Reaction gas chromatography

I. Catalytic aromatization of alicyclic and heterocyclic compounds

In contrast to the wide popularity of gas chromatography as a method for separating the products of chemical reactions, the potentialities of the technique as a tool for simultaneously carrying out reactions and analyzing the products formed have not as yet been fully appreciated.

KOKES *et al.*[1] were the first to apply this idea to the identification of hydrocarbons by catalytic cracking in a reactor attached to the inlet of a gas chromatograph. The term "Reaction Gas Chromatography" for the technique was coined by DRAWERT *et al.*[2,3] and its application illustrated through the conversion of alcohols to olefins employing a reactor packed with H_3PO_4–Sterchamol. Pyrolysis in conjunction with gas chromatography was proposed by JANAK[4] and has been successfully employed by a number of investigators to the analysis of non-volatile organic compounds. ZLATKIS *et al.* developed a method for the examination of amino acids, employing two reactors, one for oxidation of the acids and the other for cracking the aldehydes obtained[5]. Hydrogenolytic gas chromatography developed by BEROZA[6–8] for the determination of C-skeletons of organic compounds has also been used for the estimation of double bonds and certain functional groups[9].

Dehydrogenation reactions often serve as important steps in the structure elucidation of organic compounds. Conventional procedures require relatively large samples, the size of which may, however, be appreciably reduced by means of gas chromatographic analysis of the reaction products[10]. Reaction gas chromatography employing a suitable dehydrogenating catalyst permits such investigations on a micro and even submicro scale. OKAMOTO AND ONAKA[11] suggested an approach of this type when reporting the dehydrogenation of a few monoterpene compounds. Since the technique appeared to be of wider usefulness its applicability to different types of ring compounds was explored. The present investigation reports results obtained with several alicyclic and heterocyclic substances, from which a large number of compounds of pharmaceutical interest are derived.

Experimental

Apparatus

Gas chromatography. A Burrell Kromo-Tog K-2 equipped with a thermal conductivity detector and flash vaporiser unit was used. Column: a glass tube, length 225 cm and I.D. 6 mm. Packing: 20 % Carbowax 20 M deposited on alkali-washed firebrick[12]. Carrier gas: helium, 75 ml per min.

Reactor. The glass tube of the accessory flash vaporiser assembly served as reactor. The unit may readily be constructed as shown in Fig. 1. The design may be suitably modified to meet the requirements of gas chromatographs equipped with different types of injectors. The reactor tube was packed with one g of catalyst. The tapered end A of the reactor was inserted into the gas chromatograph while end B, closed with a silicone seal, served as the injection port. By manipulating valves C and D the carrier gas could be made to flow directly through the column or *via* the reactor.

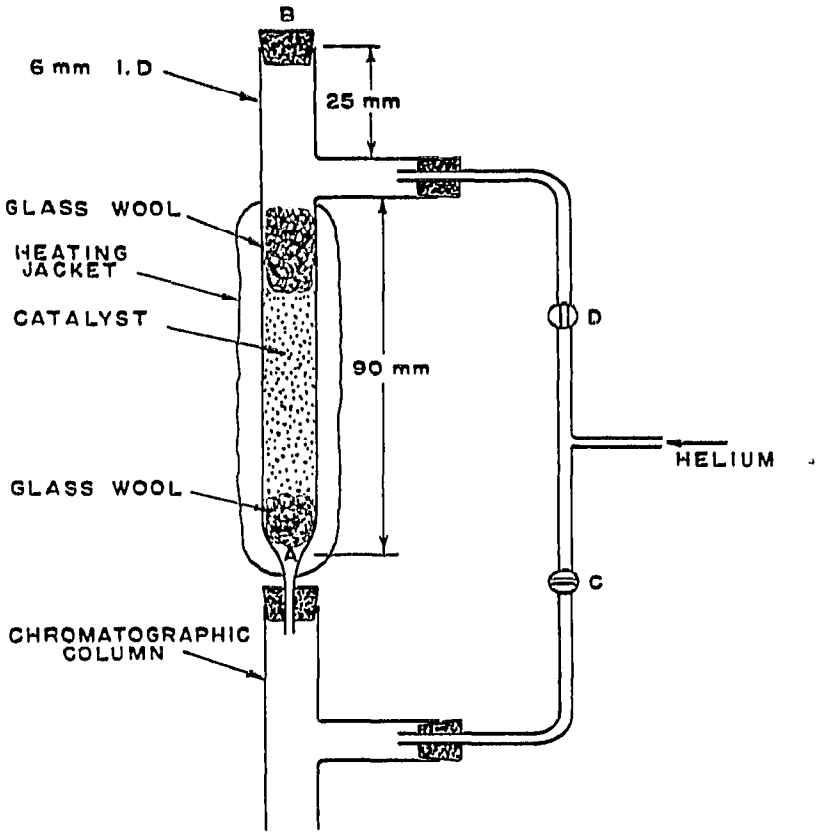

Fig. 1. Reactor for catalytic aromatization.

Catalysts. Two catalysts were employed in this study:

(1) 5 % platinum on alumina, initially obtained from Koch-Light Laboratories, Colnbrook, England, but subsequently prepared by impregnating neutral alumina (5 g) (Woelm) with an aqueous solution of chloroplatinic acid (500 mg), drying at 105° and heating in a slow stream of hydrogen while the temperature was gradually raised to 250°.

(2) 5 % platinum on alkali-washed firebrick[12] prepared in accordance by the same procedure.

Procedure

Aromatization occurred following injection of the samples (0.5–1.0 μl) into the reactor maintained at 280°. Usually dehydrogenation took place almost instantly as the vaporized material swept over the hot catalyst. In some cases, however, only slight aromatization occurred and the residence times had to be increased to realize more effective conversions. This was achieved by means of valves C and D. The carrier gas was allowed to flow directly through the column by closing D and opening C. The sample was then injected into the reactor where it vaporised and was kept under pressure by the carrier gas in the chromatographic column. After the required time for reaction had elapsed valve D was opened, C was closed and the recorder switched on simultaneously. The products of reactions were identified by comparison of their retention times with those of pure reference standards and the yields were estimated by measurement of the corresponding peak areas.

Results and discussion

Choice of reaction conditions

Catalytic dehydrogenation reactions carried out by conventional techniques generally require several hours for completion. Vapour phase reactions require less time but recycling of products is often still necessary. On the other hand reaction gas chromatography, employing the reactor assembly described, permitted very fast and efficient conversions, the short residence time of the sample in the catalyst chamber being compensated by a high catalyst/sample ratio. Minimum temperatures required for dehydrogenation were found to be dependent on the nature of the compounds. For most of the substances investigated the reaction proceeded smoothly at 280°. Helium (flow rate 75 ml/min) provided an inert atmosphere and furthermore accelerated the reaction by sweeping liberated hydrogen immediately off the sites of reaction. This also minimized the occurrence of undesirable side reactions.

Choice of catalyst

Several metals *viz.* platinum, palladium, nickel, rhodium etc., have been used as dehydrogenating catalysts. Platinum and palladium, in particular, are very widely employed. Since palladium exhibits a greater tendency to produce side reactions[13], platinum catalysts were used throughout this study. The nature of the support proved to be important. Thus a 10 % Pd on charcoal catalyst strongly adsorbed many of the compounds and their dehydrogenation products. Tetralin and decalin and their dehydrogenation products, for example, could not be recovered under the experimental conditions described. Similar observations have been reported for a Pt on charcoal catalyst[11]. Employing a 5 % Pt–alumina catalyst, however, both decalin and tetralin were quantitatively converted to naphthalene (Table I). This catalyst proved satisfactory for other alicyclic compounds as well. It was, however, generally unsuitable for analysis of nitrogeneous heterocyclic compounds which adsorbed strongly at the acidic sites of the support[14]. Platinum on alkali-washed firebrick was found to be satisfactory for these products although conversions were low (Table I).

Alicyclic compounds

The platinum–alumina catalyst proved to be more efficient than the platinum–firebrick catalyst for the aromatization of alicyclic compounds (Table I). The ease with which cyclohexene changed into benzene showed that presence of a double bond in the ring facilitates the reaction. Aromatization of cyclohexanol and cyclohexylamine probably proceeds *via* cyclohexene as an intermediate formed at active sites on the alumina[14,15]. Both these compounds gave poor yields on platinum–firebrick. On this catalyst cyclohexylamine remained practically unchanged while cyclohexanol yielded cyclohexene as the main product of reaction. The dehydrogenation of 2-methylcyclohexanone and 3-methylcyclohexanone also appears to be initiated by acidic sites on alumina. In addition to toluene (35 %), methylcyclohexane (54 %) was also obtained. Platinum–firebrick failed to aromatize these ketones to any significant extent and only small quantities of toluene were recovered. Conversions of six membered alicyclic ketones to alcohols and phenols reported to take place during catalytic dehydrogenations[16–19] were not observed with these two ketones under the present experimental conditions.

TABLE I

AROMATIZATION OF ALICYCLIC AND HETEROCYCLIC COMPOUNDS

Reactor temperature: 280°.

Compound	*Aromatic product*	*% Yield of aromatic product**	
		5% Pt on alumina	*5% Pt on alkali-washed firebrick*
Alicyclic compounds			
Hydrocarbons			
Cyclohexane	Benzene	100	2, **36**
Cyclohexene	Benzene	100	83, **93**
Methylcyclohexane	Toluene	77	nil, **7**
Decalin	Naphthalene	100	trace
	Tetralin	nil	10
Tetralin	Naphthalene	100	15
Alcohol			
Cyclohexanol	Benzene	100	6, **8**
Ketones			
2-Methylcyclohexanone	Toluene	65	trace, **4**
3-Methylcyclohexanone	Toluene	46	nil, **2**
Amine			
Cyclohexylamine	Benzene	100	trace
Heterocyclic compounds			
N-Methylpyrrolidine	N-Methylpyrrole	81	trace, **20**
Piperidine	Pyridine	—	32, **71**
N-Methylpiperidine	Pyridine	—	trace, **15**
N-Ethylpiperidine	Pyridine	—	3, **18**
Piperazine	Pyrazine	—	18

* Values in bold face denote yield of aromatic compound when sample was held in reactor for two minutes, all other figures give the yields on direct passage through the reactor.

Heterocyclic compounds

Five nitrogeneous heterocyclic compounds were used in this study (see Table I). Alumina was generally unsuitable as catalyst support for aromatizing these substances. Only N-methylpyrrolidine, a tertiary base, was effectively converted to N-methylpyrrole. The compounds were dehydrogenated on platinum–firebrick when moderate yields of aromatic products were obtained by keeping the sample in the reactor for two minutes. The aromatization of N-alkylpiperidines proceeded *via* elimination of the alkyl groups leading to the formation of pyridine. As expected N-methylpyrrolidine yielded N-methylpyrrole[20].

Scope of the technique

The technique described holds promise for wide application in the field of organic and pharmaceutical chemistry. It has already been used successfully in the author's laboratory for the determination of the C-skeleton of sesquiterpene hydrocarbons[21] and provides a novel approach to the identification and structure elucidation, on a micro scale, of compounds containing aromatizable rings. Many alkaloids possess five and six membered heterocyclic rings. Several piperidine derivatives are

used as narcotics and their detection is of forensic importance. Aromatization of cyclohexyl rings is of special interest in investigations on terpenoids. Applications of the technique to several classes of compounds of pharmaceutical interest are under study and will form the subject of forthcoming publications.

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