UDC 543.544.25:541.63

44. Nobuo Ikekawa and Yoshiyasu Masuda*1 : Gas Chromatography of Stereoisomer of Ring System.

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For the application of gas chromatography, which has been recently developed for the analysis of steroids or alkaloids, it is important to know the correlations between the structure and the retention time. Although the gas chromatographic behaviour of the stereoisomer of A/B ring system[1] and 3-hydroxy group[2] of steroids have been investigated, there is not much information about that of the stereochemical configuration.

In the previous communications, we have reported the correlations between the retention times and the structures of sterols[3], androstane and pregnane derivatives[4]. In this paper is described the gas chromatography of stereoisomers of ring systems of di-, tri- and tetra-cyclic compounds using QF-1 and SE-30 liquid phases.

Di- and Tri-cyclic Compounds

The retention times of *cis* and *trans* decaline derivatives, I and II, are shown in Table I. These two isomers can be separated with the 1% QF-1 phase, as shown in Fig. 1, but gave the same retention time using 0.5% SE-30 phase. This might be due to an insufficient amount of partitioning agent.

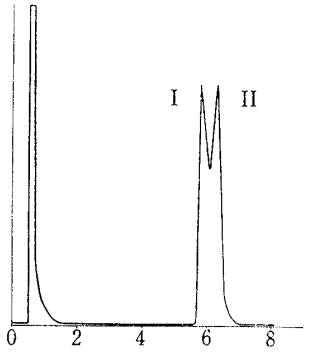


Fig. 1. Separation of a Mixture of decaline Derivatives I and II, using QF-1 phase

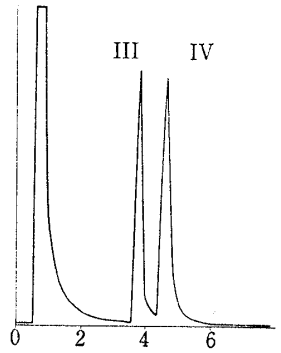
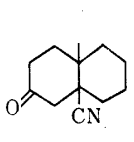
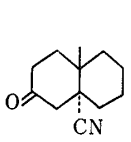


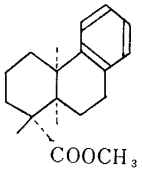
Fig. 2. Separation of a Mixture of Tricyclic Compounds III and IV, using QF-1 phase



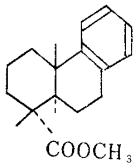
I



II



III



IV

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1) W. J. A. VandenHeuvel, C. C. Sweeley, E. C. Horning : J. Am. Chem. Soc., **82**, 3481 (1960).
2) R. B. Clayton : Nature, **190**, 1071 (1961).
3) K. Tsuda, K. Sakai, N, Ikekawa : This Bulletin, **9**, 835 (1962).
4) K. Tsuda, N. Ikekawa, Y. Sato, S. Tanaka, H. Hasegawa : *Ibid.*, **10**, 332 (1962).

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Table I and Fig. 2 show the retntion times of tri-cyclic compounds Ⅲ and Ⅳ. The *cis* isomer is eluted faster than *trans* isomer with both phases and they are separate completely.

Table I. Retention Time of Di- and Tri-cyclic Compounds

	1% QF-1 (min.)	0.5% SE-30 (min.)
cis-3-Oxodecahydro-4a-naphthalenecarbonitrile (Ⅰ)	5.8	3.2
trans-3-Oxodecahydro-4a-naphthalenecarbonitrile (Ⅱ)	6.3	3.2
Condition : column temp. 155°, sample heater temp. 190°, detector temp. 210° carrier gas N_2, 90 cc./min.		
Methyl deisopropylallodehydroabiatate (Ⅲ)	3.8	8.2
Methyl deisopropyldehydroabiatate (Ⅳ)	4.65	9.65
Condition : column temp. 172°, sample heater temp. 220°, detector temp. 220° carrier gas N_2, 80 cc./min.		

Steroids

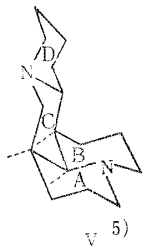
In the case of steroids, the A/B *cis* compound has a shorter retention time than the *trans* isomer.[1] The retention times of androstane derivatives are shown in Table Ⅱ. The two partitioning agents showed little difference in their ability to separate the steroidal A/B *cis* and A/B *trans* isomers.

Table Ⅱ. Retention Time of Androstane Derivertives

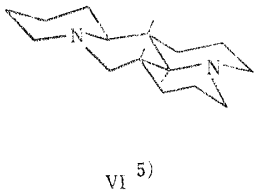
	1% QF-1 (min.)	0.5% SE-30 (min.)
17β-Hydroxy-5β-androstan-3-one Acetate	7.6	6.2
17β-Hydroxy-5α-androstan-3-one Acetate	8.4	6.75
17β-Hydroxy-5β-androstan-3-one Propionate	8.9	7.85
17β-Hydroxy-5α-androstan-3-one Propionate	9.8	8.6
Condition : column temp. 225°, sample heater temp. 250°, detector temp. 240° carrier gas N_2, 90 cc./min.		

Alkaloids

The gas chromatographic behavior of the alkaloid series, matridine, licorane and morphinan, was studied (Table Ⅲ). Matridine (Ⅴ), A/C and B/C *cis*, was eluted faster than allomatridine (Ⅵ), all *trans* (Fig. 3).



Ⅴ [5]



Ⅵ [5]

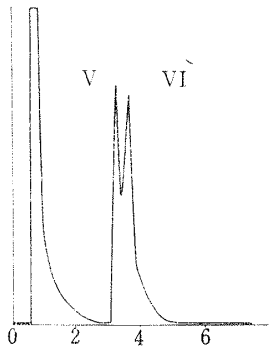


Fig. 3. Separation of a Mixture of Matridine (Ⅴ) and Allomatridine (Ⅵ), using QF-1 phase

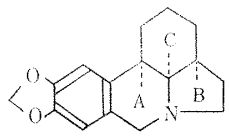
Licoranes gave sharp peaks accompanied with considerably large tailing, which may be due to the decomposition of the compounds. This phenomena is most noticeable in the case of α-licorane (Ⅸ) which may be the most thermally unstable among them. γ-Licorane (Ⅷ) (A/C and B/C *cis*), having the same configuration as the matridine, was

5) K. Tsuda, H. Mishima : This Bulletin, **5**, 285 (1957), J. Org. Chem., **23**, 1179 (1958).

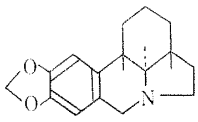
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Table III. Retention Time of Alkaloids

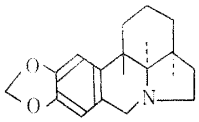
	1% QF-1 (min.)	0.5% SE-30 (min.)
Matridine (V)	3.25	4.6
Allomatridine (VI)	3.65	4.75
Condition : column temp. 145°, sample heater temp. 200°, detector temp. 200° carrier gas N_2, 80 cc./min.		
γ-Licorane (VII)	3.65	
β-Licorane (VIII)	5.05	
α-Licorane (IX)	5.8	
Condition : column temp. 174°, sample heater temp. 230°, detector temp. 220° carrier gas N_2, 95 cc./min.		
		1% SE-30
3-Methoxy-6-keto-N-methyl-morphinan (X)		4.2
3-Methoxy-6-keto-N-methyl-isomorphinan (XI)		4.75
3-Methoxy-6-keto-Δ^7-N-methyl-morphinan (XII)		4.2
3-Methoxy-6-keto-Δ^7-N-methyl-isomorphinan (XIII)		5.5
l-3-Methoxy-N-methyl-morphinan (XIV)		2.5
d-3-Methoxy-N-methyl-morphinan (XV)		2.5
Condition : column temp. 220°, sample heater temp. 250°, detector temp. 240° carrier gas N_2, 90 cc./min.		



VII



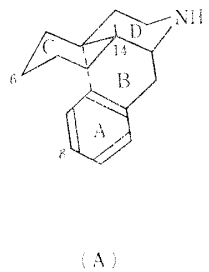
VIII



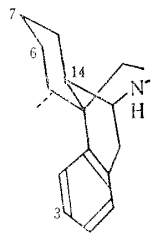
IX

eluted faster than β-licorane (VIII) ((all *trans*), and α-licorane (IX) has the longest retention time.

Morphinan derivatives (B/C *cis*, C/D *trans*) (X, XII) were eluted faster than the corresponding isomorphinan series (B/C *trans*, C/D *cis*) (XI, XIII) (Fig. 4). This may be due to their molecular size. As shown in the stereochemical formula, the morphinan molecule (A) is more compact than the iso compound (B). *l*-Morphinan (XIV) and it antipode *d*-morphinan (XV) (sinomenine series) having the same functional group gave the same retention time, as expected. The correlations between the structure of morphinan derivatives and the retention times will be published in the forthcoming paper.[6]



(A)



(B)

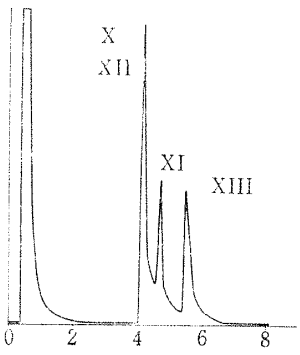


Fig. 4. Separation of a Mixture of Morphinane derivatives (X, XI, XII and XIII), using SE-30 phase

6) N. Ikekawa, Y. Masuda, Y. K. Sawa : Scientific Papers of The Institute of Physical and Chemical Research, in press.

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In all the cases investigated the *cis* isomers, which are somewhat more compact than the *trans* isomers, were eluted more rapidly. This type of behavior was observed using silicone polymer, and both SE-30 and QF-1 phase are suitable for the separation of ring junction isomer. Thus, gas chromatopraphic data may be used to obtain information about the molecular size and functional groups as well as the stereochemical configuration for compounds of unknown structure.

Experimental

A Shimadzu Seisakusyo Model GC-1B instrument (dual column, differential flame) was used in this study. It was run on the sensitivity 1000 and range 3.2. A stainless steel column of 150 cm (75 cm U-shap × 2) × 6 mm. i.d. was packed with 0.5 or 1% SE-30 (G.E., methyl silicone), or 1% QF-1-0065 (Dow Corning, fluorinated alkyl silicone) on Chromosorb W (60~80 mesh, acid washed and silanized). A typical sample was 1~2 μl of a 0.5% solution of the compound in Me_2CO.

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Summary

Gas chromatography of the stereoisomers of ring system was investigated, using SE-30 and QF-1 phases. In all of the cases, di-, tri- and tetra-cyclic (steroids and alkaloids) compounds, the *cis* isomers which are more compact than *trans* isomers were eluted faster.

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