

ESSENTIAL OILS AND THEIR CONSTITUENTS

XXIV. STUDY OF SESQUITERPENE DEHYDROGENATION REACTIONS BY GAS-LIQUID CHROMATOGRAPHY*

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INTRODUCTION

Dehydrogenation of terpenoids into readily identifiable compounds has been frequently adopted for ascertaining their carbon frameworks¹. Cyclic sesquiterpenoids yield often alkyl substituted naphthalenes and azulenes which can, in turn, be characterized *via* conversion into suitable crystalline derivatives, *e.g.* picrates and trinitrobenzene adducts².

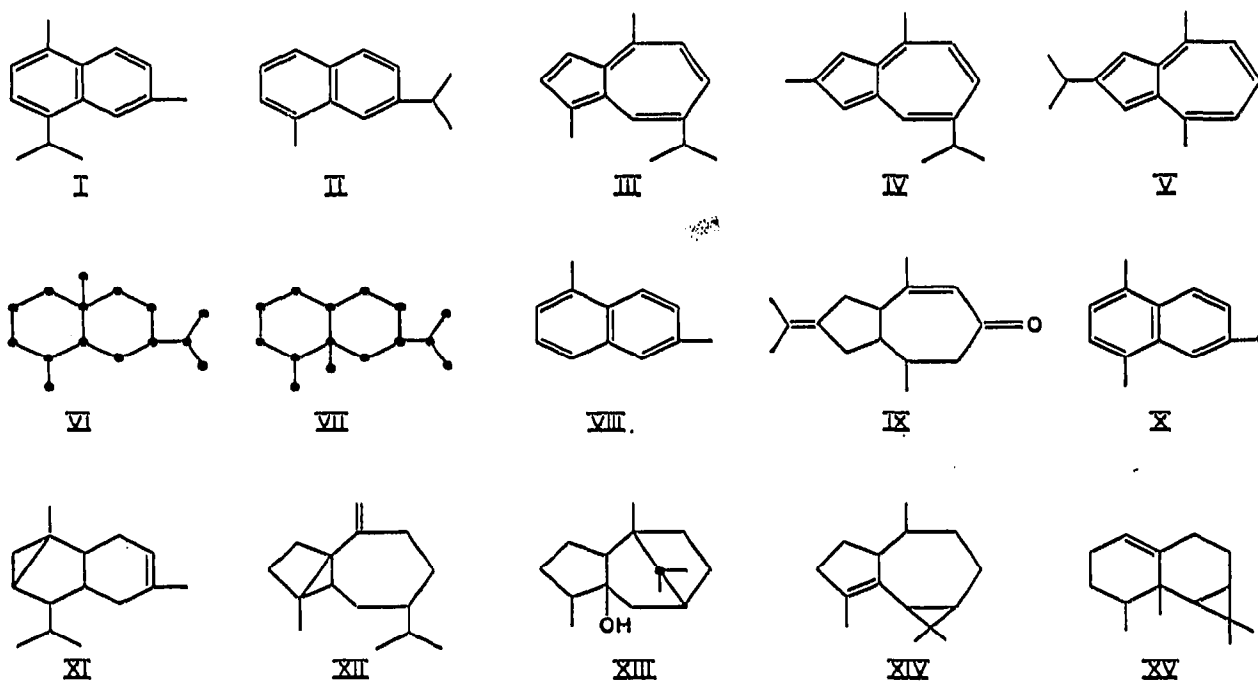


Fig. 1. Typical sesquiterpenoids and their dehydrogenation products.

Fig. 1 illustrates the structures of two substituted naphthalenes, cadalene (I) and eudalene (II), as well as three azulenes, S-guaiazulene (III), Se-guaiazulene (IV)

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and vetivazulene (V) frequently met with in such investigations. Cadalene, S-guaiazulene and vetivazulene are usually generated from parent compounds possessing the corresponding carbon skeletons. Eudalene, a C₁₄ compound, may form from either VI or VII following elimination of the angular methyl group. Se-guaiazulene, on the other hand, is a product of rearrangement of S-guaiazulene which it usually accompanies when dehydrogenation of S-guaiazulene compounds is carried out over selenium at elevated temperatures. 1,6-Dimethylnaphthalene has been observed as a dehydrogenation product of isozingiberene³.

Conventional dehydrogenations are rather drastic processes and often complex mixtures containing products of rearrangement as well as degradation are obtained. The resolution of such mixtures and identification of some of their constituents has been achieved through combination of extensive column chromatography and repeated recrystallization of their derivatives with picric acid and trinitrobenzene.

In the authors' laboratory, gas chromatography has been used successfully for some time to study the course of dehydrogenation reactions of sesquiterpenes found in essential oils. The technique proved to be a valuable analytical tool as complex mixtures were effectively resolved without recourse to tedious and time consuming operations of column chromatography, derivative formation and recrystallizations. It is the purpose of this paper to report some of the results obtained.

EXPERIMENTAL

(1) *Methods*

Dehydrogenation of sesquiterpene fractions. Selenium and sulphur were used as dehydrogenating agents. The experimental sample (250 mg) was weighed into a small bulb (3 ml). Selenium (500 mg) or sulphur (115 mg) was added and the assembly fused to an air condenser comprised of two concentric tubes. The mixture was refluxed for 24 h at $290 \pm 10^\circ$ (selenium dehydrogenation) or $200 \pm 5^\circ$ (sulphur dehydrogenation) while a slow stream of nitrogen gas was allowed to pass through the condenser. Azulenogenic sesquiterpenes were processed for only 4 h. Following reaction, the bulb was cut off, the product was dissolved in hexane, and chromatographed over 5 g of grade I basic alumina. The eluate, recovered following evaporation of the solvent, was examined by gas chromatography. Coloured effluents (azulenenic hydrocarbons) were collected separately.

Gas chromatographic analysis. The products of dehydrogenation were examined by means of a column of Reoplex 400 (20 %) on acid-washed Chromosorb W. Experimental procedures have been described⁴. Reoplex 400 (10 %) and silicone gum SE-30 (10 %) columns were also used for some of the investigations. Collection of samples for spectral identification was carried out by either depositing effluents directly on a salt plate⁵ or trapping in carbon tetrachloride.

(2) *Materials*

Products used as reference compounds were obtained in accordance with the procedures described and are listed in Table I. Acenaphthene and fluorene (commercial products) were used as internal standards.

TABLE I
PREPARATION OF REFERENCE COMPOUNDS

<i>Compound</i>	<i>Source</i>	<i>Method of preparation</i>
Cadalene	Cadinene fraction from oil of cade	Se-Dehydrogenation
Eudalene	Selinene fraction from oil of celery seed	Se-Dehydrogenation
S-Guaiazulene	Gurjunene fraction from oil of gurjun balsam	S-Dehydrogenation
Se-Guaiazulene	Gurjunene fraction from oil of gurjun balsam	Se-Dehydrogenation
Vetivazulene	Sesquiterpene fraction from oil of vetiver	Se-Dehydrogenation

RESULTS AND DISCUSSION

The gas chromatographic behaviour of naphthalenes and azulenes—see Fig. 1 (I to V and VIII)—was investigated using a polar (Reoplex 400; 20 %) and a non-polar (Silicone gum SE-30; 10 %) column. The six compounds were well separated by either substrate. Retention times were higher on the Reoplex column and a temperature of 220° had to be used to elute the compounds within 30 min. The SE-30 column could be conveniently operated at 200°.

For the separation of naphthalenes, lower column temperatures—200° for Reoplex and 185° for SE-30—were found to improve resolution, and for the separation of the high boiling azulenes a 10 % Reoplex column was found to be preferable.

Fig. 2-A illustrates the separation of a six-component reference mixture by a Reoplex column operated at 220°, and Table II shows the relative retention times of these compounds using both the Reoplex and SE-30 substrates. Fluorene and acenaphthene served as reference standards. Both these compounds displayed gas chromatographic peaks which did not overlap with any of the reaction products.

As may be seen from Table II, Reoplex 400 proved the more efficient substrate. It retained aromatics more strongly than the corresponding alicyclic and aliphatic

TABLE II
RELATIVE RETENTION TIMES OF SESQUITERPENE DEHYDROGENATION PRODUCTS

<i>Compound</i>	<i>B.P.</i> (°C)*	<i>Retention times</i> (Helium flow rate: 75 ml/min)			
		<i>SE-30</i>		<i>Reoplex</i>	
		200°**	185°***	220°**	200°***
1,6-Dimethyl-naphthalene	262–263	0.61	0.81	0.42	0.67
Eudalene	281	0.90	1.27	0.50	0.82
Acenaphthene	279	0.73	1.00	0.63	1.00
Cadalene	292	1.30	1.93	0.70	1.20
Fluorene	295	1.00	1.40	1.00	1.71
S-Guaiazulene	176/17 mm	1.89	—	1.17	—
Se-Guaiazulene	170–171/13 mm	1.95	—	1.26	—
Vetivazulene	—	2.08	—	1.37	—

* Literature values.

** Relative to fluorene.

*** Relative to acenaphthene.

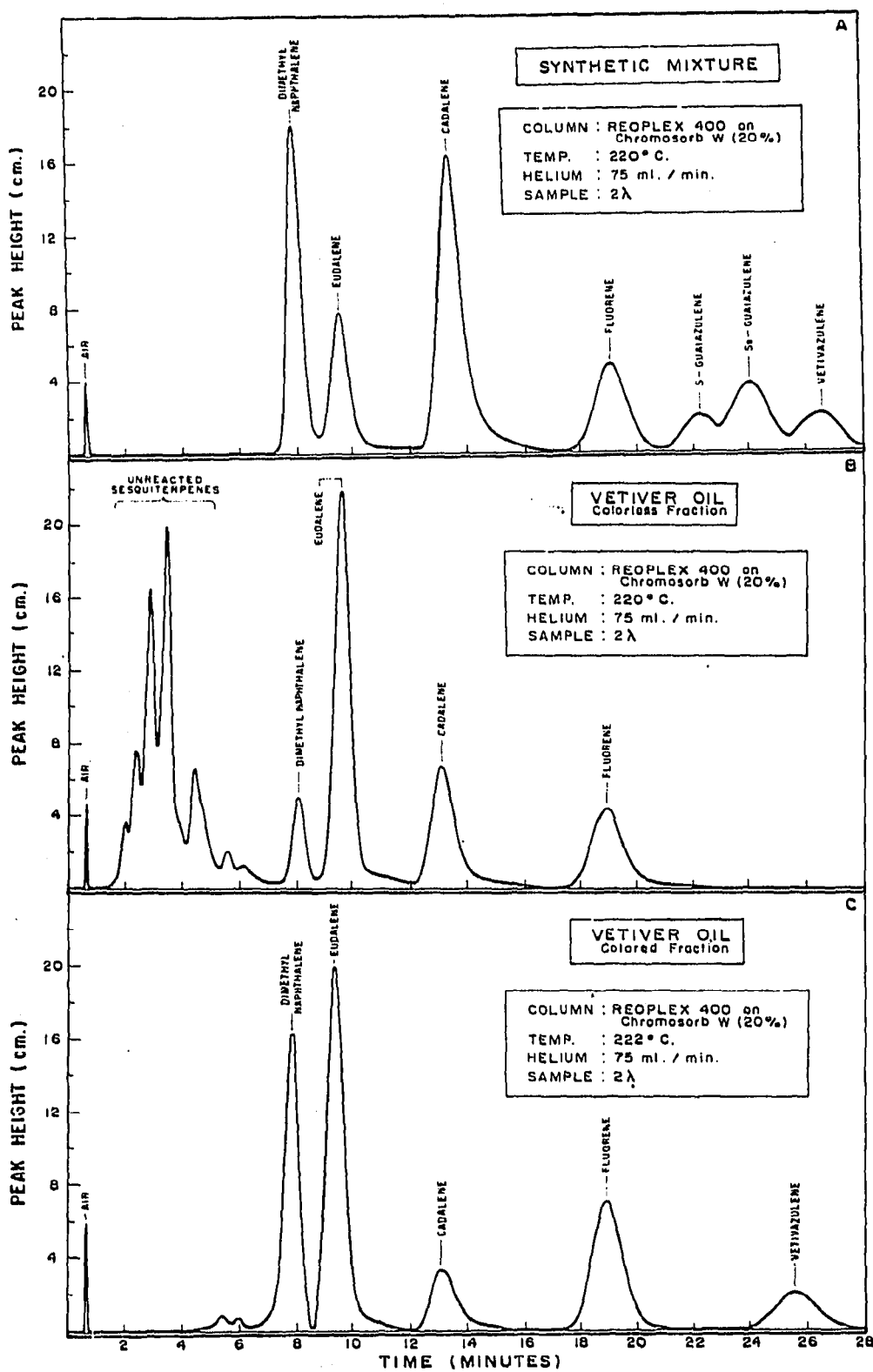


Fig. 2. Gas chromatography of sesquiterpene dehydrogenation products. Reference standard: fluorene.

compounds. The non-polar SE-30 column lacked such selectivity, its resolving properties being determined primarily by the vapour pressures of the different constituents. The Reoplex column was, therefore, found to be suited for the separation of unchanged sesquiterpenes from their aromatic dehydrogenation products. It also separated effectively lower boiling naphthalenes, formed by cracking of the larger molecules during the drastic process of dehydrogenation, from both the unreacted sesquiterpenes and their primary dehydrogenation products.

The stability of the compounds isolated under the experimental conditions described was confirmed by systematic comparison of the infrared spectra of effluents with those obtained following re-chromatography and similar analysis of the condensates collected.

The following examples serve to illustrate the scope and application of the technique.

Resolution of complex mixtures

The sesquiterpene hydrocarbon fraction of vetiver oils is known to contain compounds of various carbon frameworks including cadalenic, eudalenic and azulenic substances⁶. On dehydrogenation it yields a complex mixture of aromatic and azulenic constituents. Fig. 2-B and 2-C show how readily such a complex mixture can be analysed by gas-liquid chromatography since unreacted sesquiterpenes elute much faster than their aromatic as well as azulenic degradation products.

Dealkylations associated with dehydrogenation reactions

The earliest known example of dealkylation occurring during aromatization of sesquiterpenes is the formation of eudalene from selinene and related sesquiterpenes following elimination of the angular methyl group⁷. Dealkylation at other positions has also been observed⁸. SEIDEL *et al.* reported formation of a small quantity of 1,6-dimethylnaphthalene during dehydrogenation of isozingiberene⁹. We obtained good yields (66 %) of a low-boiling compound when preparing cadalene from cadinene fractions of cade oil in accordance with the procedure described. The infrared spectrum of this compound displayed absorptions characteristic of substituted naphthalenes. Rigorous comparison of spectral and retention time data with those of authentic samples of naphthalenes thought to be present proved the substance to be 1,6-dimethylnaphthalene. The compound was subsequently found to accompany cadalene in dehydrogenation products derived from the sesquiterpene fractions of many essential oils. This observation is in accord with the view of SEIDEL *et al.* that 1,6-dimethylnaphthalene is formed by cracking of the cadalene molecule.

Rearrangement of dehydrogenation products

Under the drastic reaction conditions of conventional dehydrogenations, the primary products formed may also rearrange to compounds possessing entirely different carbon skeletons. Examples are the formation of Se-guaiazulene from S-guaiazulene owing to migration of a methyl group, dehydrogenation of vetivones (IX) to vetivazulene, eudalene and vetivalene (X)⁹, formation of naphthalenic and azulenic compounds from tricyclic substances, *e.g.* cadalene from copaene (XI)¹⁰ and S-guaiazulene from aromadendrene (XII)¹¹ and patchoulol (XIII)¹².

A fraction of gurjun balsam oil containing α -gurjunene (XIV) and β -gurjunene

(XV) was dehydrogenated using selenium and sulphur. Gas chromatographic analysis of the reaction products showed that—as expected—selenium dehydrogenation generated both S-guaiazulene and Se-guaiazulene whereas sulphur dehydrogenation produced only S-guaiazulene. In addition to these azulenes, the presence of small quantities of cadalene, eudalene and 1,6-dimethylnaphthalene was also detected. It would appear, therefore, that eudalene originates from both α - and β -gurjunene and that cadalene, formed by rearrangement of α -gurjunene, also yields some 1,6-dimethylnaphthalene owing to cracking of its carbon skeleton.

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SUMMARY

The application of gas-liquid chromatography to the analysis of complex mixtures formed by dehydrogenation of sesquiterpenes is described. The usefulness of the technique in studying degradation and rearrangements accompanying such reactions is also illustrated.

REFERENCES

- 1 P. A. PLATTNER AND E. C. ARMSTRONG, *Newer Method of Preparative Organic Chemistry*, Interscience, New York, 1940, p. 21.
- 2 E. GUENTHER, *The Essential Oils*, Vol. II, Van Nostrand, New York, 1949, pp. 81 and 127.
- 3 C. F. SEIDEL, P. H. MÜLLER AND H. SCHINZ, *Helv. Chim. Acta*, 27 (1944) 738.
- 4 I. C. NIGAM AND L. LEVI, *Can. J. Chem.*, 40 (1962) 2083.
- 5 I. C. NIGAM, M. SAHASRABUDHE, T. W. MCCONNELL DAVIS, J. C. BARTLET AND LEO LEVI, *Perfumery Essent. Oil Record*, 53 (1962) 614.
- 6 N. T. ANH AND M. FETIZON, *France Parfums*, 6 (1963) 203.
- 7 L. RUZICKA, J. MEYER AND M. MINGAZZINI, *Helv. Chim. Acta*, 5 (1922) 345, 363.
- 8 W. COCKER, J. D. EDWARD, D. S. JENKINSON AND J. MCCORMICK, *J. Chem. Soc.*, (1952) 72; *ibid.*, (1953) 2355.
- 9 A. S. PFAU AND P. A. PLATTNER, *Helv. Chim. Acta*, 22 (1939) 640; *ibid.*, 23 (1940) 768.
- 10 F. W. SEMMLER AND H. STENZEL, *Ber.*, 47 (1914) 2555;
L. H. BRIGGS AND W. I. TAYLOR, *J. Chem. Soc.*, (1947) 1338.
- 11 A. S. PFAU AND P. A. PLATTNER, *Helv. Chim. Acta*, 19 (1936) 871.
- 12 W. TREIBS, *Ann.*, 564 (1949) 141.