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SPIRO[4,5]DECENONE - SYNTHESIS

by P. Naegeli
Givaudan Research Company
Duebendorf, Switzerland

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In view of recent reports[1,2] on cationic cyclization of α,β-unsaturated ketones we would like to put on record our own experiences in this field[3].

Treatment of allylic alcohol (1)[4] with 2,5 molar equivalents of ethyl-vinylether with a catalytic amount of phosphoric acid in an autoclave at 150°C for 90 minutes (chilling after pressure drop) gave, after neutralization with a tertiary amine and fractionation, a 70% yield of aldehyde (2)[5]. Reaction of the latter, with or without preceding catalytic reduction of the isopropenyl double bond to (3)[5], with a 3-fold excess of vinylmagnesium bromide in tetrahydrofurane gave pure allylic alcohols (4) and (5)[5] in 85% yield. Subsequent oxydation with Jones reagent in acetone at -10 to -5°C (until the orange-red colour persists for 5 minutes) furnished the α, β-unsaturated ketones (6) and (7) in over 90% yield. If either of these two ketones was treated with a 0,5 molar benzene solution of stannic chloride (1,5 molar equivalents; total concentration of ketone in benzene:ether = 6:1-solution being 0,1 molar) at room temperature for 2 to 3 hours (addition at 0°C during 30 minutes) and then quenched with cold bicarbonate solution the two isomeric conjugated spiroketones (8)+(9) or (10)+(11) were formed as main products in 40-50% and 60-70% yield respectively (after column chromatography on silicagel or fractionation under reduced pressure)[6], (table 1).

Hydrogenation experiments with the individual compounds (separated by preparative VPC) clearly showed that one had to deal with formation of cis and trans substituted spiroketones in each cyclization. Correlation with the described[7] cis-spiro[4,5]decenone (12) allowed the relative assignment, (table 2).

A further confirmation for the type of substitution and for spiroconfiguration of (10) (i.e. also for (8)) was gained through a 3-step transformation[7] into racemic acorenone[9] (plus cis-isocalamenene[13]) which was identical in all respects except for optical rotation with an authentic sample of the natural product we isolated from the essential oil of European acorus calamus L.

In the trans-substituted series we prepared the missing spiroinverted compound (15) in low yield from (11) by a described procedure[10]. Surprisingly it was not possible in the trans-substituted as well as in the cis-substituted series to assign spiroconfiguration to the cyclization products by comparative analysis of all the ^{1}H-nmr spectra. Therefore compound (11) was chemically transformed by the same 3-step procedure[7] as above into the described[12] 4-epiacorenone B and trans-isocalamenene[13] (table 3). ^{13}C-nmr studies (see table 5)[11] did allow a distinction between cis- and trans-substituted products as well as a determination of spiroconfiguration in the cis-series by interpretation of the observed γ-effects of the substituents in position 1 and 4 on the methylene carbon atom 10.

The observed stereochemistry of the cyclization products is best explained by a 1,3-hydride shift in the cationic metal enolate-intermediates A and B (table 4). Cyclopropane intermediates though cannot be ruled out because on reprotonation they would show the same stereochemical outcome.

Table 1

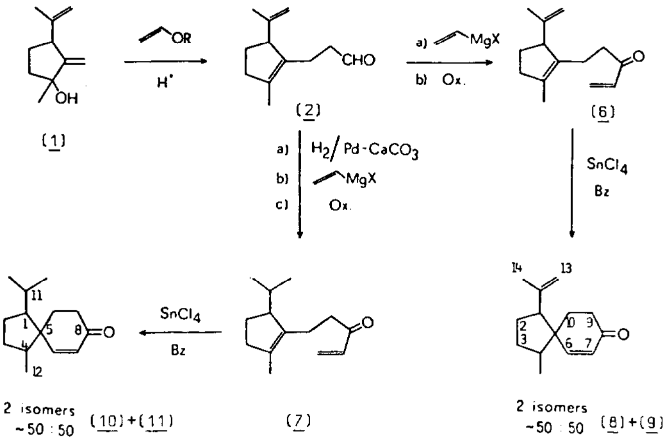

Table 2

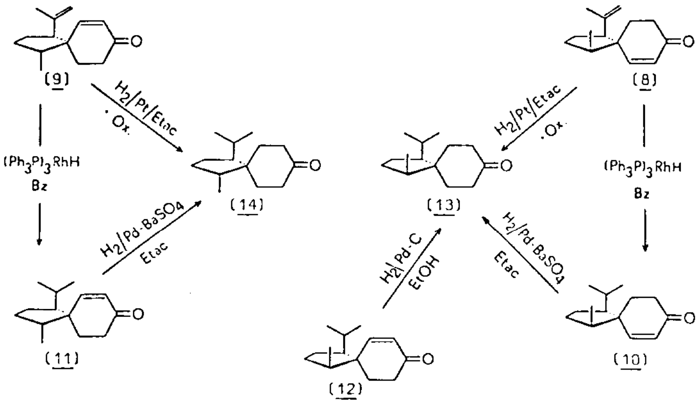

Table 3

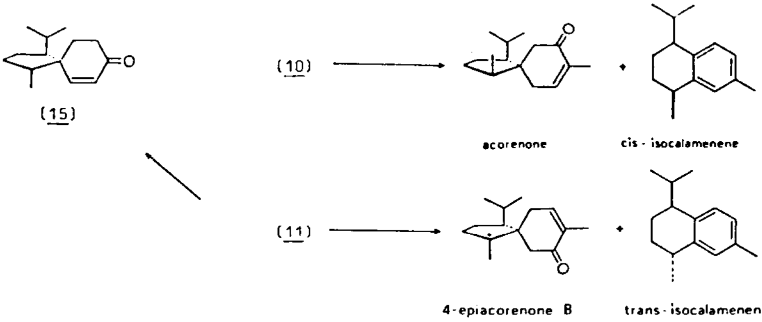

Table 4

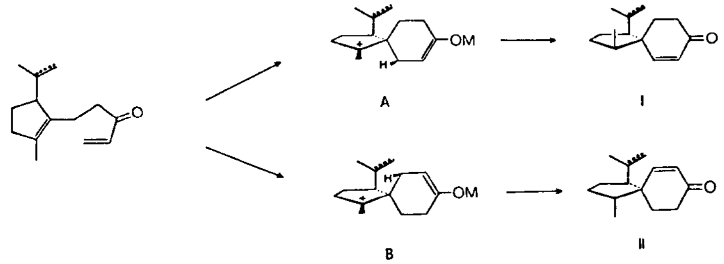

Table 5

Carbon/cpd.	(8)	(9)	(10)	(11)	(12)	(13)	(14)	(15)
1	58.0	54.6	60.1	54.3	58.3	57.5	50.5	56.2
2	26.0	28.9	28.1	26.0	25.2	25.1	25.1	29.2
3	29.9	31.7	30.2	31.9	31.5	31.0	30.3	32.2
4	46.4	43.4	46.2	45.0	46.1	43.4	38.6	42.4
5	48.6	49.3	47.9	48.7	48.8	44.3	46.2	48.5
6	158.7	157.2	160.2	157.6	153.3	24.9	⊙30.0	160.8
7	129.1	128.4	128.3	128.3	129.1	⊙38.7	38.1	127.6
8	199.4	198.9	198.9	199.0	199.3	212.1	211.3	197.7
9	34.7	34.6	35.0	34.8	35.6	⊙38.9	38.9	34.4
10	20.3	28.3	20.1	30.1	34.8	37.2	⊙31.8	28.5
11	144.0	146.2	30.5	29.7	29.2	28.0	28.4	30.0
12	15.3	15.6	15.3	15.8	17.2	16.7	16.5	19.6
13	112.6	112.6	*22.5	*20.3	*20.4	*21.0	*21.4	*22.8
14	24.7	23.6	*22.7	*23.3	*23.8	*24.9	*24.2	*23.0

Chemical shifts in ppm from TMS. (Assignments were made through induced shift experiments with Eu $(fod)_3$-d_{27} and in using the literature rules)[11].

⊙ & * assignments interchangeable.

Physicochemical data[14] :

(2) $bp_{0.2}$: 64-65°C; n_D^{20}=1.4888; ν_{max}: 3080, 2725, 1725, 1642, 1440, 1370, 1060, 895 cm^{-1}; NMR (Varian A60A): δ=9.67 (1H, s); δ=4.72 (2H, d with 1); δ=3.6-3.1 centered at 3.3 (1H, broad m); δ=1.68 (3H, s); δ=1.58 ppm (3H, s). MS: M^+ at 178, characteristic fragments at $^m/e$: 163, 150, 145, 135, 121=base peak, 107, 93, 79, 67, 55, 41.

(3) $bp_{0.001}$: 65°C; ν_{max}: 2750, 1728, 1470, 1385, 1365, 1100 cm^{-1}. MS: M^+ 180; char. fragm. at $^m/e$: 137, 119, 109, 95=base p., 79, 67, 55, 41. NMR (A60A): δ=9.81 (1H, s); δ=1.64 (3H, broad s); δ=0.91 (3H, d with 6.5); δ=0.65 ppm (3H, d with 6.5).

(4) $bp_{0.005}$: 80-85°C, $bp_{0.3}$: 97-99°C; ν_{max}: 3400, 3100, 1645, 1440, 1375, 1120, 1080, 995, 925, 892 cm^{-1}. MS: M^+ 206; char. fragm. at $^m/e$: 191, 180, 173, 163, 159, 145, 136, (133), 121, 105, 93=base p., 79, (73), 67, 55, (45), 41. NMR (A60A): δ=5.90 (1H, dd of d with 17/10/5.5); δ=5.34 and 5.17 and 5.02 (2H, 3m); δ=4.81 and 4.7 (2H, narrow m); δ=4.04 (1H, broad q with 5.5); δ=3.36 (1H, m); δ=1.68 (3H, broad s); δ=1.56 ppm (3H, broad s).

(5) $bp_{0.005}$: 80°C; ν_{max}: 3400, 3100, 1645, 1465, 1385, 1365, 995, 925 cm^{-1}. MS: M^+ 208; char. fragm. at $^m/e$: 190, 175, 165, 147, 136, 119, 105, 95=base p., 79, 67, 55, 41. NMR (A60A): δ=5.90 (1H, dd of d with 17/9.5/5.5); δ=5.32 and δ=5.15 and δ=5.01 (2H, 3m); δ=4.03 (1H, q with 5.5); δ=1.60 (3H, broad s); δ=0.88 (3H, d with 6.5); δ=0.62 ppm (3H, d with 6.5).

(6) $bp_{0.001}$: 50°C; ν_{max}: 3100, 1700/1685, 1645, 1620, 1440, 1405, 1375, 1185, 1100, 995/990, 965, 895 cm^{-1}; λ_{max} at 214 nm (9900). MS: M^+ 204; char. fragm. at $^m/e$: 189, 176/171, 161, 149, 134=base p., 119, 105, 93/91, 77, 65, 55, 41. NMR (A60A): δ=6.26 and 6.23 (2H, 2d with 8 and 4); δ=5.75 (1H, dd with 8 and 4); δ=4.71 (2H, narrow m); δ=3.29 (1H, broad m); δ=1.65 (3H, broad s); δ=1.57 ppm (3H, broad s).

(7) $bp_{0.01}$: 70°C; λ_{max} at 213 nm (7750). ν_{max}: 1700/1685, 1620, 1465, 1405, 1395, 1365, 1185, 1100, 995/985, 965 cm^{-1}. MS: M^+ 206; char. fragm. at $^m/e$: 191, 163, 145, 136, 121, 105, 93=base p., 77, 67, 55, 41. NMR: δ=6.13 and 6.26 (2H, 2d with 8 and 4); δ=5.78 (1H, dd with 8 and 4); δ=1.62 (3H, broad s); δ=0.89 (3H, d with 6.5); δ=0.64 ppm (3H, d with 6.5).

(8) $bp_{0.001}$: 50°C; mp: 34-35°C; λ_{max} at 240 nm (8100). ν_{max}: 3100, 1680, 1640, 1620, 1455, 1420, 1390, 1380, 1325, 1260, 1235, 1185, 1155, 1140, 1010, 895, 865, 825, 780, 760 cm^{-1}. MS: M^+ 204; char. fragm. at $^m/e$: 189, 176/175, 162/161, 147, 134, 123, 106, 91, 82=base p., 79, 68/67, 55/53, 41. NMR (WH 270): δ=6.59 (1H, d with 10); δ=6.04 (1H, d with 10); δ=4.91 (1H, pseudo q with ~ 1); δ=4.79 (1H, broad s); δ=2.46 (1H, broad dd with 12 and 9); δ=2.42 (2H, dd with 8 and 7); δ=2.1-1.62 (6H, several m); δ=1.72 (3H, broad s); δ=1.52-1.30 (1H, m); δ=0.98 ppm (3H, d with 6.5).

(9) $bp_{0.001}$: 50°C; λ_{max} at 230 nm (8500); ν_{max}: 3100, 1685, 1640, 1615, 1455, 1420, 1395, 1380, 1345, 1260, 1225, 1185, 1160, 895 cm^{-1}. MS: M^+ 204; char. fragm. at $^m/e$: 189, 176, 161, 147, 134, 122, 106, 94, 91, 82, 79, 68/67=base p., 55/53, 41. NMR (WH 270): δ=6.68 (1H, dd with 10 and 1); δ=5.9 (1H, d with 10); δ=4.85 (1H, small quintuplet); δ=4.77 (1H, small m); δ=2.71 (1H, broad t with 7.5); δ=2.54 (1H, dq with 17 and 9.5 and 5) and δ=2.43 (1H, dq with 17 and 7 and 5); δ=2.24-2.07 (1H, m); δ=2.07-1.90 (3H, m); δ=1.90-1.72 (2H, m); δ=1.70 (3H, broad s); δ=1.48-1.28 (1H, m); δ=0.96 ppm (3H, d with 7).

(10) $bp_{0.005}$: 40°C; λ_{max} at 241 nm (11300); ν_{max}: 1678, 1615, 1465, 1375, 1225, 1145, 895, 850, 770 cm^{-1}. MS: M^+ 206; char. fragm. at $^m/e$: 191, 164, 150, 135, 122=base p., 107, 94, 91, 79, 69, 65, 55. NMR (WH 270): δ=6.55 (1H, dd with 10 and 1.5); δ=6.01 (1H, dd with 10 and 0.5); δ=2.55 (1H, dq with 17/11.5/7) and δ=2.41 (1H, dq with 17/6.5/5); δ=2.01-1.73 (5H, m); δ=1.86-1.29 (4H, m); δ=0.97 (3H, d with 7); δ=0.88 (3H, d with 6.5); δ=0.86 ppm (3H, d with 6.5).

(11) $bp_{0.005}$: 40°C; λ_{max} at 238 nm (10900); ν_{max}: 1675, 1610, 1465, 1420, 1385, 1255, 1220, 1175, 1130, 890, 830, 775 cm^{-1}. MS: M^+ 206; char. fragm. at $^m/e$: 191, 164, 150, 135, 122=base p., 107, 94/91, 79, 69, 65, 55, 41. NMR (WH 270): δ=6.87 (1H, d with 10); δ=5.97, (1H, d with 10); δ=2.44 (2H, pseudo t with 7); δ=2.06-1.60 (7H, m); δ=1.56-1.40 (1H, m); δ=1.40-1.19 (1H, m); δ=0.97 (3H, d with 7); δ=0.90 (3H, d with 6.5); δ=0.86 ppm (3H, d with 6.5).

(13) $bp_{0.001}$: 50°C; ν_{max}: 1720, 1470, 1420, 1380, 1330, 1245, 1215, 1150, 940, 865, 755 cm^{-1}. MS: M^+ 208; char. fragm. at $^m/e$: 193, 179, 165, 152, 147, 137, 124/123=base p., 109, 95, 82, 69, 55, 41. NMR (WH 270): δ=2.58-2.27 (4H, m); δ=2.06-1.61 (8H, m); δ=1.61-1.39 (2H, m); δ=1.39-1.19 (1H, m); δ=1.03 (3H, d with 7); δ=0.96 (3H, d with 6.5); δ=0.88 ppm (3H, d with 6.5).

(14) $bp_{0.005}$: 50°C; ν_{max}: 1715, 1450, 1390/1380, 1335, 1305, 1240, 1215, 1165, 1135, 750 cm^{-1}. MS: M^+ 208; char. fragm. at $^m/e$: 193, 179, 165, 152, 147, 137, 124/123=base p., 109, 95, 82, 69, 55, 41. NMR (WH 270): δ=2.59-2.15 (5H, m); δ=2.00-1.62 (8H, m); δ=1.55-1.39 (1H, m); δ=1.36-1.18 (1H, m); δ=0.94 (3H, d with 6.5); δ=0.93 (3H, d with 7); δ=0.88 ppm (3H, d with 6.5).

(15) λ_{max} at 239 nm (8700); ν_{max}: 1685, 1610, 1470, 1385, 1225, 1170, 1130, 895, 775 cm^{-1}. MS: M^+ 206; char. fragm. at $^m/e$: 191, 178, 164, 150, 135, 122=base p., 107, 95/94/93, 84, 79, 69, 55, 41. NMR (WH 270): δ=6.81 (1H, dd with 10 and 2); δ=5.93 (1H, dd with 10 and 1); δ=2.62-2.24 (3H, m); δ=2.10-1.87 (3H, m); δ=1.81-1.49 (4H, m); δ=1.43-1.13 (3H, m); δ=1.06 (3H, d with 7); δ=1.05 (3H, d with 6.5); δ=0.94 ppm (3H, d with 6.5).

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14. IR spectra were measured as liquid films on PE 157 or 257 spectrometers, UV spectra in EtOH on a Beckman DB-G instrument, NMR spectra in $CDCl_3$ solution with TMS as internal standard on a Varian XL-100 and/or a Bruker WH 270 instruments and MS at 70 eV on a double focussing CEC 21-110 B spectrometer with an all-glass inlet system at 150°C.

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