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Rearrangement of Sclareolide to (4.3.3)-Propellanes under Strongly Acidic Conditions

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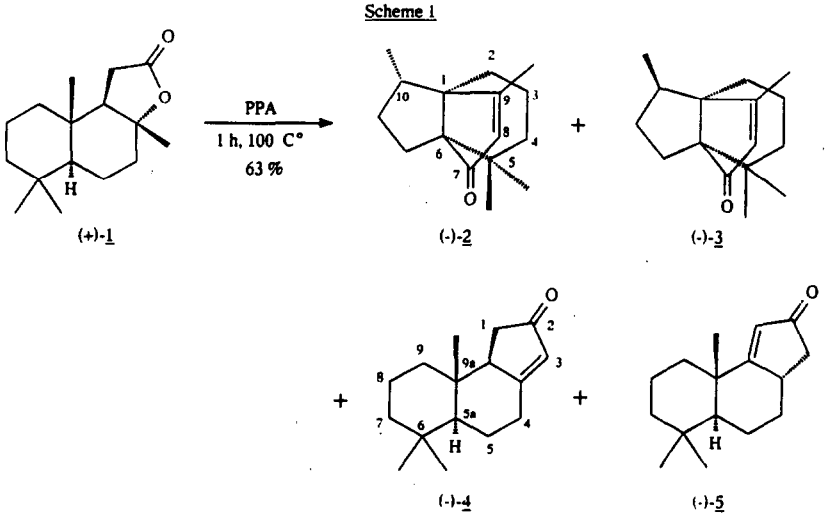
Abstract: Acid catalysed rearrangement of sclareolide ((+)-1) produces the propellanes (-)-2, (-)-3 and the linear-fused cyclopentenone (-)-5 beside the anticipated product (-)-4.

In the course of our synthetic program for the elucidation of structure-odor relationships (SOR) in the field of amber-woody compounds[1] we needed the linear-fused tricyclic cyclopentenone 4. For this purpose we considered the acid catalysed rearrangement of the γ-lactone sclareolide (+)-1 to be a workable route.[2] Consequently (+)-1 was treated with polyphosphoric acid (PPA)[2c] (1h, 100° C) and four main products were isolated (63%; scheme 1) : the two diastereomeric propellanes (-) 2 and (-)-3 in 36% yield [(-)-2 : (-)-3 ~3 : 1] and two cyclopentenones (-)-4 and (-)-5 in 27% yield [(-)-4 : (-)-5 ~ 5 : 1]. Eaton's reagent[3] (P_2O_5 in CH_3SO_3H, 1h, 105° C) furnished a mixture with the same constituents in 45% yield with completely changed selectivity [40% (-)-4 and (-)-5 in a ratio of 2.5 : 1; 5% (-)-2 and (-)-3)] from which traces (~1%) of the mechanistically important product 6 could be isolated.[4]

Scheme 1



(+)-1 (-)-2 (-)-3 (-)-4 (-)-5

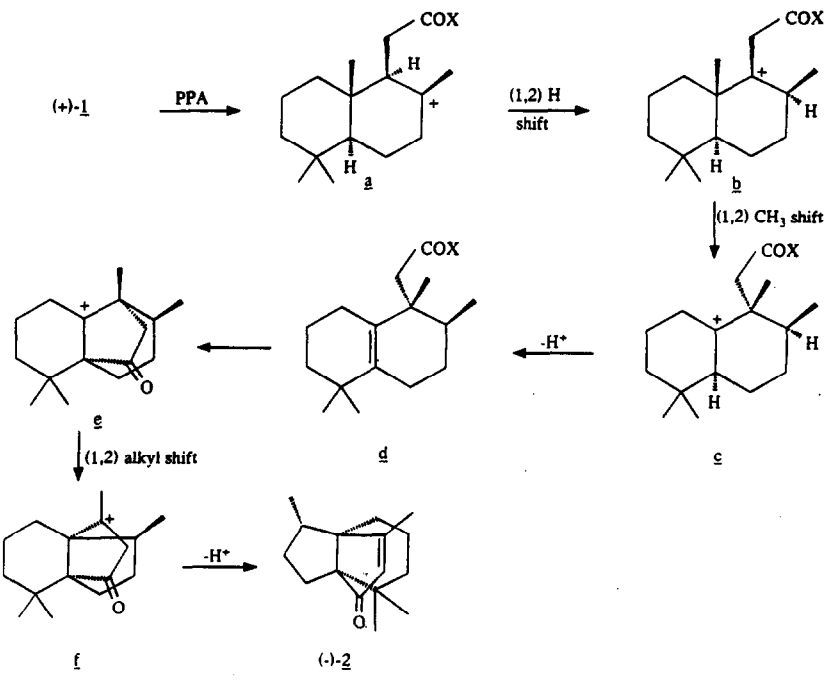
A mechanistic proposal for the formation of the propellanes (-)-2 and (-)-3 is depicted in scheme 2. From the starting carbenium ion a two consecutive syn (1,2) hydride and methyl shifts lead to c, which looses a proton to give the olefin d. The latter being a γ, δ-unsaturated acid derivative, undergoes an intramolecular olefin acylation to furnish e, which after a (1,2) alkyl shift and the loss of a proton ends up in (-)-2. The formation of (-)-3 reflects merely the well known isomerisation of sclareolide ((+)-1) to episclareolide ((-)-7),[5,6,7] from which epi-d is formed (scheme 3). Protonation of epi-d can lead to g, which is a precursor of the trace compound 6.[8]

The selective formation of (-)-4 and (-)-5 without detectable traces of the (9b)-epimer of (-)-4 and the (3a)-epimer of (-)-5 respectively is worth mentioning. Both in (-)-4 and in (-)-5 the angular protons H (9bα) and H (3aß) respectively are pseudo axial (NOE diff.), which ensures in both cases the thermodynamically most stable epimer. The generation of (-)-5 can be rationalised as taking place with episclareolide (-)-7 as an intermediate.[7]

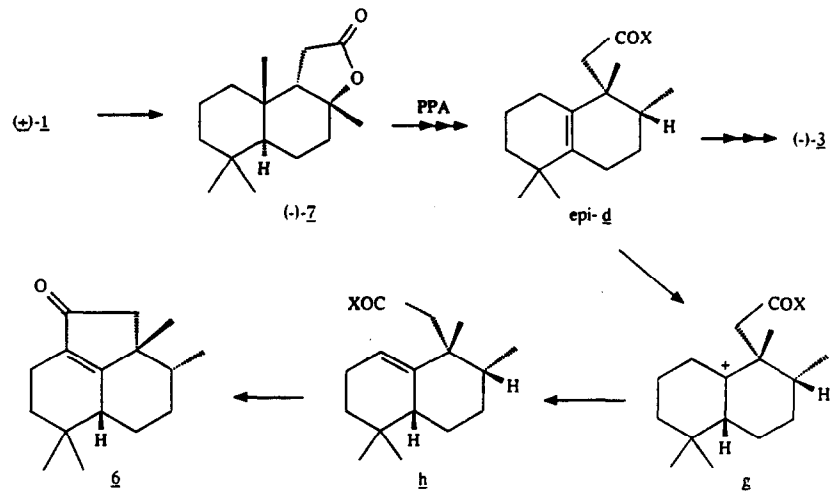
The proposed intermediate d, from which the propellane (-)-2 is formed, arises from (+)-1 after a (1,2) hydride and a consecutive (1,2)-methyl shift; these steps, which were observed here in vitro are well known in the biosynthesis of a number of diterpenes[9] (conf. ref. 8).

What concerns the step e →f (scheme 2), i.e. the transformation of a bridged-bicyclo (3,2,1)-skeleton into a bridged-bicyclo (3,3,0)-skeleton, analogous observations have been already made.[10]

Scheme 2



Scheme 3



In the sensory evaluation (-)-2 and (-)-3 turned out to have a woody, fruity and amberlike character, (-)-3 being more powerful, whereas (-)-4 and (-)-5 were only weakly woody, (-)-5 showing an additional weak camphoraceous tonality.

Acknowledgement: Thanks are due to Mr. J. Märki for the extensive NMR studies and to Mr. M. Badzong for skilful experimental work.

References and Notes

1. From the point of view of SOR and of synthesis the class of ambergris compounds is one which has been intensively worked on, corresponding to their commercial importance. We are forced to quote only reviews on this topic instead of the original works:
a) G. Ohloff, B. Winter, C. Fehr, in Perfumes; Art, Science & Technology. Ed. P.M. Müller, D. Lamparsky. Elsevier, 1991, p. 287. b) G. Fráter, D. Lamparsky, ibid, p. 533. c) G. Ohloff, in "Fragrance Chemistry", Ed. E.T. Theimer, Academic Press, 1982, p. 535.
2. For the acid catalysed transformation of unsaturated acids and γ-lactones into cyclopentenones see a) Pl. A. Plattner, A. St. Pfau, Helv. Chim. Acta. 20, 1474 (1937). b) M.F. Ansell, M.H. Palmer, Quart. Rev. 18 (2), 211, (1964). c) D.A. Rowlands, in "Synthetic Reagents", Vol. 6, Ed. J.S. Pizey; Ellis Horwood Ltd, 1985, p. 156.
3. P.E. Eaton, G.R. Carlson, J.T. Lee, J. Org. Chem. 38, 4071 (1973).
4. The structure and stereochemistry of the new compounds were deduced by means of ^{1}H, ^{13}C-NMR, $^{13}C^{1}H$-2D- and $^{13}C^{13}C$-2D INADEQUATE-spectra and NOE-diff. measurements.
(-)(1S, 6R, 10S)-5,5,9,10-tetramethyl-tricyclo (4,3,3,$0^{1,6}$) dodec-8-en-7-one (-)-2:
IR (liq): 1690, 1620 cm^{-1}. UV (EtOH) λ max: 235, (ε =8754). ^{1}H-NMR (200 MHz, $CDCl_3$): 5.76 (m,J=1.3, H-C(8)); 2.05 (d,J=1.3, CH_3-C(9)); 1.05 (s,CH_3-C(5) eq); 1.00 (d,J=7,CH_3-C(10)); 0.84 (s,CH_3-C(5)ax); ^{13}C-NMR ($CDCl_3$); 213.8 (s,C(7)); 182.9 (s,C(9)); 129.1 (d,C(8)); 65.5 (s,C(6)); 58.9 (s,C(1)); 44.1 (d,C(10)); 34.8 (s,C(5)); 33.8 (t,C(4)); 31.8 (t,C(11)); 28.4 (t,C(12)); 26.9 (q,C(14)); 26.3 (q,C(13)); 22.9 (t,C(2)); 17.9; (t,C(3)); 15.8 (q,C(16)); 15.4 (q,C(15)); MS: 232 (34 M^+), 217(11), 204(6), 189(6), 175(16), 161(15), 150(100), 135(17), 122(37), 105(15), 91(16), 77(10), 69(10), 55(11), 41(21), 28(52).$(\alpha)_D^{20}$=-145, 58° ($CHCl_3$, c=1.047).

In the diastereomer (1S,6R,10R)-(-)-3 the ^{13}C-signal of C(2) was observed at 26.3 ppm (t) vs.22.9 in (-)-2, which has been interpreted as a γ-effect of CH_3-C(10).

(-)-1,4,5,5a,6,7,8,9,9a,9b-Decahydro-6,6,9a-trimethyl-(5aS-(5aα, 9aß, 9bα))-2H-benz (e) inden-2-one ((-)-4): IR(liq): 1705, 1670, 1620. UV (CH_2Cl_2); λ max: 235, (ε =14935). ^{1}H-NMR ($CDCl_3$ 400 MHz): 5.83 (m,J=1.4, H-C(3)); 2.85 (ddd,J=14.6, J=1.4, J=4.8,H-C(4)); 2.48 (d (broad),J=6,H-C(9b)); 2.32 (dd (broad), J=7, J=12.5, H-C(4)); 2.23 (ddd, J=19,J=6.5,J=1,Hß-C(1)); 2.15 (ddd, J=19,J= 1, J=2.5, Hα-C(1)); 1.91 (ddd, J=13.4,J=2.4, J=6.4, Heq-C(5)); 1,27 (dd,J=12.5J=2.6,H-C(5a)); 0.95 (s,H_3C(11); 0.86 (s,H_3-C(10)); 0.67 (s,H_3-C(12)); ^{13}C-NMR ($CDCl_3$): 208.2 (s,C(2)); 181.7 (s,C(3a)); 126.7 (d,C(3)); 54.7 (d,C(9b)); 52.5 (d,C(5a)); 41.4 (t,C(7));39.5 (t,C(9)); 38.3 (s,C(9a)); 35.4 (t,C(1)); 32.8 (q,C(11)); 32.5 (s,C(6)); 30.0 (t,C(4)); 21.9 (t,C(5)); 21.1 (q,C(10)); 18.0 (t,C(8)); 12.0 (q,C(12)); MS: M^+ 232(11); 217(9); 204(5); 199(1); 189(5.6);175(4.4); 161(8.4); 149(10); 137(72); 123(38); 109(57); 96(100); 91(16); 81(40); 69(33.5); 55(29); 41(48) $(\alpha)_D^{20}$=-103.5° (c=1.04 $CHCl_3$).

(-)-3,3a,4,5,5a,6,7,8,8,9,9a-Decahydro-6,6,9a-trimethyl (3aS-(3aß,5aα,9aß)-2H-benz (e) inden-2-one ((-)-5): IR ($CHCl_3$): 1680, 1600 cm^{-1}. UV (EtOH) λ max: 232, (ε =11851). ^{1}H-NMR ($CDCl_3$: 5.695-5.68 (m,H-C(1)); 2.96-2.88 (m,Hα-C(3a); 2.545 (dd,J=19, J=6.8, Hα-C(3)); 2.29-2.22 (m,Hα-C(4)); 1.95 (dd,J=19, J=2, Hß-C(3)); 1.18 (s,CH_3-C(9a)); 0.93 (s,CH_3-C(6)); 0.895 (s,CH_3-C(6)); ^{13}C-NMR ($CDCl_3$): 194.5 (s,C(2)); 121.9 (d,C(1)); 53.67 (d,C(5a)); 42.4 (t,C(3)); 41.8 (t,C(7)); 39.9 (s,C(9a)); 38.3 (d,C(3a)); 37.0 (t,C(9)); 35.8 (t,C(4)); 33.9 (s,C(6)); 33.3 (q,C(11)); 21.7 (q,C(10)); 21.3 (t,C(5)); 19.3 (q,C(12)); 18.4 (t,C(8)); MS: 232 (57 M+), 217(12), 190(30), 175(30), 161(12), 147(19), 135(19), 122(26), 109(100), 91(40), 79(26), 69(27), 55(46), 41(77), 28(19). $(\alpha)_D^{20}$ = -191.8 (c=1.23 $CHCl_3$).

5. a) G. Lucius, Chem. Ber. 93, 2663 (1960). b) A. Saito, M. Matsushita, H. Kaneko, Chem. Lett. 1984, 591. c) G. Ohloff, W. Giersch, W. Pickenhagen, A. Furrer, B. Frei, Helv. Chim. Acta, 68, 2022 (1985).
6. Epi-sclareolide (-)-7 furnished under the same conditions (PPA, 100° C, 1h) essentially the same product mixture, although in somewhat lower yield.
7. The products are stable under the reaction conditions (PPA, 100° C, 1h), thus the reaction is kinetically controlled.
8. A homologue of 6 has been isolated from the acid catalysed reaction of ambreinolide: G. Büchi, W.S. Saar, A. Eschenmoser, Experientia, XII/4, 136 (1956).
9. a) D.H.R. Barton, H.T. Cheung, A.D. Cross, L.M. Jackman, M. Martin-Smith, J. Chem. Soc. 1961, 5061.b) A. Ohsaki, K. Shibata, T. Tokoroyama, T. Kubota, H. Naoki, Chem. Lett. 1986, 1585. c) R.P. Walker, D.J. Faulkner, J. Org. Chem. 46, 1098 (1981).
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