77. **Tatsuo Kariyone, Shun-ichi Naito, and Jun-ichi Chatani**: Studies on the Components of *Carpesium abrotanoides*. II.[1] Chemical Constitution of Carpesia Lactone. (1).

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Kariyone and Kono[1] first isolated a sesquiterpene lactone as an anthelmintic component from the essential oil of *Carpesium abrotanoides* and named it carpesia lactone. Carpesia lactone is a colorless viscous oil and is hard to purify. In this report, an improved extraction method of the first report is described.

Crude oil obtained by the extraction of ripe seed of *Carpesium abrotanoides* with ether at room temperature was distilled *in vacuo* to give the distillate, $b.p._2$ 195~205°, which was warmed under stirring with 10% potassium hydroxide solution. After cooling, the non-acidic portion was removed by extraction with ether from the solution and the aqueous layer was acidified with hydrochloric acid. The oily substance separated out was extracted with ether. The ethereal solution was washed with aqueous solution of sodium bicarbonate, sodium carbonate, potassium hydroxide, and with saturated solution of sodium chloride. Ether was evaporated and vacuum distillation of the residue was repeated until the distillate gave a constant infrared spectrum. The distillate thus obtained was used for this research.

Carpesia lactone easily gives azulene only by heating it at an ordinary pressure. The azulene, probably a mixture, was separated as a ferrocyanate, recovered with alkali, and purified through chromatography. The column was eluted carefully with hexane and, thus, the two principal components were obtained as their trinitrobenzene complexes. The analytical values of both coincide well with those for $C_{14}H_{16}$. One of the azulenes is a blue oil, which gives a trinitrobenzene complex of m.p. 132°, and the other, a violet oil, forming a trinitrobenzene complex of m.p. 146°.

Dehydrogenation of carpesia lactone by selenium also gives two azulenes which were proved to be the same two azulenes as above. Both the ultraviolet and visible absorption spectra of blue azulene coincide with those of chamazulene[2] (lindazulene)[3], i.e. 1,4-dimethy-7-ethylazulene, while the ultraviolet and visible absorption spectra of the violet azulene were the very image of spectra of Se-guaiazulene[4]. It is therefore assumed that the structure of the violet azulene would be best represented by 2,4-dimethyl-7-ethylazulene.

The reduction product of carpesia lactone by lithium aluminum hydride is dehydrogenated with selenium and four azulenes were obtained. They gave trinitrobenzene complexes of m.p. 150°, 153°, 132°, and 146°. A trinitrobenzene complex of m.p. 150° showed no depression of the melting point upon admixture with that of S-guaiazulene, $C_{15}H_{18}$. The ultraviolet and visible absorption spectra of both complexes were identical. A trinitrobenzene complex of m.p. 153° was proved to be identical with that of Se-guaiazulene. Trinitrobenzene complexes of m.p. 132° and 146° are identical with those of selenium dehydrogenation products of carpesia lactone.

By dehydrogenation with sulfur, the reduction product of carpesia lactone with lithium aluminum hydride gave S-guaiazulene and chamazulene. No other azulenens were obtain-

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1) T. Kariyone, N. Kono: J. Pharm. Soc. Japan, **69**, 317(1949).

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3) K. Takeda, *et al.*: This Bulletin, **1**, 241(1953).

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ed. The fact that the reduction product of carpesia lactone with lithium aluminum hydride gave two azulenes, $C_{14}H_{16}$ and $C_{15}H_{18}$, proved the presence of a lactone ring which was partially left intact on reduction with lithium aluminum hydride and bicyclo[0, 3, 5]-decane system to become part of a nucleus of carpesia lactone. Furthermore, it is evident that the position of the alkyls are at 1, 4, and 7, of which those at 1 and 4 are methyl and the one at 7 is ethyl group since the dehydrogenation of carpesia lactone with sulfur yielded chamazulene. From these experimental facts it can also be assumed that carboxyl group forming the lactone ring is situated as in Fig. 1.

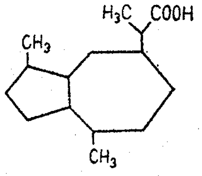

Fig. 1

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Experimental

Pyrolysis of Carpesia Lactone—50 g. of carpesia lactone was heated and 24 g. of the bluish violet oily substance distilled out. A mixture of 24 g. of this oily substance, 135 cc. of sat. aq. solution of ferrocyanate, 67 cc. of conc. HCl (sp. gr. 1.127), and 71 cc. of water was stirred for 30 mins. Brownish crystals separated was filtered and impurties were removed with petroleum ether (b.p. 40∼50°) by Soxhlet extraction apparatus. Decomposition of ferrocyanate with 5% aq. alkaline solution gave azulene, which was dissolved in petroleum ether, washed with water, and dried over anhyd. Na_2SO_4. Removal of the solvent yielded 0.7 g. of crude azulene. Distillation *in vacuo*(5 mm. Hg)gave 0.4 g. of azulenic substances. This bluish violet oil was purified by passing through a layer of alumina and the column was developed with hexane to separate into 2 fractions. They were purified as the trinitrobenzene complexes of m.p. 146° and 132° (from anhyd. EtOH). *Anal.* Calcd. for $C_{20}H_{19}O_6N_3$: C, 60.45; H, 4.79; N, 10.58. Found(for the complex of m.p. 146°) : C, 59.87; H, 4.72; N, 10.77. Found(for the complex of m.p. 132°) : C, 60.68; H, 4.90; N, 10.67.

Sulfur-Dehydrogenation of Carpesia Lactone—A mixture of 5 g. of carpesia lactone and 2 g. of S was heated at 150∼180° for 3 hrs. and at 180∼200° (bath temperature) for 2 hrs. The reaction mixture was extracted with ether. After removal of ether the residue was distilled *in vacuo* (5 mm. Hg), and the distillate was purified as a trinitrobenzene complex of m.p. 132°. Found : C, 60.58; H, 4.81; N, 10.60.

Selenium-Dehydrogenation of Carpesia Lactone—A mixture of 5 g. of carpesia lactone and 5 g. of Se was heated at 250∼300° (bath temperature) for 2 hrs. The reaction mixture was extracted with ether, distilled *in vacuo* (5 mm. Hg), distillate being taken up in petroleum ether and extracted with 86% H_3PO_4 to remove non-azulenic substances. Azulenic substances were dissolved in hexane, purified through alumina, and derived to the trinitrobenzene complex of m.p. 146° and 132°.

Reduction of Carpesia Lactone with Lithium Aluminum Hydride—To a solution of 7 g. of $LiAlH_4$ in 700 cc. of abs. ether, an abs. ethereal solution of 25 g. of carpesia lactone was slowly dropped under stirring and the resulting solution was allowed to stand overnight at a room temperature. Decomposition with dil. H_2SO_4 and extraction with ether gave, after evaporation of the solvent, colorless oil. It was distilled *in vacuo* and 20 g. of the fraction, b.p.$_5$ 198∼200°, was collected. A mixture of 4 g. of this reduction product and 4 g. of Se was heated at 280∼330° for 3.5 hrs. After cooling, the mixture was extracted with ether and dried over anhyd. Na_2SO_4. Ethereal residue was distilled *in vacuo* and 1.5 g. of the fraction of b.p.$_5$ 102∼170° was collected. The bluish violet oil distilled out was taken up in petroleum ether and extracted with 86% H_3PO_4 to remove non-azulenic substances. A total of 20 g. of the reduction product with $LiAlH_4$ was treated. 4 g. of the azulenic substance was dissolved in hexane, purified through alumina, and the column was developed with hexane. The column was further eluted with the same solvent and separated into four fractions. Their trinitrobenzene complexes showed m.p. 130°, 145°, 150°, and 153°. *Anal.* Calcd. for $C_{21}H_{21}O_6N_3$: C, 61.31; H, 5.11; N, 10.22. Found (for the complex of m.p. 150°) : C, 61.23; H, 5.21; N, 10.41. Found (for the complex of m.p. 153°) : C, 61.18; H. 5.25; N. 10.36.

Mixed melting point determination shows that trinitrobenzene complex of m.p. 132° is a chamazulene derivative, m.p. 150° S-guaiazulene, and m.p. 153° Se-guaiazulene.

Summary

Pyrolysis or dehydrogenation of carpesia lactone gave 1,4-dimethyl-7-ethylazulene and the reduction product of carpesia lactone with lithium aluminum hydride gave 1,4-

dimethyl-7-isopropylazulene. The position of the carboxyl group which formed the lactone ring in carpesia lactone was determined.

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78. **Shigehiko Sugasawa and Kitaro Mizukami**: Application of the Ball Reaction on Aromatic Alcohols. I.

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According to Ball, Goodwin, and Morton,¹⁾ polyene alcohols can advantageously be converted into the corresponding unsaturated aldehydes by means of active manganese dioxide in indifferent solvent such as petroleum ether and they succeeded in preparing vitamin A aldehyde from vitamin A. Later, Attenburrow²⁾ has shown that Ball's elegant method can be applied to α,β-monounsaturated alcohol, allyl alcohol being oxidized to acroleine, and Sondheimer³⁾ was the first to introduce this method into the field of steroid chemistry.

We are now reporting that Ball's method is also applicable to aromatic alcohols, yielding the corresponding aldehydes in good or fair yield under very mild working conditions. Our result is, therefore, at variance with that of Ball *et al.*, who reported their unsuccessful attempt to oxidize benzyl alcohol to benzaldehyde. In our case this oxidation proceeded quite smoothly at ordinary temperature, giving benzaldehyde in a good yield, when benzyl alcohol dissolved in ether was mixed with active manganese dioxide, a slight evolution of heat being observed. We cannot guess the reason for their failure but it may depend upon the activity of the manganese dioxide used, which was prepared according to Attenburrow in the present experiments.

As is shown in Table I, this method is applicable not only to isocyclic aromatic alcohols, but also to some of heterocyclic alcohols.

TABLE. I.(f)

Aldehyde	React. temp.	Time (hr.)	Yield(c) of semicarbazone (%)
Benz-	Room temp. (22°)	2	70 (215~216)(d)
Veratr-	35°	1	65 (177)
Salicyl-	Room temp. (20°)	3	60 (224)
Furfur-	Room temp. (19~20°)	3.5	40 (190~192)
3-Pyridyl-(a)	Room temp. (21°)	1.5	50 (213~214)
4-Pyridyl-(b)	35°	3	60 (213~215)(e)

a) This aldehyde is not readily soluble in ether, so $CHCl_3$ was used as a solvent.
b) Ether added with 5% EtOH was used as a solvent.
c) The yield is based upon semicarbazone once crystallized from a suitable solvent.
d) Figures in parentheses show melting or decomposition point of the semicarbazone.
e) Thiosemicarbazone, m.p. 219~221°(decomp.).
f) This table shows the result of only one experiment for each compound and no special effort was made to find out working conditions for optimal yield. The solvent used was ether unless otherwise stated.

Experiments with alcohols having other functional groups, such as nitro, hydroxyl, etc. and with polyhydric alcohols are now under progress and their results will be published in the forthcoming paper.

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