

CYCLIC HEMIACETAL AND ACYCLIC CHAIN — THE TWO FORMS OF SERRICORNIN

Masataka Mori*, Tatsuji Chuman, and Kunio Kato

Central Research Institute, the Japan Tobacco & Salt Public Corporation

6-2 Umegaoka, Midori-ku, Yokohama 227, Japan

Summary: The actual structures of the four stereoisomers of serricornin were examined by the X-ray analysis and high-field pmr spectroscopy. Each of the stereoisomers assumes either or both of two forms, cyclic hemiacetal and acyclic chain, in solution.

Serricornin, (4*S*,6*S*,7*S*)-7-hydroxy-4,6-dimethyl-3-nonanone (1), is the sex pheromone of cigarette beetle¹⁾. Regarding the relative stereochemistry at C-4,6, and 7 of 1, four enantiomeric pairs as depicted are possible, each of which was designated to SSS (4*S*,6*S*,7*S* and 4*R*,6*R*,7*R*), RSS, SSR, and RSR, respectively. In the course of our study for the relationship between the stereochemistry and biological activity upon these stereoisomers of 1, we encountered the intramolecular hemiacetal formations of the molecules²⁾.

We report herein the examination of this interesting isomerism of serricornin by the uses of high field (500 MHz) pmr spectroscopy and two dimensional (2D) nmr methods³⁾.

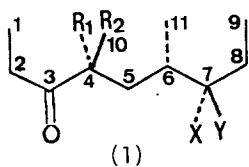
Each of the four stereoisomers of 1 could be obtained in the pure form from the non-stereoselectively synthesized mixture by the chromatographic separations and epimerizations⁴⁾.

The stereoisomer RSR is a crystalline substance (m.p. 46.5°-47.5°), and the X-ray crystallographic analysis established the cyclic hemiacetal structure in the solid state⁵⁾ (Fig. 1). This fact led us to the substantial reconsiderations for the actual structure of 1.

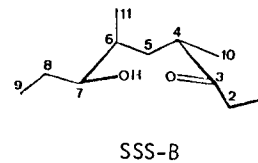
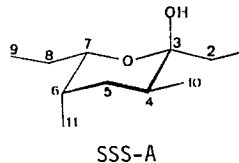
The assignments for all protons of RSR was established by the 2D-pmr methods⁶⁾. The large values of $J_{5ax,4} = J_{5ax,6} = 11.9$ Hz and $J_{6,7} = 10.0$ Hz showed that RSR preferentially assumes a cyclic conformation in C₆D₆ solution similar to that observed in the solid state. The cmr analysis of RSR confirmed the acetalic nature for the C-3 carbon, which appeared at δ 98.0 ppm.

On the other hand, RSS isomer showed a different spectroscopic features⁷⁾ from those of RSR. The pmr pattern indicated that RSS solely exists as an acyclic chain form. The low field shifts of H-2 (δ 2.15 and 2.09 ppm) and H-4 (δ 2.41) adjacent to C-3 carbonyl in comparison with those of RSR are essential. The cmr analysis also showed the C-3 carbonyl carbon at δ 214.1 ppm.

The natural and biologically active isomer SSS gave the complicated pmr and cmr⁸⁾ spectra of a binary mixture of these two forms. From the integral values of the two H-7 signals in the pmr spectrum, the ratio of cyclic hemiacetal (SSS-A) and acyclic chain (SSS-B) was determined to be 2.5:1, respectively. The full assignments of each set of the protons due to the two forms of



4	6	7	R ₁	R ₂	X	Y
S	S	S	H	Me	OH	H
R	S	S	Me	H	OH	H
S	S	R	H	Me	H	OH
R	S	R	Me	H	H	OH



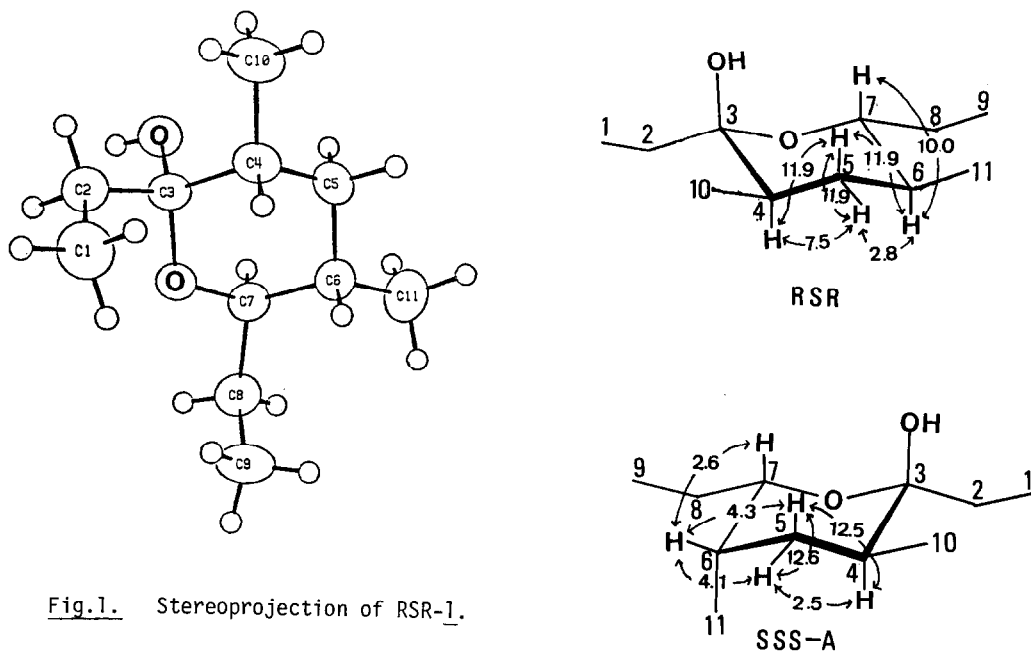


Fig.1. Stereoprojection of RSR-1.

	PROTON	SHIFT (ppm)	COUPLINGS (Hz)
SSS-A	A-1	0.911	$J_{1,2}=7.5$
	A-9	0.89	$J_{9,8}=7.5$
	A-10	0.907	$J_{10,4}=6.6$
	A-11	0.88	$J_{11,6}=7.0$
	A-2	1.61	$J_{2,2'}=13.6$
	A-2'	1.53	
	A-4	1.77	$J_{4,5ax}=12.5, J_{4,5eq}=2.5$
	A-5ax	1.88	$J_{5ax,5eq}=12.6$
	A-5eq	1.25	
	A-6	1.57	$J_{6,5ax}=4.3, J_{6,5eq}=4.1, J_{6,7}=2.6$
	A-7	3.96	
	A-8	1.52	$J_{7,8}=7.8, J_{7,8'}=6.1, J_{8,8'}=13.5$
A-8'	1.28		
SSS-B	B-1	0.96	$J_{1,2}=7.3$
	B-9	0.86	$J_{9,8}=7.5$
	B-10	0.911	$J_{10,4}=6.8$
	B-11	0.77	$J_{11,6}=7.1$
	B-2	2.10	
	B-4	2.52	$J_{4,5}=6.2, J_{4,5'}=7.6$
	B-5	1.52	$J_{5,5'}=13.1$
	B-5'	1.35	
	B-6	1.40	$J_{6,5}=8.1, J_{6,5'}=5.4, J_{6,7}=3.8$
	B-7	3.23	
	B-8	1.30	$J_{7,8}=8.5, J_{7,8'}=5.0, J_{8,8'}=13.8$
	B-8'	1.27	

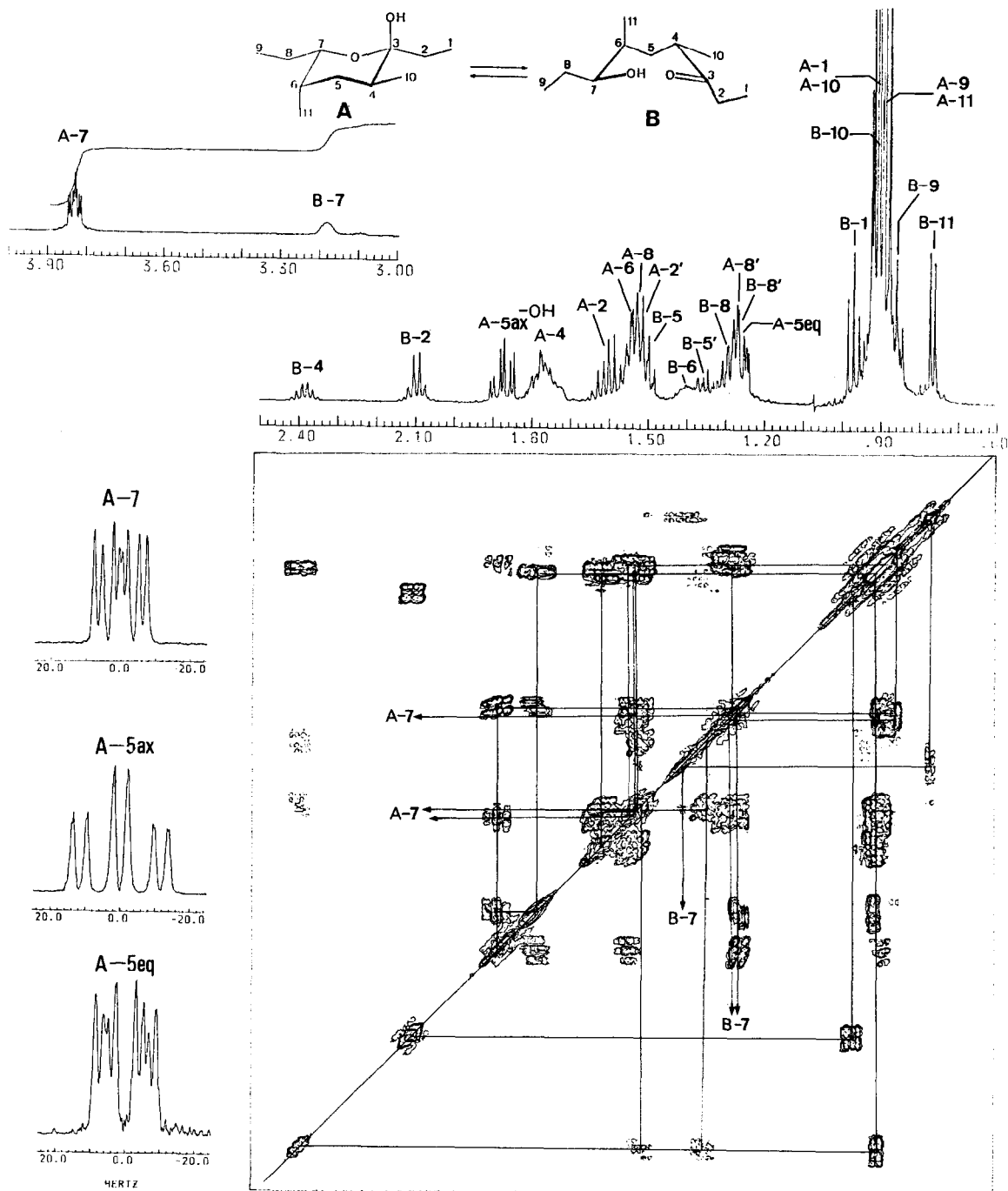


Fig. 2 2D-J-correlated (COSY⁴⁵) spectrum of SSS-1 with J-resolved A-7, A-5ax and A-5eq signals. Assignments: Upper — SSS-A, Lower — SSS-B.

SSS by 2D methods are listed in Table. The assignments for the weak or overlapped cross-peaks in the 2D-COSY45 spectrum of SSS (Fig. 2) were supported by the homo-nuclear decouplings and deuterium exchange techniques. Comparing with the data of RSR, the couplings to the geminal pair of H-5, and H-7 due to SSS-A allow an assignment of the ring conformation. Considering the large values of $J_{5ax,4} = 12.5$ Hz and the other small couplings for the ring protons, the structure depicted is the most plausible conformation for SSS-A⁹).

In addition, the residual SSR isomer showed a pmr pattern similar to that of SSS.

ACKNOWLEDGEMENT

We are grateful to Dr. K. Nakayama of Toray Research Center, Inc. for X-ray analysis of RSR-1.

REFERENCES AND NOTES

- 1 T. Chuman, M. Kohno, K. Kato and M. Noguchi, *Tetrahedron Lett.*, 2361 (1979). M. Mori, T. Chuman, K. Kato and K. Mori, *Tetrahedron Lett.*, 23, 4593 (1982). And references cited therein.
- 2 Prof. K. Mori and Mr. H. Watanabe of Tokyo University simultaneously came to a similar conclusion in their new synthesis of the optically active SSS-1; *Tetrahedron*, (1984); submitted.
- 3 Pmr spectra (500 MHz) were obtained in C₆D₆ at 27° on a Bruker AM-500 NMR. The software used for 2D spectra was the Bruker 820601.3 version. The data size of the time domain, 2D-J-correlated (COSY45) spectra used the pulse sequence [2.5 sec-90°-t₁-45°-t₂-FID] was 512(f₁) x 2K (f₂) matrix. Fourier transformation was performed with zero filling in both directions. The 256(f₁) x 2K(f₂) data matrix of the time domain, 2D-J-resolved spectra were processed in a similar way. Exact chemical shifts and coupling constants were determined by slices from 2D-J-resolved spectra and homo-nuclear decouplings. Cmr spectra (22.4 MHz) were recorded in C₆D₆ on a Hitachi R-90H NMR.
- 4 The chromatographic separations and isomerization reactions of the stereoisomers of 1 will be reported elsewhere.
- 5 Crystal data: C₁₁H₂₀O₂, M=186.3, monoclinic, space group P₂₁/c, a=11.206(1), b=10.197(2), c=10.709(2) Å, β=110.00(1)°, V=1149.9 Å³, Z=4. A total of 2592 reflections were collected on an Enraf-Nonious CAD-4 diffractometer using graphite-monochromated Cu-Kα radiation (λ=1.54184 Å), and 2362 were unique and not systematically absent. Corrections for Lorentz-polarization effects and extinction (coefficient=0.0000028) were applied to the data. The structure was solved by direct methods with final R value of 0.046. The ORTEP computer drawing is shown in Fig. 1. Details will be reported in our full paper.
- 6 For RSR: δ_H(TMS); 0.72(3H, br. d, J=6.6 Hz, H-11), 0.89(3H, t, J=7.5 Hz, H-1), 0.91(3H, d, J=6.9 Hz, H-10), 1.01(3H, br. t, J=7.6 Hz, H-9), 1.26(ddd, J=2.8, 7.5 and 11.9 Hz, H-5eq), 1.29(m, H-6), 1.37(q, J=11.9 Hz, H-5ax), 1.39(ddq, J=2.6, 13.8 and 7.3 Hz, H-8'), 1.51(dq, J=13.5 and 7.6 Hz, H-2'), 1.54(ddq, J=7.5, 11.9 and 6.9 Hz, H-4), 1.58(dq, J=13.5 and 7.5 Hz, H-2), 1.64(ddq, J=7.3, 13.8 and 7.6 Hz, H-8), 3.38(ddd, J=2.6, 7.3 and 10.0 Hz, H-7) ppm. δ_C(TMS); 7.35, 9.85, 16.59, 17.68, 26.01, 32.87, 35.34, 36.83, 37.32, 75.89(C-7), 97.96(C-3) ppm.
- 7 For RSS: δ_H(TMS); 0.82(3H, d, J=6.7 Hz, H-11), 0.89(3H, d, J=6.7 Hz, H-10), 0.91(3H, t, J=7.4 Hz, H-9), 0.97(3H, t, J=7.4 Hz, H-1), 1.02(ddd, J=5.4, 8.1 and 13.4 Hz, H-5'), 1.31(m, H-8'), 1.35(m, H-6), 1.39(m, H-8), 1.92(ddd, J=6.0, 8.7 and 13.4 Hz, H-5), 2.09(dq, J=18.4 and 7.4 Hz, H-2'), 2.15(dq, J=18.4 and 7.4 Hz, H-2), 2.41(ddq, J=5.4, 8.7 and 6.7 Hz, H-4), 3.21(br. qui, J=4 Hz, H-7) ppm. δ_C(TMS); 7.99, 10.98, 14.06, 17.71, 27.44, 34.09, 36.28, 37.23, 44.09, 75.43(C-7), 214.13(C-3) ppm.
- 8 Cmr data for SSS-A: δ_C(TMS); 7.41, 10.61, 11.68, 16.71, 26.13, 30.09, 31.22, 33.05, 36.13, 72.53(C-7), 98.45(C-3) ppm. For SSS-B: 8.02, 10.82, 13.69, 16.40, 27.44, 33.84, 35.76, 36.77, 43.75, 76.22(C-7), 213.42(C-3) ppm.
- 9 Considering the anomeric effect, the orientation of C-3 hydroxyl group was tentatively assigned to be axial. A small signal which may be due to H-7 of the C-3 epimer was observed in the pmr spectrum of SSS at δ 3.10 ppm (ddd, J=2.7, 5.4 and 8.1 Hz).

(Received in Japan 24 February 1984)