tdd J_{bc} = J_{bd} = 13.0 Hz, J_{ba} = 8.4 Hz, $J_{bd'}$ = 3.4 Hz), 1.31 (H$_d$, t J_{db} = $J_{dd'}$ = 13.0 Hz), 1.20 (3, s); ^{13}C NMR δ 141.0 (s), 139.1 (d), 121.2 (d), 113.5 (t), 73.6 (s), 47.2 (d), 46.1 (d), 44.9 (d), 44.6 (d), 42.3 (t), 29.1 (t), 27.3 (q), 26.2 (t), 24.9 (t), 23.1 (t), 22.0 (t).



The ^{1}H NMR coupling constants were determined on 1D-COSY spectra with semiselective excitation using shaped pulses generated by the selective excitation unit on a 400 MHz spectrometer (ref. 12). For example, by irradiation of H$_d$, the clear pattern of H$_b$ appeared and the coupling constants were determined.

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13. Dialkylation of the 2,5-hexanedione monoethyleneketal (**9**). (1*S**, 2*R**, 5*R**, 6*R**)-1,6-Dimethyl-2,5-divinyl-9-oxabicyclo[4.2.1]nonane (**10**, 20 %) : IR (film) 3080, 1640, 1000, 915 cm^{-1}; ^{1}H NMR δ 6.13-5.15 (2, m), 5.20-4.63 (4, m), 1.22 (3, s), 1.10 (3, s); ^{13}C NMR δ 142.1 (d), 140.5 (d), 115.2 (t), 113.4 (t), 86.7 (s), 84.2 (s), 55.7 (d), 55.2 (d), 43.0 (t), 31.9 (t), 31.7 (t), 30.4 (t), 29.2 (q), 28.5 (q); HRMS calcd for $C_{14}H_{22}O$ 206.1670, found 206.1654.

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