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SYNTHESIS OF dl-(2E,6Z,10E)-CERICERENE FOR ELUCIDATION OF THE PROPOSED STRUCTURE OF CERICEROL-I[1)]

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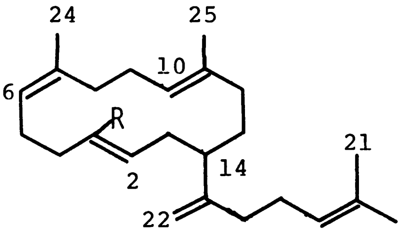
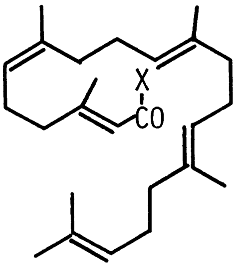
dl-(2E,6Z,10E)-Cericerene was synthesized and its spectral data were compared with those of cericerene derived from cericerol-I, revealing that the reported arrangement of annular double bonds of cericerol-I and related compounds should be revised.

Many sesterterpenoids have been isolated from the insect wax secreted by Ceroplastes (genus),[2,3)] which is known to be a rich source of sesterterpenes as exemplified by cericerol-I. Structural elucidation was carried out mainly on the basis of spectroscopic data, in which cericerene, a skeletal hydrocarbon derived from cericerol-I, played an important role. Structures 1 and 2 with R configuration at C-14 were proposed for cericerol-I and cericerene, respectively. Although it is evident that cericerene has a 14-membered monocyclic skeleton, the arrangement of annular double bonds, particularly the position of the cis-double bond, does not necessarily seem to be established.[2,3)] In order to clarify this aspect, we undertook the synthesis of 2, the result of which is described in this communication.



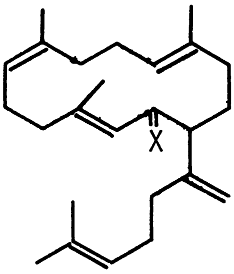
1 $R = CH_2OH$
2 $R = CH_3$

(2E,6Z,10E)-Geranylfarnesic acid (3) was prepared in 47% yield starting from (2Z)-geranylgeraniol via known method.[5)] The acid chloride (4) derived from 3 ($SOCl_2$, py, 0°C) was treated with 0.3 mol equivalents of $SnCl_4$ in CH_2Cl_2 at -95°C for 1 h and the reaction was quenched with excess pyridine at the same temperature. Without purification, the resultant mixture of chlorides was subjected to dehydrochlorination[6)] with LiBr-Li_2CO_3 in DMF at 105°C for 6 h and the products were purified by SiO_2 column chromatography, providing ketones (5 and 6) in 15 and 25% yields, respectively. Presence of isopropenyl group in 5 was shown by decoupling experiment in the ^1H NMR spectrum. As summarized in Table 1, ^{13}C NMR spectra[9)] of 5 and the hydrocarbon (7) derived therefrom[10)] support the structure of hitherto unknown 18-membered ketone (5).[11)] The structure of 14-membered ketone (6) is based on the close similarity of its ^1H and ^{13}C NMR spectra with those of the relevant ketone (8).[5)]



3 X = OH

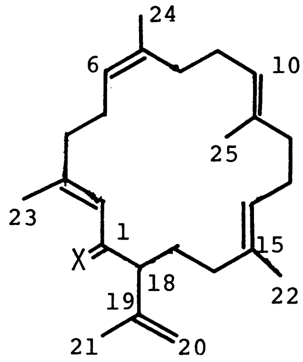
4 X = Cl



6 X = O

9 X = H,OH

11 X = H,OAc



5 X = O

7 X = H_2

Reduction of 6 with AlH_3 at -95°C afforded the allyl alcohol (9) in 45% yield as major product accompanied by 2,3-dihydro ketone (10). 9 was converted to the corresponding acetate (11) quantitatively (Ac_2O, py). In the ^1H NMR spectrum, 1-H of 11 appeared at 5.51 ppm with $J_{1,2}$ = 7 and $J_{1,14}$ = 2.7 Hz. Acetylation of 1-OH of 9 caused the 14-H signal to shift downfield by 0.3 ppm. These observations suggest the partial stereostructure of 9 as depicted in 9a although the complete conformation is left uncertain due to the mobility of the 14-membered ring.

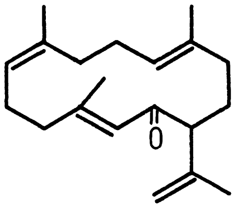
Treatment of 11 with Li in $EtNH_2$ (-78°C, 20 min) furnished a hydrocarbon (2) in 26% yield after purification with $AgNO_3$-SiO_2 column chromatography. Although its mass fragmentation was identical to that reported for cericerene from natural cericerol-I,[2b)] spectroscopic data were not identical. Therefore, the arrangement of annular double bonds of cericerene and of the compounds which have been related to cericerene[2b)] should be revised. Recently, Y. Naya has concluded that cericerene has a (2Z,6E,10E)- and not a (2E,6Z,10E)-skeleton.[12)]

Table 1.

^{13}C-NMR chemical shifts of (2E,6Z,10E)-cericerene and its synthetic intermediates

C-atom	II	III	V	VI	VII	VIII	XI
1	30.00c)	172.59	200.79	201.58	32.11d)	201.46	72.81
2	127.60	115.41	125.07a)	126.77	125.32b)	126.40	124.11
3	133.59	162.73	159.47	152.75	135.18a)	153.03	134.15
4	39.34b)	41.58	41.06	39.23	39.89c)	39.13	39.51
5	24.31	25.91	25.13	24.74c)	24.83	24.63	24.89a)
6	124.41	123.51	122.20a)	126.12	123.06b)	125.96	120.79b)
7	134.10a)	135.32	134.01b)	135.06	133.54a)	135.03a)	139.08c)
8	30.32	32.05	32.25	30.16	32.61d)	30.09	29.97
9	26.83	26.83	26.57d)	25.98c)	26.68e)	25.92	23.84a)
10	124.41	124.48	124.16a)	126.12	123.20b)	125.96	126.93b)
11	134.50a)	136.43	136.23b)	133.43	136.41a)	133.42a)	134.62c)
12	35.08b)	39.75	39.17c)	37.73	38.92c)	37.55	37.02
13	30.06c)	26.70	27.22d)	28.07	28.18e)	27.12	26.60
14	43.59	124.22	124.94a)	56.14	125.11b)	57.74	46.23
15	153.44	134.93	134.34b)	147.85	135.47a)	144.10	149.65
16	34.70	39.75	37.21c)	35.38	37.16c)	20.61	34.02
17	26.36	26.50	27.68d)	26.63	29.65		26.60
18	123.76	123.96	59.99	123.90	46.88		123.64
19	131.36	131.14	143.61	131.66	148.62		131.39
20	25.69	25.72	113.45	25.65	110.40		25.63
21	17.73	17.69	20.26e)	17.76	19.29		17.99d)
22	107.99	15.99	15.60	111.75	15.53	112.78	110.17
23	16.44d)	19.19	20.43e)	19.97	16.91	20.02	17.99d)
24	22.19	23.37	23.30	22.32	23.25	22.25	22.13
25	17.23d)	15.99	16.06	14.88	16.56	14.82	17.61d)
$OCOCH_3$							170.22 21.16

a-e) Assignments denoted by same alphabet are interchangeable.



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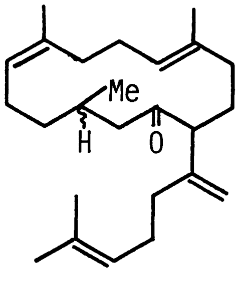

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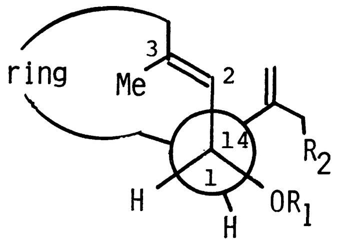

9a $R_1 = H$

$R_2 = CH_2CH{=}CMe_2$

References

1) This constitutes part 37 of the series, Cyclization of Polyenes. Part 36, M. Aoki, T. Uyehara, and T. Kato, Tetrahedron Lett., in press (1983).

2) a) T. Kusumi, T. Kinoshita, K. Fujita, and H. Kakisawa, Chem. Lett., 1979, 1129;
   b) F. Miyamoto, H. Naoki, T. Takemoto, and Y. Naya, Tetrahedron, 35, 1913 (1979);
   C) Y. Naya, F. Miyamoto, K. Kishida, T. Kusumi, H. Kakisawa, and K. Nakanishi, Chem. Lett., 1980, 883;
   d) F. Miyamoto, H. Naoki, Y. Naya, and K. Nakanishi, Tetrahedron, 1980, 3481.

3) Albocerol having 2Z-geometry was isolated from the same genus.4) All the reports related to Ceroplastes albolineatus.

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6) Dehydrochlorination was also attempted by silica gel7) and Al_2O_3,8) giving no satisfactory result.

7) H. Takayanagi, T. Uyehara, and T. Kato, Chem. Commun., 1978, 359.

8) T. Yanami, M. Miyashita, and A. Yoshikoshi, J. Org. Chem., 45, 607 (1980).

9) In addition to the ^{13}C NMR data, each structure was supported by the following ^{1}H NMR spectra (90 MHz).

   5 (CCl_4) 1.53 (3H, bs), 1.60 (3H, bs), 1.63 (3H, bs), 1.68 (3H, d, 1.1 Hz), 2.05 (3H, d, 1.2 Hz), 2.93 (1H, dd, 6.9 and 5.7 Hz, 18-H), 4.78 (2H, m), 4.8-5.2 (3H, m), and 5.98 (1H, d, 1.2 Hz) ppm.

   6 (CCl_4) 1.54 (3H, bs), 1.60 (3H, bs), 1.67 (6H, bs), 1.98 (3H, d, 1.2 Hz), 2.93 (1H, dd, 11.4 and 2.9 Hz, 14-H), 4.63 (1H, bd, 9 Hz), 4.75 (2H, m), 4.8-5.2 (2H, m), and 5.80 (1H, d, 1.2 Hz) ppm.

   7 ($CDCl_3$) 1.57 (9H, bs), 1.67 (6H, bs), 4.68 (2H, m), and 4.8-5.3 (4H, m) ppm.

   11 (CCl_4) 1.54 (3H, bs), 1.59 (6H, bs), 1.67 (3H, s), 1.75 (3H, d, 0.9 Hz), 1.90 (3H, s), 2.63 (kH, m, 14-H), 4.71 and 4.80 (each 1H, bs), 5.19 (1H, bd, 7.8 Hz), 4.8-5.2 (2H, m), and 5.51 (1H, dd, 7.8 and 2.7 Hz) ppm.

10) 7 was prepared from 5 by reduction with $LiAlH_4$ to allyl alcohol followed by acetylation (Ac_2O, py) and then reduction (Li/$EtNH_2$, -78°C).

11) Numbering of 5 is based tentatively on that of cericerene.

12) Private communication from Dr. Y. Naya, to whom we appreciate for her generous sending of her manuscript prior to publication.

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