B

Kurzmitteilung / Short Communication

Acid-Catalyzed and Lewis Acid-Promoted Synthesis of 6-Hydroxybicyclo[4.3.0]nonan-3-ones

Dieter Schinzer* and Martin Ruppelt

Institut für Organische Chemie der Technischen Universität Braunschweig, Hagenring 30, D-3300 Braunschweig (F.R.G.)

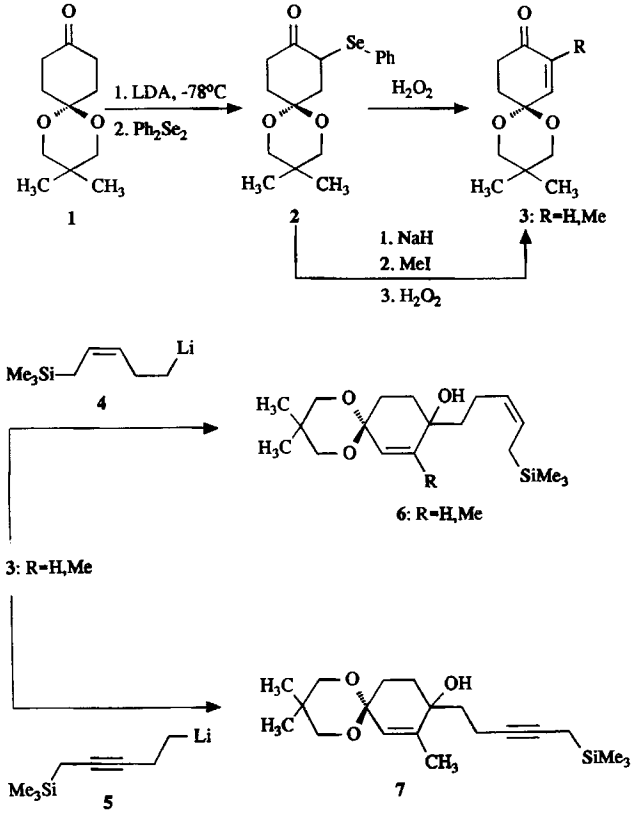
Received, September 14, 1990

Key Words: 6-Hydrindanones / Heart glycosides / Bicyclo[4.3.0]nonanone

3a-Hydroxy-6-hydrindanones of type **10** and **11** can be obtained by acid-catalyzed or Lewis acid-promoted cyclization reactions of ene-ketals of type **6** and **7**. The compounds described are interesting building blocks for biologically active heart glycosides.

The synthesis of 3a-hydroxy-6-hydrindanones as useful ring C,D units for the biologically active steroid skeleton has been reported[1-3]. In connection with our studies on intramolecular additions of allylic and propargylic silanes to enones and dienones we have described the stereoselective synthesis of 5-, 6-, 7-, and 8-membered ring systems[4].

In this communication we wish to report on the synthesis of 3a-hydroxy-6-hydrindanones of type **10** or **11** by intramolecular additions of allylic and propargylic silanes to ene-ketals. For the first time we have been able to promote the cyclization under acid catalysis using ene-ketals as starting compounds.



The starting material of type **6** and **7** may easily be obtained from the commercially available ketone **1**, which can be transformed in a short sequence into compounds of type **3**. Addition of organolithium compounds **4** and **5** produces the cyclization substrates **6** and **7**[5].

The cyclization of ketal **6** occurs in aqueous methanol in the presence of a trace of *p*-toluenesulfonic acid to afford a mixture of ketones **10** in 67% yield.

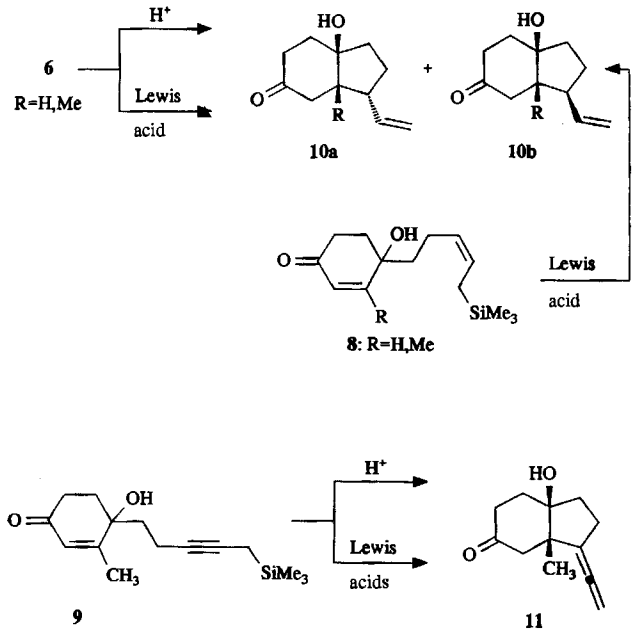
In the presence of Lewis acids ($EtAlCl_2$, $TiCl_4$, Et_2O-BF_3) both ene-ketals **6** and enones **8** and **9** can smoothly be cyclized. With ene-ketals, $TiCl_4$ gives the best results. The desired enones **8** and **9** can be obtained quantitatively by stirring the ketals in THF in the presence of silica gel. The Lewis acid of choice for enone cyclizations is Et_2O-BF_3. The stereochemical outcome of the cyclization is dependent on the Lewis acid used (see Table 1).

In the presence of Et_2O-BF_3, the major product is the *anti* product **10a** (see Table 1, R = Me). The diastereoselectivity can be reversed with $TiCl_4$ and $EtAlCl_2$ to yield compound **10b** (see Table 1, R = Me).

Table 1. Conditions of conversion **6**, **8**, **9** → **10**, **11**, ratio of diastereomers **10a** and **10b**, and yields of **10**, **11**

Reaction	Acid or Lewis Acid	Ratio **10a** : **10b**	% Yield
6 → **10** (R=H)	p-TsOH	20 : 80	67
6 → **10** (R=H)	Et_2O-BF_3	25 : 75	55
6 → **10** (R=H)	$TiCl_4$	9 : 91	99
6 → **10** (R=Me)	p-TsOH	55 : 45	22
6 → **10** (R=Me)	Et_2O-BF_3	60 : 40	66
6 → **10** (R=Me)	$EtAlCl_2$	28 : 72	29
6 → **10** (R=Me)	$TiCl_4$	34 : 66	76
8 → **10** (R=H)	Et_2O-BF_3	20 : 80	81
8 → **10** (R=Me)	Et_2O-BF_3	61 : 39	32
8 → **10** (R=Me)	$TiCl_4$	46 : 54	9
9 → **11**	p-TsOH	-	20
9 → **11**	Et_2O-BF_3	-	94
9 → **11**	$TiCl_4$	-	5

  0009-2940/91/0101-0247 $ 3.50+.25/0



In summary, these results clearly show that the intramolecular Sakurai reaction effectively produces hydrindanones with two quaternary centers, one of them carrying a hydroxy function. It is important to note that the sensitive tertiary alcohol can be tolerated under the acid cyclization conditions without forming a phenol by elimination of water. Consequently, this new cyclization technique can be used to form functionalyzed bicyclic ketones containing a second oxygen functional group.

Experimental

High-resolution mass spectra: Finnigan MAT 312 spectrometer. – IR spectra: Perkin-Elmer 580 and FT 1710 spectrometers. – NMR spectra: Bruker AM 300, WM 400, and WM 600 spectrometers. – All reactions were run under inert gas (nitrogen), and pure products were obtained after flash chromatography using the solvent system ethyl acetate/petroleum ether (boiling range 60–70°C). Compounds **10** and **11** are quite volatile oils, therefore we could not get elemental analyses.

6-Hydroxy-9-ethenylbicyclo[4.3.0]nonan-3-one (**10**, R = H): IR (CCl_4): $\tilde{\nu}$ = 3611 cm^{-1}, 3460 br, 3082, 2956, 2871, 1719, 1640, 1216, 919.

10b: ^1H NMR (600 MHz, $CDCl_3$): δ = 5.68 (ddd, *J* = 17 Hz, *J* = 10 Hz, *J* = 7.5 Hz, 1H), 5.01 (ddd, *J* = 17 Hz, *J* = 1.6 Hz, *J* = 0.7 Hz, 1H), 4.99 (ddd, *J* = 10 Hz, *J* = 1.6 Hz, *J* = 0.5 Hz, 1H), 2.61 (dd, *J* = 15.5 Hz, *J* = 6.7 Hz, 1H), 2.55 (ddd, *J* = 17 Hz, *J* = 11.2 Hz, *J* = 5.8 Hz, 1H), 2.20 (dd, *J* = 15.5 Hz, *J* = 5.4 Hz, 1H), 2.20 (ddd, *J* = 17 Hz, *J* = 6 Hz, *J* = 5 Hz, 1H), 2.1–1.6 (m, 9H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 212.55, 140.36, 115.18, 78.77, 52.46, 50.60, 40.49, 39.93, 35.62, 34.55, 29.53.

10a: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 212.61, 137.85, 115.93, 80.18, 50.52, 45.74, 39.40, 38.63, 36.37, 35.17, 27.98. – MS: *m/z* (%) = 180 (3), 179 (19), 162 (14), 161 (100), 120 (67), 110 (46), 109 (69), 107 (61), 105 (53), 91 (46), 83 (45), 81 (61), 79 (78), 67 (50), 55 (52). – HR-MS: 180.1151, calcd.: 180.1150 ($C_{11}H_{16}O_2$).

1-Methyl-6-hydroxy-9-ethenylbicyclo[4.3.0]nonan-3-one (**10**, R = Me): IR (CCl_4): $\tilde{\nu}$ = 3619 cm^{-1}, 3082, 2959, 2880, 1721, 1639.

10a: ^1H NMR (600 MHz, $CDCl_3$): δ = 5.62 (ddd, *J* = 16.7 Hz, *J* = 10.6 Hz, *J* = 8.1 Hz, 1H), 5.15–4.95 (m, 2H), 2.80–1.70 (m, 11H), 1.6 (s, br., 1H), 0.94 (d, *J* = 0.8 Hz, 3H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 210.78, 137.30, 116.83, 79.18, 52.31, 51.53, 45.85, 38.34, 34.67, 33.44, 25.58, 17.89.

10b: ^1H NMR (600 MHz, $CDCl_3$): δ = 5.65 (ddd, *J* = 17.1 Hz, *J* = 10.2 Hz, *J* = 8.3, 1H), 5.06 (ddd, *J* = 10.2 Hz, *J* = 1.8 Hz, *J* = 0.7 Hz, 1H), 5.00 (ddd, *J* = 17.1 Hz, *J* = 1.8 Hz, *J* = 1.1 Hz, 1H), 2.80–1.60 (m, 12H), 0.94 (s, 3H). – ^{13}C NMR (75 MHz, $CDCl_3$): δ = 211.67, 138.06, 116.92, 81.17, 51.03, 49.60, 47.26, 37.13, 36.53, 36.04, 25.06, 17.38. – MS: *m/z* (%) = 194 (2), 193 (9), 176 (5), 175 (27), 140 (19), 125 (61), 97 (100), 95 (39), 79 (32), 69 (46), 67 (27), 55 (34). – HR-MS: 194.1307, calcd.: 194.1307 ($C_{12}H_{18}O_2$).

Standard Procedure for Enones (Compound **9**): To a solution of 93 mg (0.35 mmol) of **9** in 30 ml of CH_2Cl_2 0.1 ml of Et_2O-BF_3 (0.89 mmol) is added at 0°C. The solution is stirred at 0°C for 2 h and then poured into 10 ml of brine. The organic layer is extracted three times with 20 ml of CH_2Cl_2 and then dried with $MgSO_4$. The crude product is flash-chromatographed with ethyl acetate/petroleum ether (25:75) to yield 64 mg (94%) of **11**. – IR (CCl_4): $\tilde{\nu}$ = 3618 cm^{-1}, 3450, br., 2962, 2934, 2870, 1962, 1723, 1035, 909, 854. – ^1H NMR (600 MHz, $CDCl_3$): δ = 4.80 (t, *J* = 4.5 Hz, 2H), 2.64 (m, 1H), 2.535 (dddd, *J* = 15.0 Hz, *J* = 9.5 Hz, *J* = 5.5 Hz, *J* = 1.5 Hz, 1H), 2.47 (m, 1H), 2.415 (dd, *J* = 14.5 Hz, *J* = 1.5 Hz, 1H), 2.27 (m, 1H), 2.24 (dd, *J* = 14.5 Hz, *J* = 1.5 Hz, 1H), 2.06 (ddd, *J* = 14.0 Hz, *J* = 9.5 Hz, *J* = 5.3 Hz, 1H), 2.01 (ddd, *J* = 14.0 Hz, *J* = 9.5 Hz, *J* = 5.0 Hz, 1H), 1.94 (ddd, *J* = 13.5 Hz, *J* = 7.0 Hz, *J* = 6.0 Hz, 1H), 1.88 (ddd, *J* = 13.0 Hz, *J* = 10.2 Hz, *J* = 6.5 Hz, 1H), 1.65 (s, br., 1H, OH exchangable with D_2O), 1.09 (s, 3H). – ^{13}C NMR (150 MHz, $CDCl_3$): δ = 209.81, 202.18, 108.22, 79.32, 79.19, 51.04, 48.13, 37.43, 34.83, 34.28, 24.41, 21.39. – MS: *m/z* (%) = 192 (5), 191 (27), 132 (47), 121 (59), 91 (71), 79 (100), 77 (51). – HR-MS: 192.1150, calcd.: 192.1149 ($C_{12}H_{16}O_2$).

CAS Registry Numbers

6 (R = H): 130434-25-2 / **6** (R = Me): 130434-26-3 / **8** (R = H): 130434-24-1 / **8** (R = Me): 130434-27-4 / **9**: 130434-23-0 / **10a** (R = H): 130434-18-3 / **10a** (R = Me): 130434-20-7 / **10b** (R = H): 130434-19-4 / **10b** (R = Me): 130434-21-8 / **11**: 130434-22-9

[1] E. Mutschler, *Arzneimittelwirkungen*, p. 422, Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart 1986.
[2] S. E. Denmark, J. P. Germanas, *Tetrahedron Lett.* **25** (1984) 1231.
[3] M. E. Jung, K. M. Halweg, *Tetrahedron Lett.* **22** (1981) 3929.
[4] D. Schinzer, *Synthesis* **1988**, 263.
[5] M. Ruppelt, *Dissertation*, University of Hannover 1989.

[310/90]