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Reaction Gas Chromatography.*1 (Determination of Skeletal Structure by Means of Reaction Gas Chromatography

The gas chromatographic technique which involves a reaction simultaneously, was first reported as a micro-catalytic technique by Emmett and co-workers,[1] and the same kind of idea was applied to the gas chromatographic analysis of nonvolatile compounds. For example, amino acids were analyzed after conversion to aldehyde on a ninhydrin reactor column,[2] and the pyrolytic gas chromatography of organic substances was reported to be effective for the qualitative identification of relatively nonvolatile materials.[3,4] Drawert carried out the analysis of alcohols after conversion to olefines on the H_3PO_4-Sterchamol reactor and named such technique "Reaction Gas Chromatography."[5,6]

The authors have planned to investigate the application of gas chromatography from the similar point of view and been studying various kinds of combination of chemical reaction and gas chromatographic analysis. In the present communication, they wish to describe the reaction gas chromatography about the dehydrogenation, hydrogenation and dealkylation of monoterpene series.

Apparatus and Procedure

Reaction gas chromatography is in general carried out by the equipment which is shown in Fig. 1. A glass U-tube reactor containing the suitable catalyst (Fig. 2) is placed between the sample evaporator and the analytical column. The catalyst is heated by electric heater to desired temperature. The sample, injected in the evaporator, reacts on the catalyst in the reactor, and then the products are separated by the column directly attached to the reactor, and detected.

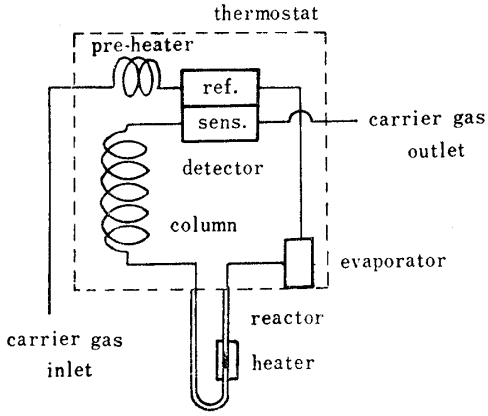


Fig. 1.
Flow Diagram of
Reaction Gaschromatography

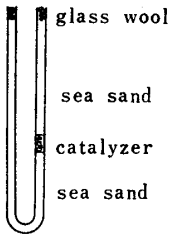


Fig 2.
Reactor Column

*1 This work was presented at the 6th Annual Meeting of Kanto Branch of Pharmaceutical Society of Japan (Symposium on Gas and Thin Layer Chromatography), November 24, 1962 (Tokyo). Abstracts of Papers, page 35. After our presentation, Beroza published an article[7] independently which concerned the hydrogenation reaction.

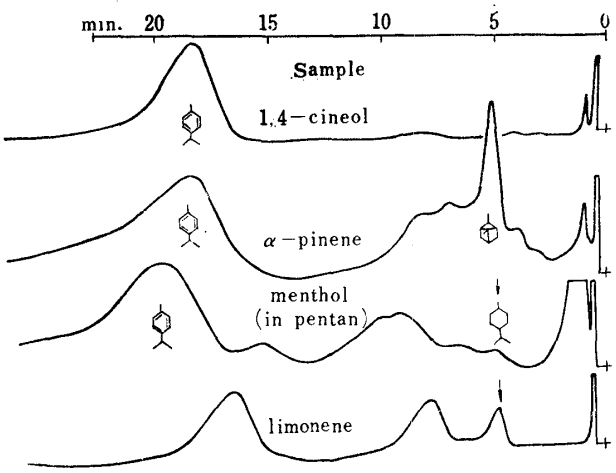
1) R. J. Kokes, H. Tobin, Jr., P. H. Emmett : J. Am. Chem. Soc., **77**, 5860 (1955).
2) A. Zlatkis, J. F. Orō, A. P. Kimball : Anal. Chem., **32**, 162 (1960).
3) J. Janak : Nature, **185**, 684 (1960).
4) K. Ettre, P. F. Váradi : Anal. Chem., **35**, 69 (1963).
5) F. Drawert, R. Flgenhauer, G. Kupfer : Angew. Chem., **72**, 555 (1960).
6) F. Drawert, K. H. Reather : Chem. Ber., **93**, 3066 (1960).
7) M. Beroza : Nature, **196**, 768 (1962); *Idem* : Anal. Chem., **34**, 1801 (1962).

Dehydrogenation and Hydrogenation Reaction Gas Chromatography

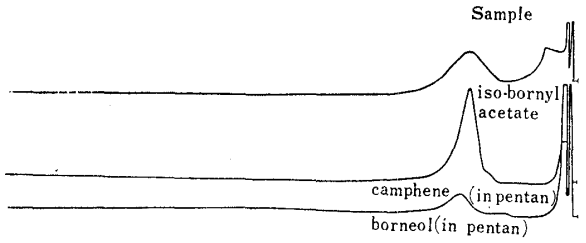
The chromatographic "spectra" of dehydrogenation products of monoterpenes were measured by means of reaction gas chromatography employing various kinds of catalyst. Among them the most satisfactory result for dehydrogenation was achieved by palladium on silica gel (2~20%), which was especially recommended to be rather aged and deactivated. Fig. 3 shows dehydrogenation "spectra" of typical monoterpenes using this catalyst and hydrogen as a carrier gas. From these "spectra," monoterpenes can be classified into two groups depending whether it forms *p*-cymene (Group A) or not (Group B). The group A consists of two types, the one possesses the *p*-cymene skeleton (limonene and menthol) and the other cleaves easily to form *p*-cymene by dehydrogenation(*α*-pinene and 1,4-cineol).

The group B includes bicyclic and aliphatic monoterpenes which can be hardly dehydrogenated to aromatic compounds. The peaks indicated by the arrow in Fig. 3 was considered to be *p*-menthan from the fact that it disappeared when the reaction was carried out in carrier gas of helium where no simultaneous reduction took place. As the reactions in hydrogen and in helium are different, it seems to be useful to compare the chromatographic "spectra" taken with both carrier gases.

Employing platinum-charcoal[8] as a catalyst, the products with higher boiling points did not elute due to strong adsorptive property of the catalyst. Palladium-Celite*[2] turned out to be a weak catalyst for dehydrogenation and the reaction was not complete. On



Group A (Reactor temperature 360~370°)



Group B (Reactor temperature 370~450°)

Fig. 3.

Chromatographic conditions :
Column : 15% TCP on Fuji N-2 Firebrick 1/4" × 2 m. Cu tube 110°
Reactor : Pd-silica gel (1:5) 2 cm. in 1/4" glass tube
Carrier gas : H_2 50 ml./min.

*[2] This is an suitable catalyst with moderate reactivity and little adsorptive property for reduction gas chromatography.

8) K. Packendorff, L. Leker-Packendorff : Chem. Ber., **67**, 1389 (1938).

zinc or nickel, cyclohexane could not be dehydrogenated at all (under the reaction temperature up to 450°).

Dealkylation Reaction Gas Chromatography

Using the same apparatus as mentioned above, alkyl benzenes reacted over 15~50% palladium-silica gel catalyst at 380~460°, and dealkylation "spectra" were obtained. Hydrogen is recommended as the carrier gas and the reaction proceeds more perfectly when the reactor temperature is higher and/or flow rate slower. Fig. 4 shows that *p*-cymene gives *p*-ethyltoluene, *p*-xylene, toluene and benzene. The formation of *p*-xylene, which has methyl group reminicent of the isopropyl group of original compound, implies the possibility to elucidate the position of the alkyl substituent in complex aromatics. Gas phase products were analyzed on dimethylformamide-squalane-alumina[8] or active charcoal column. It is of interest that the largest alkyl substituent can be detected as the largest hydrocarbon in the dealkylation fragments. (*e.g.* *p*-cymene gave propane, ethane and methane while *p*-ethyltoluene gave ethane and methane only).

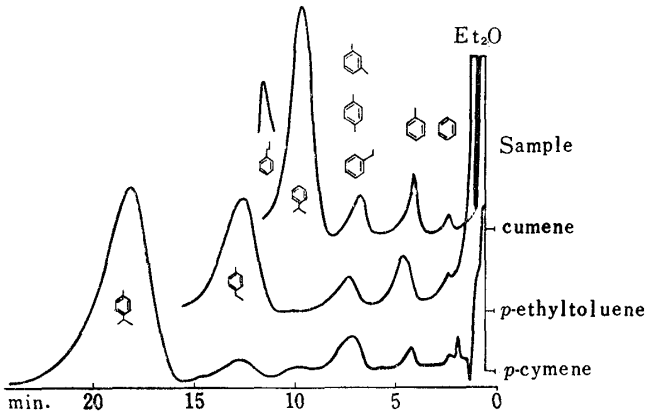


Fig. 4.

Column : 15% TCP on Fuji N-2 ¼ × 2 m. Cu 110°
Reactor : Pd-silicagel (1:5) 2 cm. in glass tube 440~460°
Carrier gas : H_2 50 ml./min.

Whereas the usual dehydrogenation reaction for determination of the skeletal structure has the limitation of the poor yield of degradation products owing to troublesome procedure of its isolation and purification, the dehydrogenation gas chromatography can overcome this difficulty because of its simple procedure, clear-cut separation and high sensitivity. And the dealkylation gas chromatography supplies the valuable informations about the species of alkyl substituents of the aromatics, which were produced by the dehydrogenation gas chromatography.

In some cases, the peak broadening and tailing are observed in the reaction gas chromatography and especially the compounds with higher boiling points afford broad peaks with poor resolution.....no elution in the extreme case. But, as far as the technique is applied to the compounds having lower molecular weight (*e.g.* up to C_{10} compounds), it still remains an elegant and effective method for structural determination.

Further survey of reaction gas chromatography of other reactions is in progress, and application of the dehydrogenation and dealkylation technique to more complex natural products is also being studied.

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9) N. Hara, H. Shimada, A. Ishikawa, K. Dohi : Bull. Japan Petrol. Inst., 2, 33 (1960).