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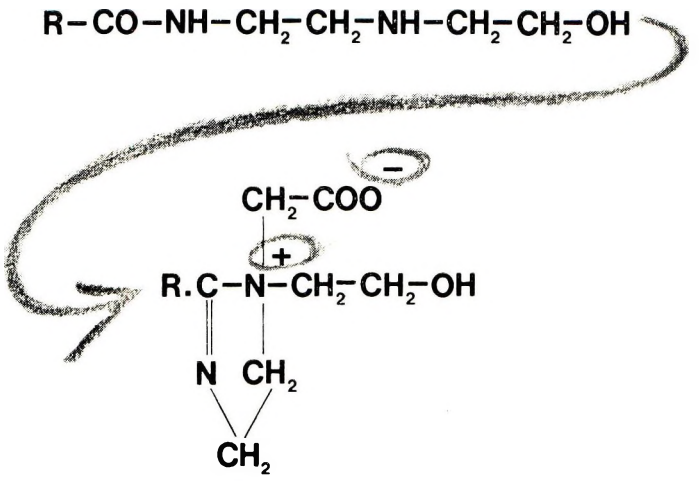
Contents



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INDEX TO ADVERTISERS

SYNOPSES FOR CARD INDEXES

The following synopses can be cut out and mounted on 127×76 mm index cards for reference without mutilating the pages of the Journal.

Decision analysis and its relevance to subjective testing: A. H. CHRISTER. *Journal of the Society of Cosmetic Chemists* **25** 159–181 (1974)

Synopsis—This paper introduces some of the basic concepts of decision analysis and discusses how decision analysis might be applied to a variety of decision situations to be found within the cosmetic and perfumery industry. In particular, the decision situation in which only subjective information is available is discussed.

Response of the frog olfactory system to controlled odour stimuli: T. MICHAEL POYNDER. *Journal of the Society of Cosmetic Chemists* **25** 183–202 (1974)

Synopsis—The electrical events which occur in the nose of a frog when it is stimulated with odorants have been studied.

For this study new techniques were developed for applying stimuli of known composition and controlled concentration in a reproducible manner. The concentration and timing of the stimuli in the nose cavity has been monitored by means of a new device consisting of a sampling probe connected to a flame ionization detector.

The ranges of concentration used have been wider than those reported previously and the form of the relationship between concentration and response size is now seen more clearly. It is that to be expected for a Langmuir type adsorption of odorant molecules on the receptor surface.

Sesquiterpenes in the perfumery industry: H. R. ANSARI and A. J. CURTIS. *Journal of the Society of Cosmetic Chemists* **25** 203–231 (1974)

Synopsis—The developments in sesquiterpenoid chemistry are reviewed with especial reference to their application in perfumery.

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Decision analysis and its relevance to subjective testing

A. H. CHRISTER*

Presented at the 2nd Joint Perfumery Symposium organized by the British Society of Perfumers and the Society of Cosmetic Chemists of Great Britain at Eastbourne on 7–9th May 1973

Synopsis—This paper introduces some of the basic concepts of DECISION ANALYSIS and discusses how decision analysis might be applied to a variety of decision situations to be found within the COSMETIC and PERFUMERY INDUSTRY. In particular, the decision situation in which only subjective information is available is discussed.

INTRODUCTION

The purpose of this paper is to introduce the fundamental ideas of decision analysis and to discuss in particular how it might be employed to assist in making subjectively based decisions within the perfumery and cosmetic industry. Here we are not so much concerned with the mechanism of subjective testing, Pridmore (1), as with the way in which the results of any such subjective measure might be incorporated into a decision procedure.

General business use of decision analysis is very much in its infancy, but growing. Perhaps the main gain to be obtained by the use of such analysis is that it enables decisions to be made in a logical manner, consistent with available information and the designated objective of the decision-maker. In this sense its use can be said to enhance management's ability to make

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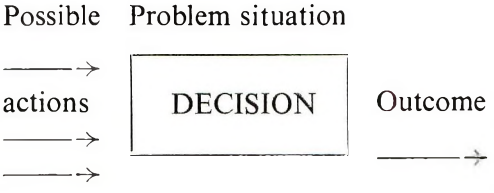
good choices in situation of risk and uncertainty. Of course, many decisions can be and are made without any fuss because the best solution is obvious. When this is not the case, however, decision analysis can provide a framework within which the pertinent decision may be discussed in a logical and objective fashion.

The decision procedure

We define here some of the terms and concepts of decision analysis. In essence, the decision process can be represented as follows:



Here the decision-maker views the alternatives available and selects that one which leads to the most desirable outcome. For a decision to be taken, it is clear that:

(a) there must be at least two or more alternative courses of action possible;
(b) the process of decision will select from these alternatives only one course of action which will actually be carried out; and
(c) the selection process is made so as to accomplish some designated purpose.

Alternatives, or strategies

Alternatives or strategies comprise all the factors which are within the decision-maker's control. Such factors could be the following.

How much/many to make.
What type of advertising media to use.
What size and shape of container to market a product in.
A stock control policy.
The size and location of a new factory or extension.

We denote the ith strategy by X_i.

Environments

The assemblage of all factors outwith the control of the decision-maker constitute the environment. States of nature and environments are interchangeable terms. Possible environmental factors are:

weather conditions	a price index
availability of raw material	availability of labour
cost of raw material	competitors' marketing strategy
demand for a product	

A particular choice of strategy could influence an environmental factor but not determine it, e.g. advertising policy and demand for a product. Unless otherwise stated, it is here assumed the environment is under no intelligent control. Should such a control exist the situation is likely one of gaming. We denote the jth state or environment by Z_j.

Result/Outcome

The result is the outcome R that will be observed when a given strategy X_i and specific environment Z_j appear together, and is denoted by R_{ij}. Clearly R_{ij} is some function of both X_i and Z_j, so we may write

$$R_{ij} = f(X_i, Z_j).$$

If in any situation this function were known, for example $R_{ij} = aX_i + bZ'_j$, the result of each strategy environment interaction could be calculated. Such a result might be written as follows:

Results		Environments			
		Z_1	Z_2	Z_3	Z_4
	X_1	R_{11}	R_{12}	R_{13}	R_{14}
Strategies	X_2	R_{21}	R_{22}	R_{23}	R_{24}
	X_3	R_{31}	R_{32}	R_{33}	R_{34}

Possible sources of difficulty

This simple notation conceals a number of problems. For example, it may not be possible to identify and define all environments pertinent to a specific decision. The environments considered in any decision situation will be those the decision-maker thinks most likely to occur or influence the problem. Obviously the sheer size of certain problems will cause some environments and strategies to be disregarded. It is interesting to observe

that this possible restriction exists whether or not decision-analysis is used, and represents an initial and subjective identification of a 'sub-decision' on the part of the decision-maker. Starr (2) refers to the resulting problem as decision-making under ambiguity.

A second difficulty can arise when evaluating the results R_{ij}. This matrix can sometimes be compiled by direct observation, but more likely costly experimentation or an operational research type study is required. White (3) defines the process of evaluating R_{ij} given environment Z_j and strategy X_i as the object study.

Having determined R_{ij}, there is still the problem of deciding an order of preference between results. Any specific result R_{ij} could be viewed in a multitude of ways. Consider, for example, the decision concerned with the selection of a marketing policy for a product. The results of various policies could be measured by

r_1 = value of sales in the first 6 months,
r_2 = value of sales in the first 2 years,
r_3 = total net profit gained over first year,
r_4 = expenditure on advertising over first 6 months.

Clearly there are numerous other measures one might be concerned with here such as possible counter measures by competitors, etc. If the result R is restricted to the above four measures, we see it has the form of a four-dimensional vector $R(r_1, r_2, r_3, r_4)$ with different strategies and environments giving rise to different values of r_1. Suppose the two possible strategies X_1, X_2 (under a specific environment) give rise to

$$X_1 \rightarrow R(5\,000, 23\,000, 2\,000, 1\,400)$$
$$X_2 \rightarrow R(8\,000, 19\,000, 1\,900, 1\,850)$$

which result is preferred? Before this question is answered it is necessary for the decision-maker to have a clear idea as to his objectives in making the decision. Perhaps the objective is to maximize profits. If so, over what period of time? Should a period of time be specified: presumably the decision-maker would wish to select that policy which maximizes his profits over this period, subject to his company being in a viable trading position for the subsequent period of time. The true objective is seldom simple in reality and will likely be reviewed within a dynamic context.

There are some techniques available to assist with this preference selection procedure. Suppose in the above marketing problem the decision-

maker decided that the order of paramount importance and concern was r_3, r_4, r_2 and r_1, and a fractional increase in r_3 was preferable to any increase in r_4, r_2 and r_1: that a fractional increase in r_4 was preferable to any extent of increase in r_2 and r_1: and that an increase in r_2 was superior to any increase in r_1. Then the order r_3, r_4, r_2 and r_1 is a lexicographic ordering (3) of the outcome parameters for the decision-maker. His choice of R would be that with the best value of r_3. Should two or more policies have the same best value of r_3, the choice is made between them on the basis of the next most important variable r_4, and so on.

Alternatively, it might be possible to determine a value function V, whose argument is an outcome R_s, with the property

$$V(R_s) > V(R_t)$$

if and only if R_s is preferred to R_t (3). Clearly the decision function is itself dependent upon the decision-maker. The existence of such a decision function reduces the selection procedure to a mathematical problem, namely find R^* where

$$V(R)^* = \max V(R_i).$$

Yet another approach to the problem exists using utility theory (4). Here each outcome is given a single numerical value (utility) which reflects its desirability as measured by the decision maker. The most desirable outcome is that with the greatest utility.

The final difficulty we shall mention here is that due to the uncertainty introduced through the unknown environment Z. According to the type of uncertainty, decision problems are divided into those of certainty, uncertainty and risk. In what follows, we will assume the result R can always be determined, and furthermore, that it is a scalar quantity such as cash or time. This being so, most of the difficulties mentioned in this section will not apply.

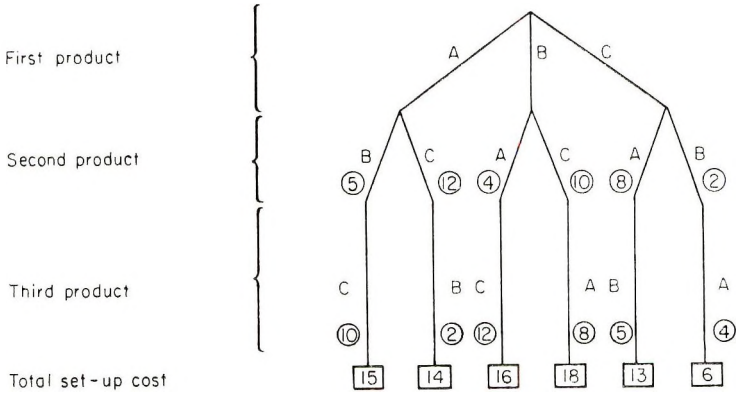
Decisions under certainty

In this case an outcome R is known for certain once the alternatives are specified. Any uncontrolled events are assumed known or irrelevant to the decision. Here either the environment is unique or the decision is independent of the environment. Thus the result R is a function of X only, i.e. $R = R(X_i)$.

A typical problem of decision under certainty is the selection of a production schedule when the cost and times associated with production are known. For example, consider a company about to manufacture a quantity of three cosmetics or perfumes, A, B and C. Before production can begin there is a certain amount of preparation required, such as adjustment of machinery, cleaning of apparatus, etc. The standard of preparation is dependent upon the product to be manufactured, and the amount of cleaning is dependent on what the plant produced last and what it is to produce next. Let these 'set up' costs in suitable units be as follows.

		followed by		
		A	B	C
1st product	A	—	5	12
	B	4	—	10
	C	8	2	—

The problem is to select the production order A, B, C, A, C, B, etc, so as to minimize the set up costs. Each order (A, C, B) is a possible strategy X_i. This problem is conveniently tabulated by means of a decision tree, as follows.



Circled numbers represent the set-up costs for the associated product under the policy concerned. Clearly the best policy from the point of view of such costs is (C, B, A) at a minimum cost 6.

In terms of the decision problem the above problem is as follows.

		Z_1 – one environment	
	X_1	$R_{11}=15$	
	X_2	$R_{21}=14$	
	X_3	$R_{31}=16$	
	X_4	$R^1{}_1=18$	optimum $R_{ij}-R_{61}$
	X_5	$R^2{}_1=13$	therefore decision is X_6
	X_6	$R^3{}_1=6$	
X_1 = (A, B, C)	X_3 = (B, A, C)		X_5 = (C, A, B)
X_2 = (A, C, B)	X_4 = (B, C, A)		X_6 = (C, B, A)

Decisions under uncertainty

Decisions are sometimes made in a situation in which environments can be identified, but nothing is known as to the likelihood or probability of a specific event pertaining.

To be specific, consider a cosmetic company who have produced an innovatory skin preparation. Suppose they are considering the price at which to market the preparation, but as yet have no ideas as to the likely market response, that nothing like it has been marketed before and, as yet, no consumer test has been conducted. Management may be willing to consider the market response (environments) on a three-point scale, poor, average and good. Suppose further the strategies are to market the product in one of three sizes at a cost of £2, £1.50 or £1, and also, associated with these strategies and environments, an estimate of the likely profit over a year has been established as follows.

	Profit (suitable units)	Good	Average	Poor
	X_1 (£2)	7	3	1.5
Strategy	X_2 (£1.50)	3	4	4
	X_3 (£1)	4	2	5

Hence the decision-maker has to choose between the policies X_1, X_2 and X_3 knowing nothing whatsoever as to the likely market response. Clearly the headings good, average and poor may be erased at this point since they communicate no usable information. Assuming the objective is to maximize profit over the year, how is the choice to be made?

Laplace's criterion for this choice is based upon the Principle of Insufficient Reason. Here there is no reason to suppose one environment any

more or less likely than the other. This being so, environments are assumed equally likely and strategies accordingly measured by the average outcome across the environments. Thus we have $X_1 \sim 11.5/3$, $X_2 \sim 11/3$, $X_3 \sim 11/3$ and X_1 is accordingly chosen.

There are many other ways of making this selection. Each policy could be viewed in terms of its worst possible outcome, in which case X_2 would be chosen since it has the best worst outcome. This procedure of choice is the pessimist's criterion of Wald. Of course, one could equally well make the choice on the basis of the very best possible outcome, or a mixture of the best and worst outcomes.

One selection criterion of interest to us here is that due to Savage–minimax regret criterion. The selection is made on the basis of the policy with the minimum maximum regret where, for each environment, regret is measured as the difference between what was obtained and the best that could have been obtained had the environment been known. For the above problem, we have for the regrets:

Regret	Good	Average	Poor	Max regret
X_1	0	1	3.5	3.5
X_2	4	0	1	4
X_3	3	2	0	3

The chosen strategy is here X_3 since it has the minimum maximum regret. Now suppose initially market prices of £2 and £1 are considered. If the decision-maker were to choose on the basis of Savage's criterion, the price would be fixed at £2. However, we have just seen using the same criterion to choose between £2, £1 and £1.50, the choice is £1. This irrational behaviour is caused by the criterion concerned being non-transitive. Transitivity, sometimes referred to as coherence, is a very important concept in decision analysis. A decision-maker's preferences are transitive if, when A is preferred to B, and B preferred to C then A is preferred to C. With this condition unsatisfied, the decision-maker has no best choice between A, B and C.

Few business men would be content to make decision under conditions of uncertainty. Most likely they would attempt to obtain further information as to the prevailing environment. This leads to a situation of risk.

Decisions under risk

In the case of decision-making under risk, the decision-maker assigsn probabilities to each of the environments indicating his degree of belief that

each particular one will prevail. The probabilities may either be objective or subjective in nature.

Consider the situation of a marketing manager whose firm is contemplating a special promotion for a new product during October and must decide upon the promotion now. Assuming his objective is profit maximization over a specified period of time, there are two alternatives open to him

X_1 approve the promotion,
X_2 reject the promotion.

It has been calculated the production and promotion costs will be £100 000. No objective information is available concerning customer reaction, but it is assumed customer reaction can be measured on a three-point scale say, 'very favourable', 'favourable' and 'unfavourable'. The manager summarizes his feelings about the various categories in the following table.

Profit £	Very favourable Z_1	Favourable Z_2	Unfavourable Z_3
X_1	250 000	60 000	−100 000
X_2	0	0	0
$p(Z)$	0.4	0.3	0.3

$p(Z)$ is a probability (subjective in this case) giving a measure of the manager's personal degree of belief the various environments will prevail. It is suggested a decision should here be made on the basis of expected outcome, that is for each policy X_i, the choice is based upon

$$X_i \sim \sum_j R_{ij}\, p(Z_j). \tag{1}$$

In the present case, therefore,

$$X_1 \sim £250\,000 \times 0.4 + £60\,000 \times 0.3 - £100\,000 \times 0.3 = £88\,000$$
$$X_2 \sim \quad £0 \times 0.4 + \quad £0 \times 0.3 + \quad £0 \times 0.3 = £0$$

and policy X_1 is chosen since it has the greatest expected value £88 000. It is assumed here the decision-maker has no overpowering objection to the possible loss of £100 000. Of course, the decision-maker will never actually get £88 000 in any single case. Clearly his gain is fixed as one of £250 000, £60 000, —£100 000 or £0. The interpretation of this result is: if the situation is as represented in the above table, and the identical decision has to be made not once but on numerous independent occasions, then the expected average return from policy X_1 is £88 000.

An obvious problem here is, of course, determining the probabilities of customer reaction. Some objective evidence may be available based on experience with similar problems in the past. Either way, the marketing manager has his own opinion, albeit subjective, as to the likelihood of various events. With or without this approach the manager's decision will be based upon the available information such as it is. This particular format asks that his opinion become numerically explicit and that the decision be arrived at in a logical fashion, consistent with his beliefs. Further reading on this point of an introductory nature may be found in Raiffa (5) and Lindley (4).

Information problem

Only a rather unusual kind of marketing manager would seriously consider launching a new and untried product to the extent of a £100 000 investment without some quantitatively based information as to the likely market response. Most probably he will spend some time and money so as to conduct a market survey to sample the response for his product. This being the case, how much should he be willing to pay for a market survey? It is suggested the value of information should be measured by the extent to which the expected return on a consequential decision increases due to its use.

Let us return to the above problem and assume the information derived from a market survey is perfect, that is the correct environment would be determined. With this assumption we have for the expected return to be realized under a policy X_3—conduct a market survey and invest if the environment is found to be favourable and do not invest if unfavourable.

Profit	Very favourable Z_1	Favourable Z_2	Unfavourable Z_3
X_3	250 000	60 000	0
$p(Z)$	0.4	0.3	0.3

Here the probabilities express the marketing manager's degrees of belief the market survey will indicate each particular environment prevails. The expected value of X_3 is seen to be £118 000. Consequently, using a market survey, the manager would increase his expected gain by £118 000—£88 000

= £30 000, and would be unwise to pay more than this sum for the survey. More generally, the expected value with perfect survey information is

$$\sum_j \left\{ \max_i R_{ij}\, p(Z_j) \right\} . \tag{2}$$

The value of information is therefore given by

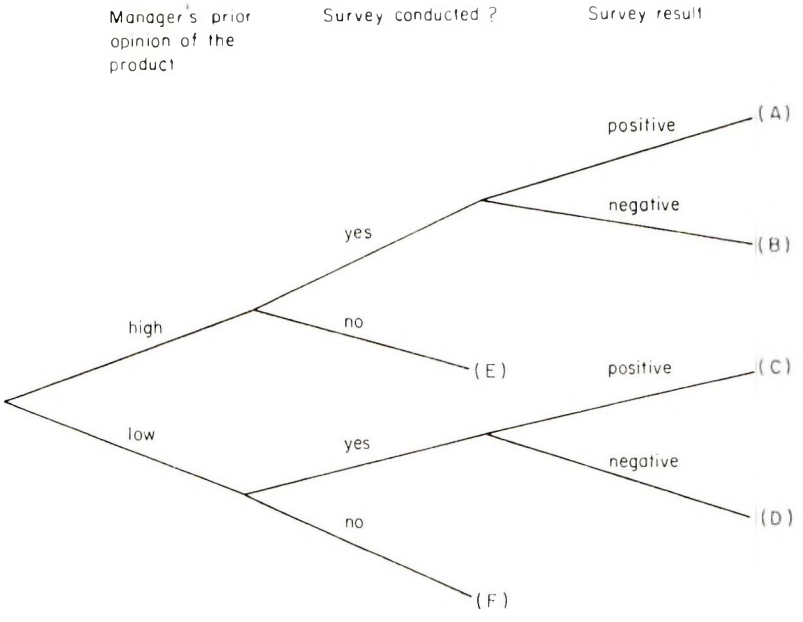
$$\left\{ \sum_j \left\{ \max_i R_{ij}\, p(Z_j) \right\} - \max_i \sum R_{ij}\, p(Z_j) \right\} . \tag{3}$$

Another way of arriving at the 'value of information' is to consider the effect it has had upon the decision. If environments Z_1 and Z_2 prevail, the purchase of information has added to the costs but not to the return since decision X_1 would have been taken anyway. If, however Z_3 prevails, the purchase of information prevents a loss of £100 000. Since the prior probability of Z_3 is 0.3, the information offsets an expected loss of £100 000 × 0.3 = £30 000.

As already stated, on expected value grounds, provided the cost of a market survey is less than £30 000, policy three will be selected. In other words, a market survey will be carried out and policy X_1 or X_2 selected, depending upon the findings of the survey. This analysis indicates whether or not a market survey can be justified in a manner consistent with the manager's knowledge and judgement of the situation as expressed by his probability distribution $p(Z)$.

Imperfect information

The assumption of infallibility of a market survey is, of course, not realistic. Accepting the fact that such tests are subject to error, how much is a survey worth and how would the results be used? Presumably one would not pay more for imperfect information than one would for perfect information. Here the decision-maker may or may not have a high prior feeling as to the potential of his new product. He may or may not conduct a market survey which may or may not endorse his views. This situation is best represented by a tree as follows, where a positive and negative test result represents a survey recommendation to market and not market respectively Six possible decision points can arise (A, B, C, D, E, F). First consider E. and F. Here the decision is based only on the manager's prior knowledge and would, presumably, be made in accordance with section on 'Decisions



under risk'. If a survey is undertaken, the decision point could be A or D, that is the manager's prior notion and the market test are in agreement. If this is so, the test has contributed to the cost of the decision but not, presumably, to the actual return on the decision, since the same decision for points A and D will likely be made as for points E and F respectively. Consider the remaining decision points B and C. Here the survey results and manager's priors are in conflict and we still have a problem. Is the decision to be made on the basis of the manager's priors, the survey information or perhaps a mixture of both? It would appear the purchase of imperfect information is either costly and useless or leads to a situation equally imponderable with the initial decision! To confuse the issue further, at any particular stage the actual environment is unknown. In other words, even if the manager's prior feeling and the test result are in agreement, they could both be wrong!

Bayes theorem gives a way out here. This is a theorem concerning probabilities and may be written (4)

$$p(Z \mid X) = \frac{p(Z \text{ and } X)}{p(X)}$$

In words, the probability of an environment being Z, given information X, is the probability of Z and X divided by the probability of obtaining information X. Since $p(Z \text{ and } X) = p(X \text{ and } Z)$, we have

$$p(Z \mid X)\, p(X) = p(X \mid Z)\, p(Z). \tag{4}$$

Returning to our problem, the manager has a prior distribution $p(Z)$ for the probability that various environments will prevail, and based solely on this information would make a decision on the basis of that policy X_i which maximizes his expected return $\Sigma_j R_{ij} p(Z_j)$.

Having now received the information X, say, of the survey, presumably the manager can be expected to 'revise' his probability distribution from $p(Z)$ to $p(Z \mid X)$—that is the probability of Z given information X. This being the case, the expected return on policy X_i is now

$$\Sigma R_{ij} p(Z_j \mid X) p(X)$$

which using (4) becomes

$$\Sigma_j R_{ij} p(X \mid Z_j) p(Z_j).$$

In the particular case under discussion, there are two possible pieces of information X resulting from the survey: $\overset{(1)}{X}$—a favourable environment and therefore advise invest, and $\overset{(2)}{X}$—an unfavourable environment. For each value of X, the policy leading to the greatest expected value will, of course, be selected. This being so, the expression may accordingly be written

$$EV(X_i) = \Sigma_x \left\{ \max_i \Sigma_j R_{ij} p(X \mid Z_j) p(Z_j) \right\}$$

$$= \max_i \Sigma_j R_{ij} p(\overset{(1)}{X} \mid Z_j) p(Z_j) + \max_i \Sigma_j R_{ij} p(\overset{(2)}{X} \mid Z_j) p(Z_j). \tag{5}$$

Suppose, for the purpose of demonstration, an analysis of past experience with survey tests indicates they can be expected to give the correct result some 80% of the time (it is assumed the statement 'correct result' in this context is understood). This being so, we have the following situation.

Profit	Very favourable	Favourable	Unfavourable	$\sum_j R_{ij}p(X\ Z_j)p(Z_j)$	
	Z_1	Z_2	Z_3	$\overset{(1)}{X}$	$\overset{(2)}{X}$
X_1	250 000	60 000	− 100 000	88 400	− 400
X_2	0	0	0	0	'0'
$p(Z)$	0.4	0.3	0.3		
$p(\overset{(1)}{X} \mid Z)$	0.8	0.8	0.2		
$p(\overset{(2)}{X} \mid Z)$	0.2	0.2	0.8		

For $X_i = X$, $X = \overset{(1)}{X}_1$, $\sum_j R_{ij}p(X \mid Z_j)p(Z_j)$ is given by

$$250\,000 \times (0.8) \times (0.4) + 60\,000 \times (0.8) \times (0.3) - 100\,000 \times (0.2) \times (0.3) = 88\,400$$

and for X_1, $\overset{(2)}{X}$ by

$$250\,000 \times (0.2) \times (0.4) + 60\,000 \times (0.2) \times (0.3) - 100\,000 \times (0.8) \times (0.3) = -400.$$

From expression (5) we now have for the expected value of X_1 and X_2 using the imperfect survey information

$$EV(X_1) = £88\,400 + £0,\ EV(X_2) = £0.$$

Thus the value of perfect information is given by
£88 400 − £88 000 (expected value without information) = £400, and the decision procedure is X_1 if $\overset{(2)}{X}$ obtains, otherways X_2.

Evidently the manager would be ill advised to pay more than £400 for this particular survey since the expected value of his decision will only increase by this amount. It is a matter of common sense that a manager with a low opinion as to the marketability of a product is unwilling to pay much for further information. The above process provides us with a numerical value for this information. A slightly more general expression for the value of imperfect information here is

$$\sum_z \left\{ \max_i \sum_j R_{ij}p(X \mid Z_j)p(Z_j) \right\} - \max_j \sum_j R_{ij}p(Z_j)$$

which represents the difference between the expected value with imperfect information and that without it.

This, the Baysian approach to a decision problem, uses all the information available in a logical and consistent manner to analyse the decision situation. When evaluating a numerical measure of the expected consequences of a particular choice X_i, use is made of both the manager's priors

and the sample result X. This seems reasonable since the information X is a function of the number of people surveyed, the format of the survey, etc., whereas the manager's priors $p(Z)$ are based upon a different source of information, namely his experience and knowledge to date. Here the broadest possible data base is used for the decision. For further reading on this topic, the reader is recommended to look at (4) and (5).

Subjective tests and information

In the previous section are discussed the use of information which was essentially an objective measure of a specific quantity such as market share. We discuss in this section the value and use of tests and information which are subjective in nature.

Consider the situation of, say, a soap manufacturer who wishes to perfume his product. His procedure might be to compile a perfume specification and duly invite say six perfumers to submit a sample as tender. Presumably the perfume specification indicated any price limit the manufacturer wished to impose. If all six perfumers submit tenders, the manufacturer needs to choose between six perfumes, S_1, S_2, S_3, S_4, S_5, S_6 for his product.

It appears a common method employed to make this choice is to use a consumer panel. Here a team of 30 or so individuals are requested to give their opinion and preference on the samples S_i, and a particular one S^* selected on the basis of this information. Such a process has the attraction of being simple to operate and also of avoiding any real decision on the part of the manufacturer in a highly subjective area.

Panel tests

An obvious question here is how one would recognize a good choice of S^* and also what is expected of it? Before we discuss these points further, it will be useful to consider some possible problems associated with a panel test of the type described above. We shall assume each and every member of the panel to be a coherent individual capable of giving an informed opinion. Being coherent individuals, their preferences are transitive in that if

$$S_iPS_j \text{ and } S_jPS_k \text{ then } S_iPS_k$$

where P denotes preferred to.

Suppose three firms A, B and C have submitted perfume tenders, and the preference orderings of a seven man panel is as follows:

		three samples					two samples		
Panel member	1	A	P	B	P	C	A	P	B
	2	A	P	B	P	C	A	P	B
	3	A	P	B	P	C	A	P	B
	4	B	P	A	P	C	B	P	A
	5	B	P	A	P	C	B	P	A
	6	C	P	B	P	A	B	P	A
	7	C	P	B	P	A	B	P	A

Now, if $N(Y)$ is the number of times perfume Y is the most perfumed choice, and the group decision is made on the basis of the highest value of $N(Y)$, with some further criterion for decision in the case of a tie, in the above case with three samples we have,

$$N(\mathrm{A}) = 3, \quad N(\mathrm{B}) = 2. \quad N(\mathrm{C}) = 2$$

Accordingly perfume A is selected out of the set A, B and C. If, however, only two samples are considered by the panel, say A and B, we see from the second table above which is obtained by deleting perfume C from the first table,

$$N(\mathrm{A}) = 3, N(\mathrm{B}) = 4$$

and so B would be chosen from the set A, B.

In short, even though each member of a panel is coherent, it is possible for a group decision procedure to be incoherent.

As a further example of the kind of problem that can arise in group decision-making, consider the following three panel member, three product problem

Panel member	1	A	P	B	P	C
	2	B	P	C	P	A
	3	C	P	A	P	B

Let the mechanism for producing a panel choice be as follows: each individual ranks the alternatives as shown: for each pair (X, Y), the number $N(X,Y)$, being the number of times perfume X is preferred to Y, is determined: the alternatives for the panel are then ranked on the basis of the numbers $N(X, Y)$. We find that

$$N(\mathrm{A}, \mathrm{B}) = 2 \quad \mathrm{N}(\mathrm{B}, \mathrm{A}) = 1$$
$$N(\mathrm{B}, \mathrm{C}) = 2 \quad N(\mathrm{C}, \mathrm{B}) = 1$$
$$N(\mathrm{C}, \mathrm{A}) = 2 \quad N(\mathrm{A}, \mathrm{C}) = 1$$

If the first pair discussed is A and B, B is discarded in favour of A. In the next comparison between A and C, A is discarded and perfume C selected. Now, had the first perfumes compared been B and C or A and C, the choice would have been A and B respectively. Thus we have a panel of coherent members with a decision rule for obtaining a group choice which has the undesirable quality of being dependent upon the order of consideration of the samples.

It is now evident the process of obtaining a group choice needs to be transitive, or coherent, if any useful information is to result. What is required is a 'Welfare function, W', whose input data are the coherent preferences of the panel members, and whose output are the unique panel choice. This function is, by definition, a coherent function.

We return for the moment to the question of recognizing a good choice S^* from S_i. It is evident the choice S^* is a function of both the specific panel used and the welfare function—or panel choice procedure. It is arguable that by having a sufficiently large panel, the individual preferences of panel members will in some sense be evened out and two panels of similar composition and sufficiently large size would be expected to give the same choice given a specific welfare function. This assumption is directly measurable.

If, as is often assumed, a sufficiently large panel will produce a choice which is more or less independent of the individual panel members, the choice S^* is directly determined by the welfare function used. This being so, the main choice the soap manufacturer has to make is the selection of a welfare function W. Presumably he will value highly any welfare function he believes reflects the preference of the market at large. How can this selection of welfare function be made?

Suppose the manufacturer has, say, two possible welfare functions, W_1 and W_2, and is contemplating perfuming a product. Following the usual procedure, tenders S_i are invited and a panel test to determine preferences duly conducted. Since the market as such might object to the particular product in question being perfumed, the manufacturer may well append a non-perfumed product S_0 to those submitted to the panel. Now, if both welfare functions give the same choice, that is

$$W_1(S_i, S_0) = W_2(S_i, S_0) = S^*$$

the perfume choice S^* is clear. If this is not the case, the welfare function to choose is ideally that which will lead to the greatest increased profit for the manufacturer over a specific period. An analysis of past occasions in which

W_1 and W_2 have been used could resolve this issue on the basis of expected increase in profit due to the selection procedures W_1 and W_2 respectively.

The perfumer's tendering decision

Consider now the situation of the perfumer when selecting a particular perfume to tender for a specific contract. In the normal course of events, the perfumer might create three or four possible candidates in response to the perfume specification and then choose one as a tender. How can this choice be made? There are two classes of problem here.

(a) The perfumer knows the customer's (soap manufacturer) welfare function W.

(b) The perfumer is ignorant of the customer's welfare function.

Welfare function known

Here the perfumer has the opportunity of performing a panel test himself and use the known welfare function to identify which, of his set of perfumes, would be the most desirable according to the customer, and so increase his chance of gaining the contract. How much is this increased chance worth to the perfumer?

Suppose over the past 50 tenders submitted for similar types of contract, the following information is available.

	Number of tenders	Number of contracts awarded
X_1—no panel test used	25	8
X_2—panel test used	25	12

On the basis of this information, the probability of a successful tender given no panel test is used in its selection is $p(S \mid X_1) = 8/25, = 0.32$ and that when a panel test is used is $P(S \mid X_2) = 12/25 = 0.48$. This is a quantified expression of experience to date. Consider a new contract worth £4 000 say, in which the development costs are £300, and should the subsequent tender be accepted, expected production cost of £1 000 would be incurred. If a panel test costs £250, should it be used?

The following actions are open,

(X_1) do not tender,

(X_2) tender, but do not use a panel test,

(X_3) tender and use a panel test with known welfare function to select sample. If S and S^1 denotes the events tender accepted and rejected respectively, we have the following situation:

Policy	Payoff		Probability	
	S	S^1	S	S^1
X_1	0	0	0	1
X_2	2 700	− 300	0.32	0.68
X_3	2 350	− 550	0.48	0.52

Accordingly, we have the following expected values for the various policies

$$EV(X_1) = £0$$
$$EV(X_2) = £2\,700 \times (0.32) - £300 \times (0.68) = £660$$
$$EV(X_3) = £2\,350 \times (0.48) - £550 \times (0.52) = £842$$

Based upon previous experience, therefore, if the sample selection decision were to be based upon the expected values of policies X_1, X_2 and X_3, procedure X_3 would be chosen.

The above example embodies numerous assumptions which may or may not be acceptable in any particular case. For instance, the data table of past tenders is in a very idealized form. In any particular organization it could be that the chances of obtaining a contract were dependent upon the number of, and particular firms competing, the size of the contract as well as whether or not a panel test is used. Hopefully, however, information will be available to determine a probability measure for the likelihood of securing a contract of a particular size and type given X_1 and X_2. It is worth noting here that with policy X_2, the manufacturer's welfare function is known, but not used explicitly. No doubt knowledge of W will in some way influence the sample selection under X_2. A consideration of how X_2 might be made is discussed in part in the next section.

Welfare function unknown

When the manufacturer's welfare function is unknown, the perfumer is unable to determine the customer's preference for the three samples say produced. This being the case, what is the point in the perfumer performing a panel test, presumably with his own welfare function? For all the perfumer knows, the manufacturer's group decision procedure could be incoherent! Selection procedures have been used in the past and it is not unreasonable to judge them accordingly by their results.

Past selection decision could be analysed according to contract value, expected profit, number and type of competing companies, whether or not a panel test was used, etc., and the recommended selection procedure based upon this analysis. Suppose, for the sake of simplicity, it appears reasonable to assume the likelihood of winning a contract is independent of the number of firms competing, and also the value of the contract. (If these assumptions are not valid, the same subsequent analysis may be performed but consideration restricted to, and based upon data from contracts within a value range, say £8 000–£10 000, and with a specific number of competing firms.)

We have, therefore, information such as

Number of contracts	S	S^1
X_3	n_3	m_3
X_2	n_2	m_2

where the number of successful and unsuccessful tenders selected on the basis of a panel test (X_3) and a specific welfare function W are n_3 and m_3 etc. Based upon this information, the probabilities of successful tenders using and not using a panel test are respectively

$$P(S \mid X_3) = \frac{n_3}{n_3 + m_3} \qquad p(S \mid X_2) = \frac{n_2}{n_2 + m_2}.$$

On the basis of these probabilities the same cost analysis as before may be performed.

Non-panel decision

Under policy X_2, the selection of the tender sample is made within the company without recourse to a panel test. Presumably the decision or selection criterion is some function of the considered opinion of perhaps

$a^{(1)}$ the chief perfumer; $a^{(2)}$ the marketing manager; and $a^{(3)}$ the production manager.

Each of these individuals has his own opinion as to the most likely candidate to submit as a tender and this opinion is based on his or her own subjective understanding and knowledge of perhaps current trends and fashions in perfumery, or even upon some subconscious consideration. If the individual

preferences of these experts have been recorded along with the actual group choice X_2, —or was to be recorded over a period of time, information of the following nature would be available.

	Number of occasions $a^{(i)}$ and X_2 agreed		Number of occasions $a^{(i)}$ and X_2 disagreed
	S	S^1	Result of tender $a^{(i)}$ unknown
X_2	7	18	0
$a^{(1)}$	5	6	14
$a^{(2)}$	6	7	11
$a^{(3)}$	4	1	20

This table indicates the number of times each individual agreed with a selection which was subsequently found to be either successful or unsuccessful, or to have disagreed with a selection decision which was unsuccessful. Accordingly it is possible to associate a prediction measure to each of the individuals and so identify, on historic grounds, the 'best' predictor. One possible such measure is to give, say, one mark to each correct prediction, 0 to a known incorrect prediction and perhaps $1/n$ (where n is the number of competing firms) in the case of an unknown result. Thus, if $n = 4$ we have for a preference measure

$$X_2 = 7$$
$$a^{(1)} = 8.1/2$$
$$a^{(2)} = 8.3/4$$
$$a^{(3)} = 9.$$

In this particular instance, the current practice of using X_2 could be superseded by any $a^{(i)}$ with an anticipated increase in successful tenders. The best apparent predictor is, of course, $a^{(3)}$, or in this case the production manager. With $a^{(3)}$ the prior probability measure of success is $9/25 = 0.36$ as opposed to 0.28 with X_2. Clearly such a prediction measure could and should be updated as results of each tender become available.

Care must be taken when deciding upon a 'measure' of prediction performance. Above we used the principle of Insufficient Reason to assign equal probabilities to a set of events of unknown probability. Equally well one may have reasoned as follows: the production manager has made 25 selections, five of which we know split into four successful selections and

one unsuccessful. It might be assumed, therefore, the unknown results will split in the same ratio given a total of 20 successful selections and five unsuccessful selections. Here there is a danger of putting too much trust in too little information. If, for instance, another party, the Managing Director, say, had only agreed with X_2 once, and on this occasion the selection was successful in gaining the contract, his expected prediction rating would be top at 25, or 100%.

Panel test used

If a panel test is used, the perfumer has the task of selecting a welfare function W. There are two immediate approaches to this problem.

(a) Knowing the preference orders of panel members over past sets of decisions, it is possible to experiment with various welfare functions over this data and perform an analysis similar to the above, where individual preferences $a^{(i)}$ are now replaced by welfare function selection $W^{(i)}$. That welfare function $W^{(i)}$ leading to the best expected number of successes is then selected. Of course, this analysis may be complicated by different costs associated with evaluating the various welfare function. The analysis of non-panel decision would presumably be incorporated here by defining $W^{(1)} = a^{(1)}$, $W^{(2)} = a^{(2)}$ etc., that is the relative effectiveness of the simplest welfare function, an individual's preference, and more sophisticated function $W^{(i)}$, $i > 3$, would be measured.

(b) It might be possible, knowing the soap manufacturer's problem, to predict to some degree the welfare function, or likely welfare function, W^* of the manufacturer. Suppose the perfumer thinks welfare function $W_1, W_2, \ldots W_n$ are likely candidates, and also in his opinion the probability of W_1 being used is p_1 and in general of W_i being used is p_i etc . . . $i = 1, -, n$.

If there are three possible tender samples to choose between S_1, S_2, S_3, using function W_i the choice is $S_i^* = W_i(S_j)$, $i = 1, -, n$. We form a weighted sum of the number of times S_i is selected as S^*, namely $N(S_i) = \sum_j p_j$, where j is such that $S_j^* = S_i$.

The selection is then made on the basis of selecting S_i to maximize $N(S_i)$. An example will make this procedure clear.

Ex. $W_1(S_2, S_2, S_3) = S_1 = S_1^* \quad p_1 = 0.2$
$W_2(S_1, S_2, S_3) = S_2 = S_2^* \quad p_2 = 0.2$
$W_3(S_1, S_2, S_3) = S_3 = S_3^* \quad p_3 = 0.3$

$$W_4(S_1, S_2, S_3) = S_2 = S_4^* \qquad p_4 = 0.1$$
$$W_5(S_1, S_2, S_3) = S_1 = S_5^* \qquad p_5 = 0.1$$
$$W_6(S_1, S_2, S_3) = S_3 = S_6^* \qquad p_6 = 0.1$$

$N(S_1) = 0.3$, $N(S_2) = 0.3$, $N(S_3) = 0.4$, so on the basis of the prior distribution p_i, S_3 is selected as tender.

Concluding remarks

The above remarks concerning subjective tests and their use and value are by no means complete. In discussing the subject it has been necessary to make numerous simplifying assumptions presenting a rather idealized situation. This is not so much a consequence of the decision analysis approach as the need here to simplify the discussion as much as reasonably possible. In discussing a variety of decision situations our object has been to see how a decision may be made which is logical, coherent and consistent with all available information. It is eminently clear from the last section that in the final analysis, decision procedures should be judged by their consequences.

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REFERENCES

(1) Pridmore, W. A. *Sensory testing—a statistician's approach*, Proceedings—Symposium on Perfumery (1970) (Society of Cosmetic Chemists of Great Britain).
(2) Starr, M. K. *Management: A Modern Approach* (1971) (Harcourt Brace Jovanovich, New York).
(3) White, D. J. *Decision theory* (1969) (Allen and Unwin Ltd, London).
(4) Lindley, D. V. *Making decisions* (1971) (Wiley Interscience, New York).
(5) Raiffa, H. *Decision analysis* (1970) (Addison-Wesley, London and Massachusetts).

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Response of the frog olfactory system to controlled odour stimuli

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Presented at the 2nd Joint Perfumery Symposium organized by the British Society of Perfumers and the Society of Cosmetic Chemists of Great Britain at Eastbourne on 7–9th May 1973

Synopsis—The electrical events which occur in the nose of a frog when it is stimulated with ODORANTS have been studied.

For this study new techniques were developed for applying STIMULI of known composition and controlled concentration in a reproducible manner. The concentration and timing of the stimuli in the nose cavity has been monitored by means of a new device consisting of a sampling probe connected to a FLAME IONIZATION DETECTOR.

The ranges of concentration used have been wider than those reported previously and the form of the relationship between concentration and response size is now seen more clearly. It is that to be expected for a Langmuir type ADSORPTION of odorant molecules on the RECEPTOR surface.

INTRODUCTION

This investigation concerns the slow changes of electric potential which take place at the surface of an animal's olfactory mucosa when it is stimulated by an odorant. These changes can be observed only in the region of the olfactory receptor cells and can be presumed to result from processes essential to olfactory perception. Their study should therefore help towards an understanding of the receptor mechanism.

In practice the changes in electric potential are recorded using a pair of electrodes, one of small tip diameter placed on the surface of the olfactory

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mucosa, and the other larger one on inactive tissue. The plotted time course of the potential is called the ElectroOlfactoGram or EOG. *Fig. 1* illustrates a typical EOG resulting from a 5-s stimulus of 1,8 Cineole.

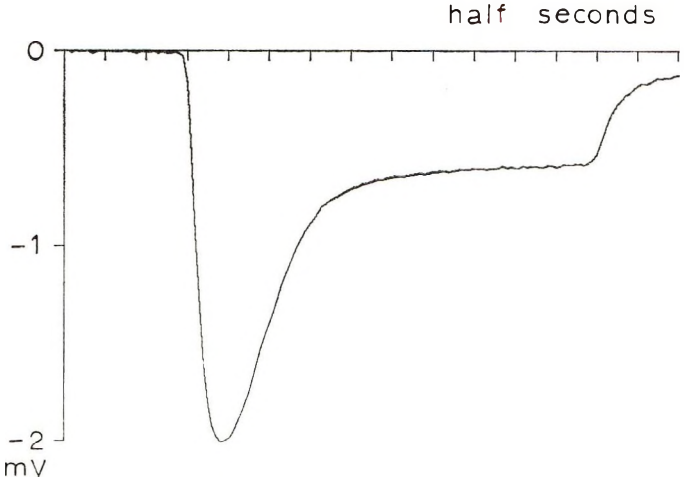

Figure 1. EOG resulting from a 5-s stimulus of 1,8 Cineole.

EOG's were first recorded by Hosoya and Yashida in 1937 (1). They were not systematically studied until nearly 20 years later. In 1956 Ottoson published his classic *Analysis of the electrical activity of the olfactory epithelium* (2). This was a lengthy and thorough investigation of EOG's in frogs. In it much attention was paid to the relationship of EOG size and shape to strength, duration and quality of the stimulus used. The conclusions of Ottoson's research remain practically unchanged today. This is a remarkable tribute considering the relatively simple apparatus which he had at his disposal.

It has been an object of the present research to look again and more closely at some of the factors investigated by Ottoson, taking advantage of modern instruments and technology to control and define as precisely as possible the chemical composition, concentration and time course of the stimuli used at the location where it matters—close to the olfactory epithelium.

Apparatus has now been evolved to meet these requirements (3) to a large degree. A feature of the stimulus applicator is that it can handle up to six different odour streams switching them on and off independently of each other and so close to the point of discharge that practically no time is

needed for a steady state to be reached. The apparatus may therefore be used for experiments which have not, it seems, been possible before. One of its first uses has been in the investigation of the relationship between stimulus concentration and the amplitude of the resulting EOG.

METHODS

The animals and their preparation

Common frogs (*Rana temporaria*) were used for the EOG recordings.

A frog was first anaesthetized by placing it in 15 ml of 10% aqueous urethane in a beaker. As soon as the frog lost its reflexes, it was rinsed with water and placed in a holder. The frog remained anaesthetized by this treatment for the whole course of the experiment and it was not allowed to recover.

The olfactory epithelium was exposed by dissecting away the dorsal wall of the nasal cavity opposite to the eminentia olfactoria. The opening thus made was 2–3 mm across and provided access for the recording electrode and the stream of air carrying the stimulus.

The stimulation system

The stimulation system may best be described by reference to *Fig. 2*. It consists of a constant stream of clean moist air which plays on the olfactory epithelium all the time. This prevents the mucus from drying up, prevents

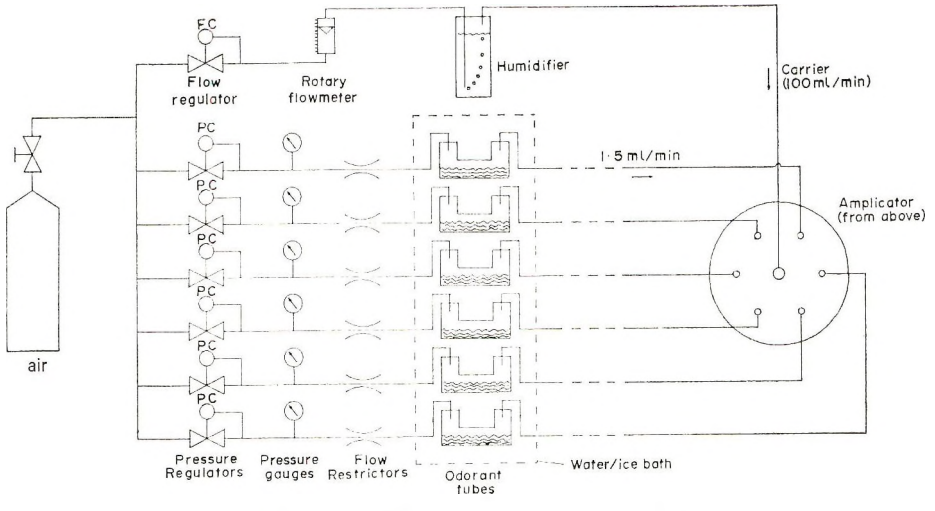

Figure 2. Diagram of the arrangement of odorant streams.

extraneous odours and, when required, carries the odour stimulus to the sensory area. This stream flows at 50 ml min^{-1} and emerges from a jet 1 mm inside diameter in laminar flow. (Mean linear velocity = 100 cm s^{-1} approx.)

The six odorant streams are switched into the carrier stream as close to the point of discharge as possible so that downstream there is minimum dead space and wall surface to delay delivery. The volume of the dead space is in fact about 0.15 ml so that with a flow rate of 50 ml min^{-1} there would be a delay of 0.18 s before a stimulus reached 63% ($= 1 - 1/e$) of its full strength. This would represent the worst possible case, i.e. instantaneous forward mixing in the nozzle causing 'rounding' of the stimulus profile. (If there were no forward mixing in the nozzle, the stimulus would still take 0.18 s to reach the orifice but would arrive there at full strength.)

The odorant streams (up to six in number) are generated by passing clean dry air over pools of liquid odorants held in U tubes. These U tubes have a straight central portion so that the air stream passes over about 8 cm^2 liquid surface without bubbling through it. This prevents formation of spray which might be carried forward and upset the concentration. The air flow through each tube can be regulated from about 1 ml min^{-1} to 5 ml min^{-1} by controlling the pressure to a sintered stainless steel flow restrictor before the U tube—or up to 10 ml min^{-1} by changing the flow restrictor. At these small flow rates the vapour leaving the U tube is practically in equilibrium with the liquid odorant. If necessary the U tubes can be immersed in a water bath to keep their temperature constant at or below room temperature.

The odorants used are chemicals whose purity has been checked by glc analysis of head-space samples. They are used either neat or diluted with water or paraffin oil. (The paraffin oil used is first deodorized by treatment with activated silica.) This dilution is the means most used to provide widely different rates of delivery of odorant. The rates can also be regulated by adjusting the air flow rates or by cooling the U tubes in order to lower the vapour pressures.

The odorants are conveyed to the applicator (where they are switched into the main carrier stream) by means of PTFE tubing of inside diameter 0.4 mm. This tubing is conveniently flexible and is easily and cheaply replaceable. It does absorb some of the odorant but, some minutes after starting the flow, it reaches a steady state which is not disturbed by the switching operation since the flow is not thereby interrupted. It is an important feature of the design of the system that this should be so. All

changes in flows and concentrations are confined to the switch and nozzle of the applicator itself. Contamination of one odorant by another and adsorption effects are therefore reduced to a minimum.

The function of the applicator is to enable odorant streams to be added to and mixed with the main carrier stream so that odour stimuli of predetermined duration and sequence can be directed into the frog's nasal cavity. The applicator, which is illustrated in *Fig. 3*, consists of three parts. These are the stream switching part, the mechanism for operating the switches and the nozzle which mixes and directs the gas stream towards the animal. The switches and nozzle are shown on a larger scale in *Fig. 4*. There

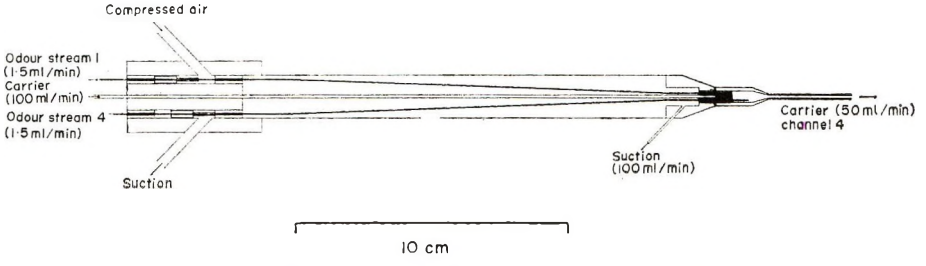

Figure 3. Scale drawing of six-channel odour applicator. (Saggital section, channel 1 off, channel 4 on.)

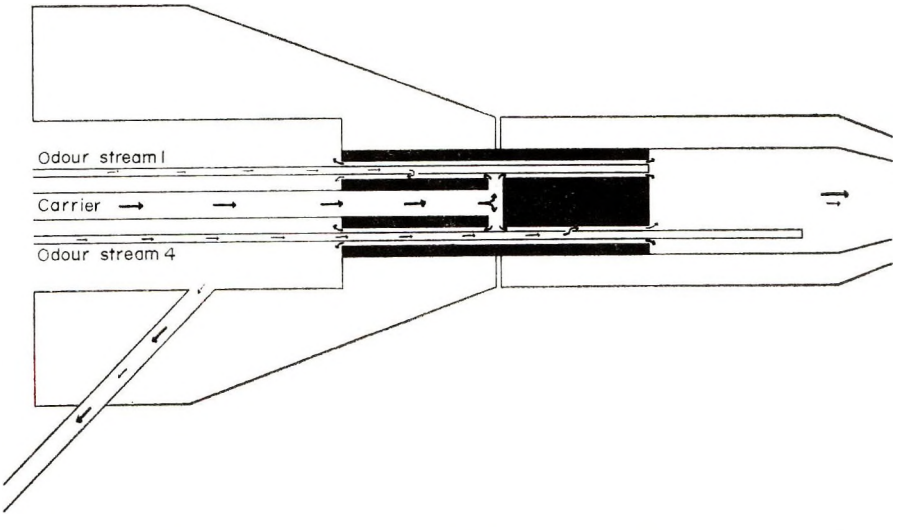

Figure 4. Detail of applicator stream switching system, showing channel 1 'off' and channel 4 'on'. (Glass nozzle on right is not all shown.)

are six switches, one for each odorant stream. Each switch operates on the following principle. The carrier gas divides at a T junction one branch of which leads to a vent while the other leads to the nozzle and the frog. Odorant is introduced into one or other branch of the T by means of a movable, loose-fitting inner tube. It is swept by the carrier either to vent or to the nozzle according to which branch the orifice of the odorant tube is moved into.

The switches are designed so that each can be actuated independently of the others. Carrier gas flowing at 100 ml min^{-1} splits into six radially disposed ducts. Each of these then divides at one of the abovementioned T junctions. Therefore 100/12 ml min^{-1} gas issues from each of the 12 branches of the T's. Six of these streams recombine as they enter the nozzle which therefore delivers 50 ml min^{-1}, while the other six lead away to a vent. Odorant streams not being applied and escaping at the vent are prevented from entering the room by an extraction duct.

The movable, loose-fitting inner tubes which convey odorant into branches of the T's are stainless steel tubes of outside diameter 0.3 mm. They are moved parallel to their axes by means of pistons which are fixed to them and which run in cylinders. The cylinders are each connected at one end to a source of compressed air or to suction. The change from compressed air to suction is made by solenoid valves which are actuated according to a preset programme by a timing device.

The nozzle of the applicator is designed to ensure good mixing of the odorant into the carrier stream. At first various designs were tried in which baffles were inserted in the nozzle to break up the flow Surprisingly these did not bring about the desired mixing. The best way was found to be to rely on diffusion and the problem was simply and effectively solved by extending the 1 mm bore outlet tube from 1 cm to 3.5 cm in length. The fact that the gases were not mixed properly in the original 1 cm long outlet tube was revealed by means of the vapour monitoring system described below.

Monitoring system for the odour stimuli (4)

This part of the apparatus is shown diagrammatically in *Fig. 5*. It is used to indicate the concentration of organic vapours in any particular locality such as in the stream issuing from the applicator jet. It consists essentially of a short probe tube connected directly into a standard flame ionization detector (fid) supplied by Pye Unicam Ltd. A sample of the vapours to be tested is drawn continuously into the fid through the probe by applying suction to the fid outlet. The probe tube is 4 cm long and 0.4 mm outside

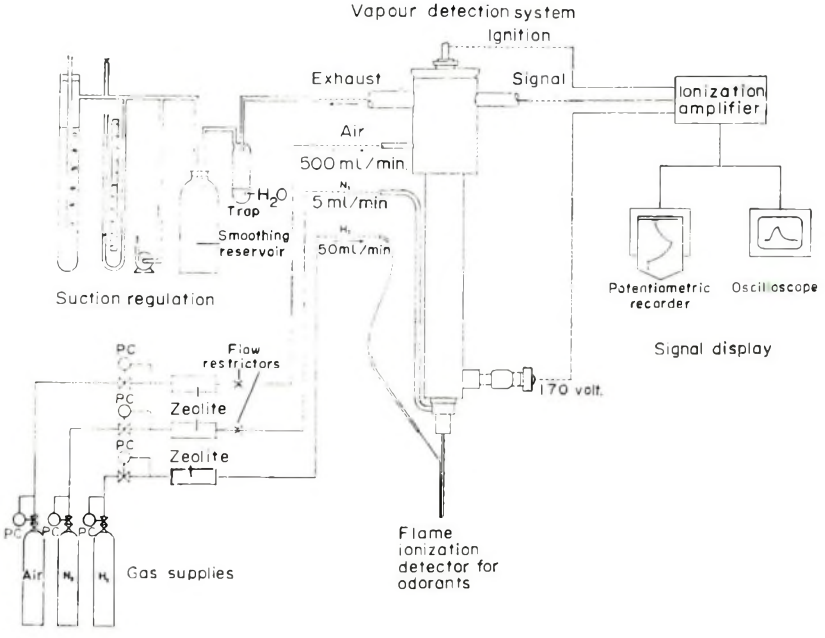

Figure 5. Diagram of monitoring system for odour stimuli.

diameter (od). The flow of sample being withdrawn by this probe needs to be small compared with the whole flow of gases being sampled. On the other hand the sample flow needs to be large enough for low concentrations of vapour to be measured by the fid. A sample flow rate around 2 ml min^{-1} is normally used. The transfer of sample towards the fid is slowed up by adsorption of organics on the inside walls of the probe. In order to minimize this delaying effect, the hydrogen for the flame is also introduced via the probe tube. This is done by means of a smaller tube (0.3 mm od) the end of which is bent and hooked $\frac{1}{2}$ mm into the open end of the probe. The probe inlet is thus nearly closed and offers resistance to sample flow such that a suction of about 50 cm water gauge needs to be applied to the fid exhaust to maintain this flow.

The suction (50 cm water gauge) needs to be adjustable and free of drift and pulsations. This is achieved, as shown in *Fig. 5*, by means of an adjustable dip-leg submerged in water and a 3 litre bottle to smooth out pressure pulses. The exhaust from the fid leads downhill to a trap to catch water formed in the flame. The fid itself is lagged to prevent condensation of water vapour inside it, to keep the fid at a steady temperature and to stop heat radiation affecting the frog.

The vapour monitoring system has been used mainly for determining the concentration of odour stimuli delivered by the applicator. Its fast response facilitates the adjustment of the odorant streams so that the desired concentrations are delivered. Once the odorant solutions and flow rates have been adjusted, it is unnecessary always to check the concentrations during a series of olfactory response measurements but only before and after the series. Only when solutions of very volatile substances are used is there any change noticeable in the composition over the period of an experiment.

The vapour monitoring system has other important uses. One of these, as mentioned above, was to check the mixing of odorant and carrier streams in the applicator jet. This was done by moving the probe tip 0.2 mm at a time across the 1-mm diameter of the jet orifice with an odorant switched on. The concentration profile so obtained was asymmetrical when mixing was not complete. Incidentally this experiment demonstrated that the sampling system was capable of discerning differences between points only 0.2 mm apart.

When the concentration profiles are determined for diameters progressively further and further away from the jet, a three-dimensional picture may be built up showing concentration on the vertical scale and displacement from the jet axis on the horizontal scale. Such a diagram is shown in *Fig. 6*. This may be the first time that an odorant jet stream has been mapped in this way and it is interesting to note that the concentration has fallen to half its original at a distance 12 mm from the orifice due to the spreading sideways of the odorant. Obviously the positioning of the applicator jet relative to the nasal cavity is of considerable importance. It would be useful to know also how the humidity of the jet stream—originally saturated—falls off for the same reasons. The olfactory mucus does sometimes become dry in spite of the precaution of saturating the carrier gas with water vapour.

Another use of the vapour monitoring system has been to check the efficiency of the applicator switching and to obtain some idea of the time course of build-up and fall-off of concentration when an odorant is switched on and off. It was found that, even with much smaller carrier gas flow and increased odorant stream flows, the device reliably and completely switched on and off. *Fig. 7* shows the three fid response curves to 2-s applications of acetone, cineole (strong) and cineole 1 000 times more dilute. Ideally the traces should be rectangular. The rounding of the shoulders is due largely to the slow movement of sample up the probe tube

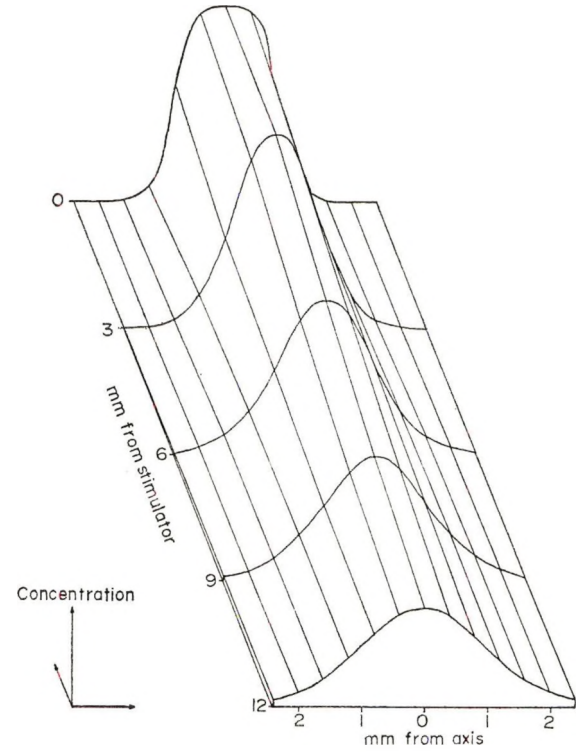

Figure 6. Concentration profile of applicator jet stream shown in 3-dimensional perspective. Measured by Fido.

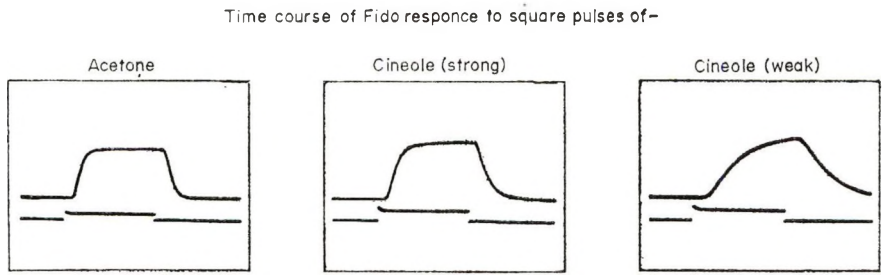

Figure 7. Response of the fid monitoring system to 'square' pulses of odorants lasting 2 s. Horizontal axis is time, vertical concentration.

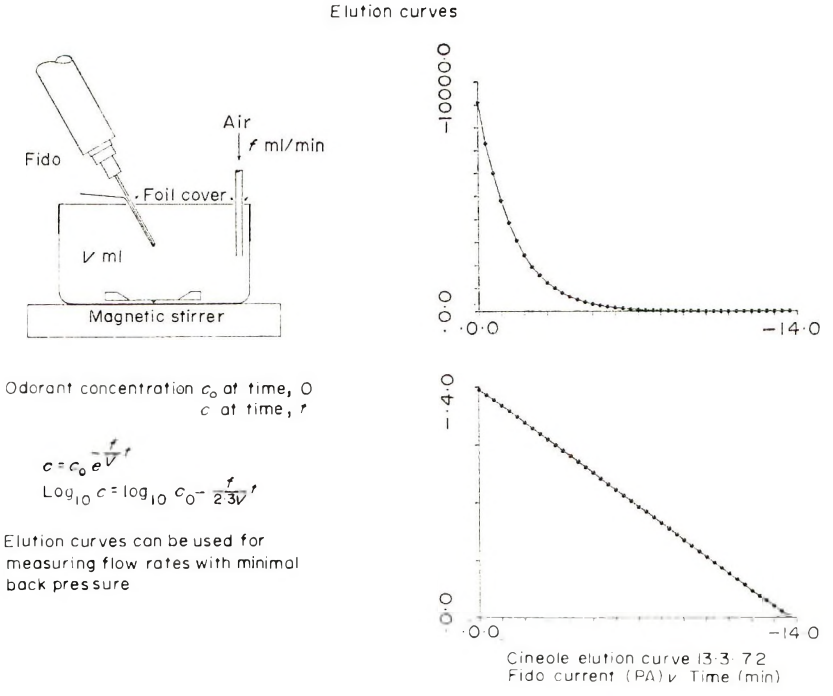

Figure 8. Arrangement showing how the vapour monitoring system can be used for measuring gas flow rates.

due to adsorption on the walls. That this was so was shown by applying a 'square' odorant pulse by a different method in which there was no possibility of a 'rounded' application. The response curves were only slightly sharper than before. It is interesting to observe, in *Fig. 7* the marked increase in adsorption effects when dealing with the more dilute odorant. This emphasizes the need for an applicator system such as that described here especially when studying physiological responses to very dilute odour stimuli.

The concentration time courses of odorants delivered by the applicator have more recently been studied by directing the jet stream directly into an improvised fid having a cut-away side for access. The time constant of the applicator has been shown to be about 0.12 s or more depending on the material being handled.

Yet another use of the vapour monitoring system has been in the measurement of gas flow rates without appreciably increasing the resistance to their flow. This has been done by using the flow to be measured to elute

an organic vapour from a nearly enclosed space of known volume. The concentration in this enclosed space is kept uniform by mechanical mixing (if diffusion alone is not adequate) and is measured continuously by the vapour monitor. The arrangement is illustrated in *Fig. 8*. The volume of enclosed space divided by the time constant of the exponential fall in concentration gives the flow rate of the eluting gas. This method has been used with advantage to measure the flow of gas from the applicator nozzle where back-pressure of most conventional flow meters would have altered the flow being measured.

This concludes the description of the apparatus for generating, applying and monitoring odour stimuli. It has been somewhat detailed because it is hoped that some of the ideas will be useful to those researching in this field and perhaps to others also. Moreover it seems desirable to place more emphasis on this side of any study of stimulus–response relationships than has been accorded hitherto. There is now the means of investigating more thoroughly firstly the relationship between stimulus concentration and physiological response, secondly the interactions between different odours applied simultaneously or sequentially and thirdly the time course of physiological events following an odour stimulus. All these can provide useful information about olfactory receptor mechanisms and it is with the first that the experimental part of this paper is concerned.

The electrode system for recording EOG's

The electrodes used for recording EOG's were similar to those used by Ottoson (3). The recording electrode was a Pyrex glass pipette having a tip diameter of 50–100 μm and filled with normal saline containing 2% agar. Electrical connection was through a AgCl–Ag wire inserted in the pipette. The second electrode was a AgCl–Ag plate wrapped in lint, soaked in normal saline and inserted in the frog's mouth.

The signals picked up by these electrodes were led to a high input resistance preamplifier, a main amplifier and the EOG's recorded on a strip chart.

Procedure for EOG experiments

In each experiment one frog was used for the study of EOG's resulting from one odorant chemical at different concentrations. The vaporizer tubes were charged with the odorant made up to different dilutions with a suitable solvent (usually deodorized light paraffin oil). Typically the dilutions were chosen so that the applicator delivered a set of stimuli in which each was 10

times weaker than the preceding one. Stimuli of intermediate strength were obtained by altering the gas flows in each channel by a factor of three. In this way stimuli having concentrations covering up to four decades in half decade steps were available.

The actual concentrations of stimuli were, of course, measured by the vapour monitoring system and this was done just before an experiment with a frog. Arbitrary units were used since for the purpose of the present investigation this was all that was necessary. In the case of certain odorants the lowest concentration gave fid signals obscured by noise and several readings had to be averaged to arrive at an estimate.

An anaesthetized frog was prepared and placed in a head holder. The applicator was positioned with its nozzle pointing into the opened nasal cavity and about 4 mm away from it. The recording electrode was lowered by means of a micromanipulator so that its tip just touched the surface of the mucus overlying the eminentia olfactoria.

The recordings required for this investigation were of the peak EOG voltages which are in fact reached soon after the onset of stimuli (see *Fig. 1*). Stimuli could therefore be switched off as soon as this peak voltage had been reached and doing this helped to minimize fatigue effects especially for strong stimuli. Also to combat fatigue 2 or 3 min were allowed for recovery between each stimulation with the higher concentrations.

The stimuli were usually applied in both ascending and descending order of concentration so that two EOG readings were obtained at each concentration.

The odorant chemicals for which EOG data are reported in this paper are:

Amyl acetate,
1,8 Cineole,
Linalol, and
Butyl acetate.

Results

The results are shown entirely in the form of graphs on which all the experimentally determined points are plotted. These graphs are shown in *Figs. 9–13*.

The abscissae in every case are the logarithms (base 10) of the concentrations in arbitrary units of the stimuli used. The EOG amplitudes in millivolts are plotted as the corresponding ordinates in *Figs 9(a)*, *10(a)*, *11(a)*,

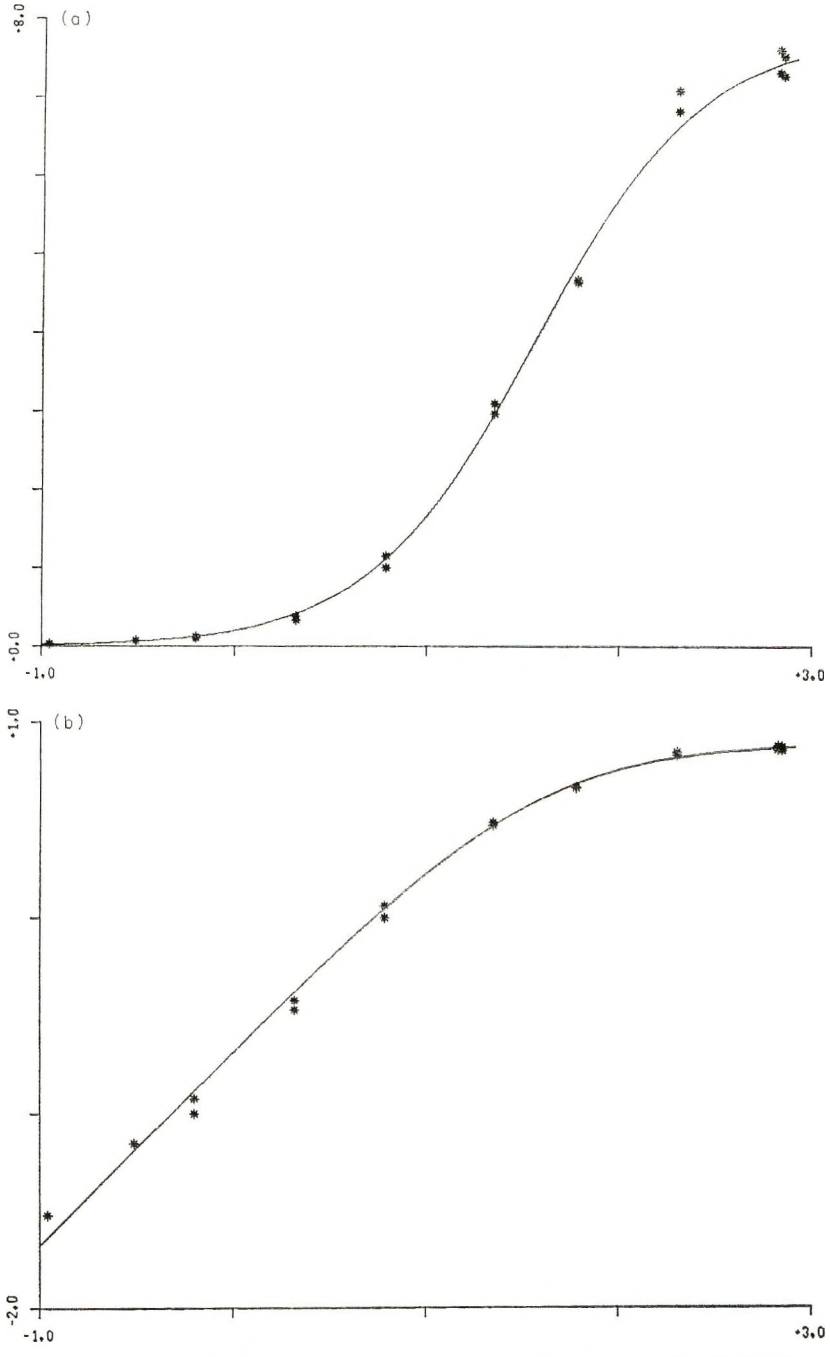

Figure 9. (a) EOG (mV) *v.* log concn. Amyl acetate. EOG max = 7.9 mV. (b) log EOG *v.* log concn. Amyl acetate.

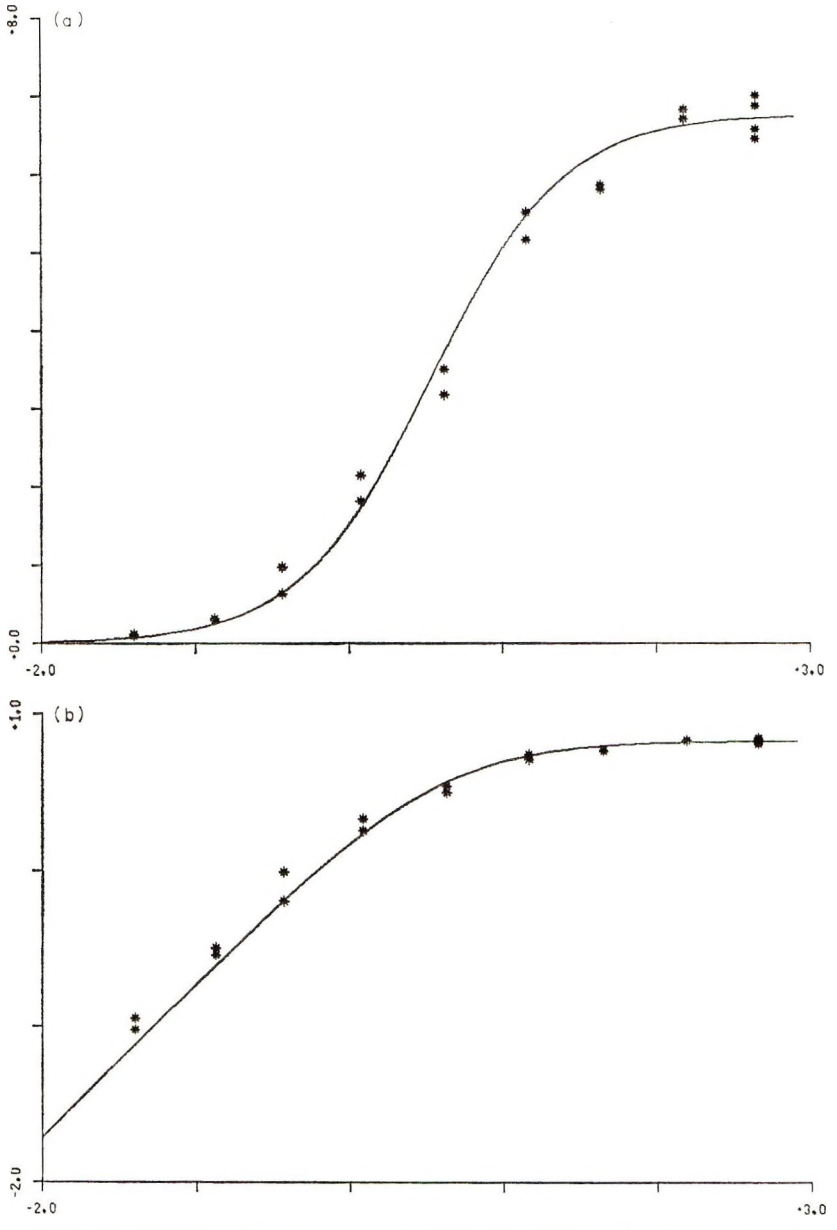

Figure 10. (a) EOG (mV) *v.* log concn. 1, 8 Cineole. EOG max = 6.8 mV. Concn. for half max EOG = 3.5. (b) log EOG *v.* log concn. 1, 8 Cineole.

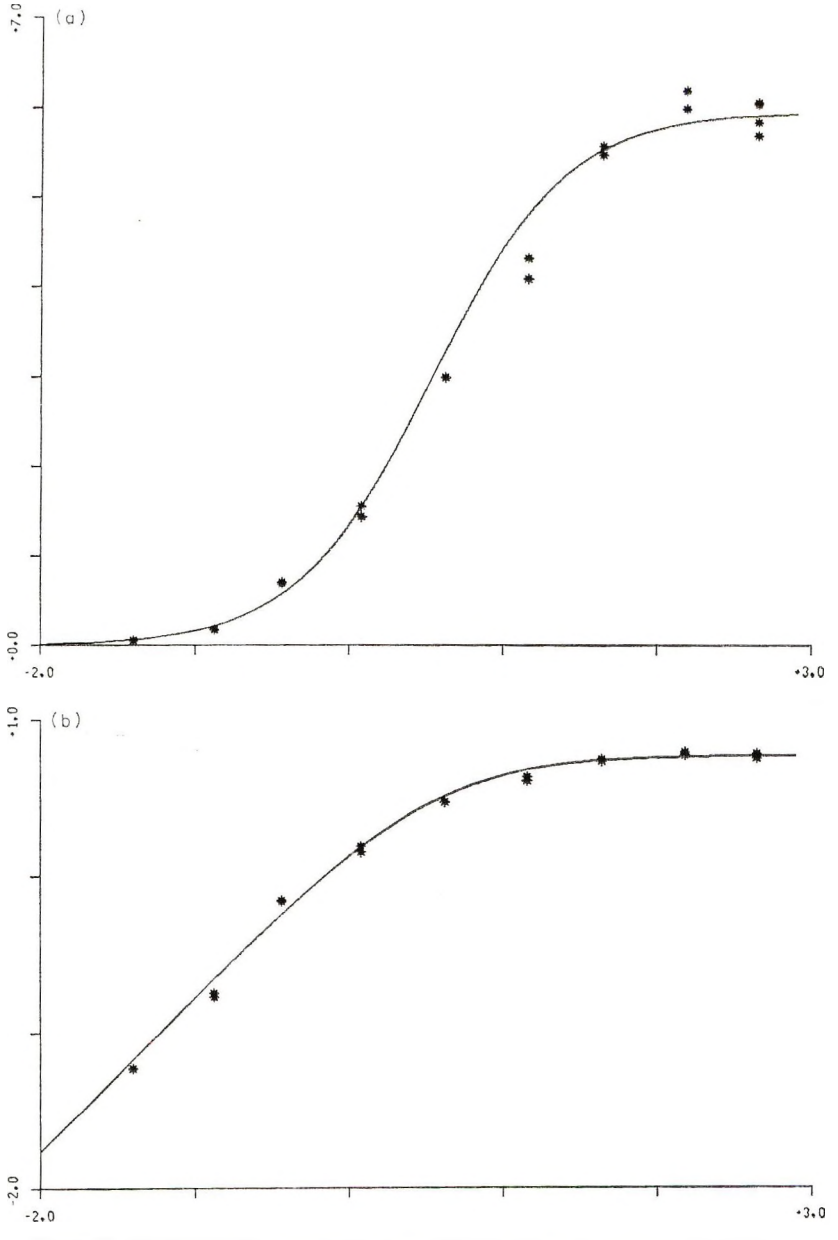

Figure 11. (a) EOG (mV) *v.* log concn. 1, 8 Cineole. Repeat experiment. EOG max = 6.0 mV. Concn. for half max EOG = 3.5. (b) log EOG *v.* log concn. 1, 8 Cineole.

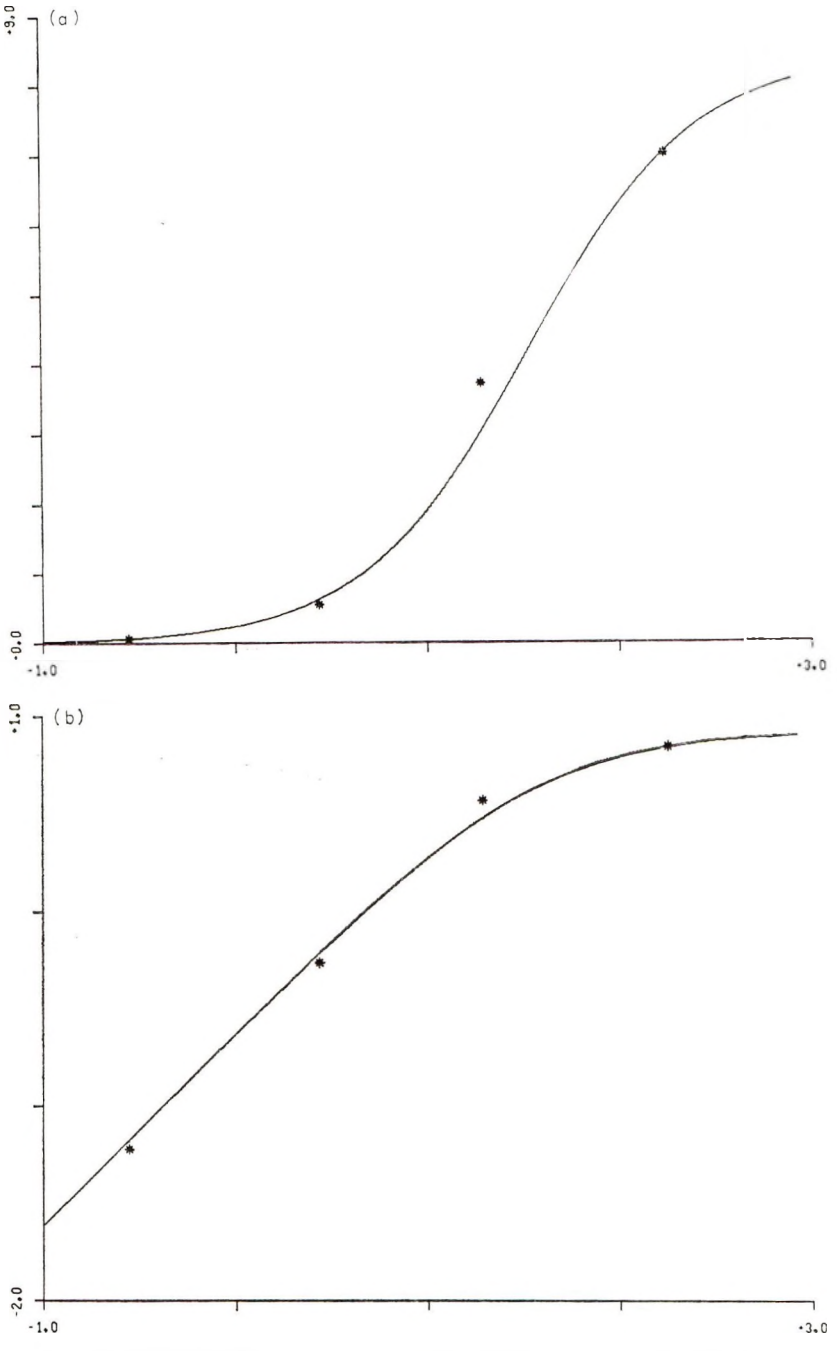

Figure 12. (a) EOG (mV) *v.* log concn. Linalol. EOG max = 8.4 mV. (b) log EOG *v.* log concn. Linalol.

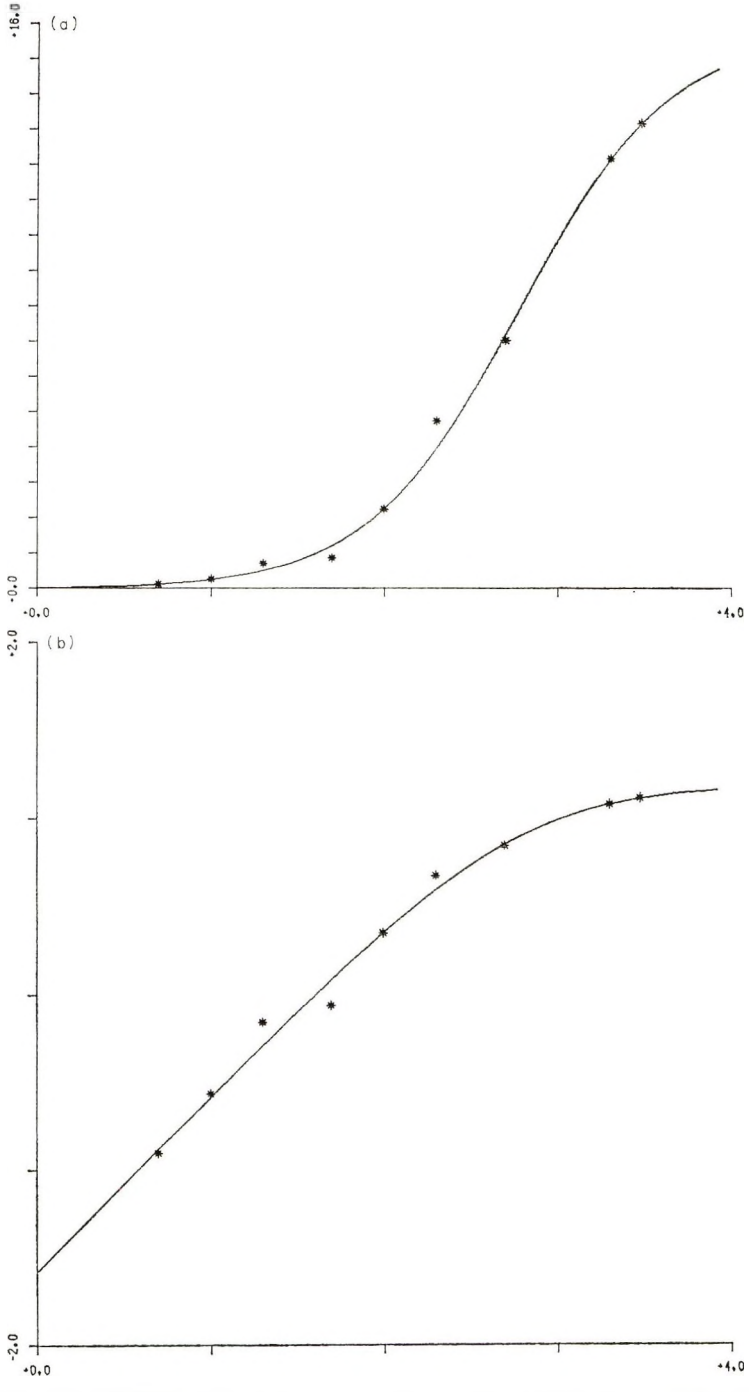

Figure 13. (a) EOG (mV) *v.* log concn. Butyl acetate. EOG max = 15.8 mV. (b) log EOG *v.* log concn. Butyl acetate.

12(*a*) and *13*(*a*) and the logarithms (base 10) of the EOG's are in *Figs 9*(*b*), *10*(*b*), *11*(*b*), *12*(*b*) and *13*(*b*). Thus for each experiment there is a pair of graphs representing the same data in two different ways:

(a) log stimulus *v.* response, and (b) log stimulus *v.* log response.

The curves drawn on the graphs represent a postulated mathematical relationship between stimulus and response analogous to the Langmuir adsorption isotherm (5). (See Discussion.) This postulated relationship contains only two arbitrary constants which define (a) the EOG for infinite stimulus concentration, and (b) the stimulus concentration required for half this (hypothetical) maximum EOG. These constants have been chosen in the case of each experiment to make the curve fit the experimental points as closely as possible. The values of the maximum EOG's are shown in the legends under each figure.

Discussion

In order to discuss the significance of the foregoing results it will be helpful to have a picture in one's mind of the events as far as they are known which give rise to an EOG.

The origin of the potential is the electrical polarization which exists between the inside and outside of cells forming the olfactory epithelial layer. This layer is formed by a mosaic of mainly two kinds of columnar cells. One kind is the receptor cells and the other the supporting cells. Odorant molecules in the mucus overlying these cells spread by diffusion and interact with receptor sites which form some part of a cell membrane. This interaction results in an increase of membrane permeability to certain ions. An ionic current then flows which depolarizes the receptor cell. (It is this depolarization of the receptor cell which causes it to generate action potentials.) The ionic current flows in a circuit through receptor cell, supporting cell and overlying mucus. Each of these components of the circuit contributes some resistance so that there is a potential difference between the surface of the mucus and the base of the receptor cells. The EOG is the summed effect of the 5 000 or so receptor cells which lie within range of the electrode tip. The magnitude of the EOG can therefore be considered in terms of the local circuits at cellular level.

Suppose that the EMF of the circuit is E, that the active membrane has a variable resistance, R_m, depending on presence of odorant and that the other resistances of mucus and tissue total R_t which is constant.

Then the potential, V_t, across the constant resistance, R_t, is given by

$$V_t = E.\frac{R_t}{R_t + R_m}.$$

If membrane conductance, G_m, is $1/R_m$ then

$$V_t = E.\frac{R_t.G_m}{1 + G_m R_t} \quad . \tag{1}$$

If it is assumed that the membrane conductance is a linear function of odorant concentration, $G_m = k.c$, then

$$V_t = E.R_t.\frac{kc}{1 + kc\ R_t}.$$

V is to be our estimate of the EOG so that

$$\text{EOG} = \frac{Ac}{1 + Bc}\ ,\ \text{where } A \text{ and } B \text{ are constants.}$$

Up to this point the argument has followed that of Tucker and Shibuya (6). But the above assumption that the membrane conductance is a linear function of concentration is clearly not correct because a saturation must soon be reached. Instead let us assume that there is a limited number of gates in the membrane corresponding to a maximum conductance of G_M.

Then, analogous to the Langmuir adsorption isotherm, we have

$$G_m = G_M.\frac{kc}{1 + kc} \text{ where } k \text{ is a constant.}$$

Combining this with equation (1) we get

$$V_t = \frac{E.R_t.G_M.k.c}{1 + (k + G_M.R_t.k).c}$$

$$\text{so EOG} = \frac{Ac}{1 + Bc} \text{ where } A \text{ and } B \text{ are constants as before.} \tag{2}$$

Therefore it may after all be expected that the EOG's would follow equation (2).

The curves plotted on the graphs of results are in fact those obtained from equation (2) with values of A and B chosen to make them fit as well as

possible the experimental points. The curves fit well especially having regard to the wide range of concentrations used and there is no evidence to suggest that the relationship is other than that deduced.

Earlier researchers (2, 7 and 8) have worked with smaller concentration ranges. When their results were plotted on log–log axes, the points fell approximately on straight lines implying a power function relationship. The lines for different substances had different gradients and it was thought that the gradients (exponents) were characteristic of the substance.

The results of the present study have also been plotted on log–log axes and it can be seen that for low concentrations the relationship is indeed practically linear. However, in no case is there suggestion that the gradient is other than 1 for low concentrations. Another feature of the results is that there is no evidence for a threshold concentration below which there is no EOG response.

In conclusion it may be noted that the sense of smell now seems to fall into line with other senses in following a stimulus–response relationship which is sigmoidal in form when plotted on semi-log paper.

Acknowledgments

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REFERENCES

(1) Hosoya, Y. and Yashida, H. Ueber die bioelektrische Erscheinungen an der Riechschleim haut. *Jap. J. Med. Sci.* 3 *Biophys.* **5** 22 (1937).
(2) Ottoson, D. Analysis of the electrical activity of the olfactory epithelium. *Acta Physiol. Scand.* **35** suppl. 122 1 (1956).
(3) Bostock, H. and Poynder, T. M. Apparatus for delivering and monitoring a sequence of odour stimuli. *J. Physiol.* **224** 14P (1972).
(4) *British Patent* Appln. 10851/72.
(5) Langmuir, I. Adsorption of gases on plane surfaces of glass, mica and platinum. *J. Amer. Chem. Soc.* **40** 1361 (1918).
(6) Tucker, D. and Shibuya, T. A physiologic and pharmacologic study of olfactory receptors. *Symp. Qualitat. Biol.* **30** 207 (1965).
(7) Drake, B., Johansson, B., Sydow, E. von and Dϕving, K. B. Quantitative psychological and electrophysiological data on some odorous compounds. *Scand. J, Psychol.* **10** 89 (1969).
(8) Ottoson, D. The electro-olfactogram. *Handbook of Sensory Physiology Vol. IV/I* 95 (1972) (Springer-Verlag, Berlin).

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Sesquiterpenes in the perfumery industry

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Presented at the 2nd Joint Perfumery Symposium organized by the British Society of Perfumers and the Society of Cosmetic Chemists of Great Britain at Eastbourne on 7–9th May 1973

Synopsis—The developments in SESQUITERPENOID CHEMISTRY are reviewed with especial reference to their application in PERFUMERY.

Sesquiterpenes are the group of terpenoids which are formed by the combination of three isoprene units and are found widely distributed in many essential oils in the high boiling fraction. These represent a collection of highly complex and diverse structural systems. Although certain sesquiterpene-based essential oils, such as oil of sandalwood and vetiver, have been used in perfumery since antiquity, the detailed study of sesquiterpene chemistry commenced only about 20 years ago. This progress has been possible mainly due to modern methods of isolation, structural determination and synthesis. It is generally believed that the future of our industry lies in simulating as many essential oils as possible and hence lessen its dependence on the natural oils. In this respect the detailed and more comprehensive analysis of essential oils is revealing that many commercially important oils contain a number of sesquiterpenes which are important to the overall odour of such oils. Consequently, in many cases the scope of commercially producing synthetic oils will depend on the availability of

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such sesquiterpenes. Another use of sesquiterpene compounds in perfumery is to convert the readily available natural sesquiterpenes into various odoriferous compounds on lines similar to monoterpenes. However, the complex nature of this class of compounds coupled with the lack of commercially feasible methods of synthesis have prevented a real breakthrough.

The increased demand of perfumery materials has pressurized the industry to look for, and accept, synthetic equivalents of the natural products, despite the odour differences between the two. This has led to the commercial production of materials such as geraniol, nerol, citronellol, menthol, citral and the ionones whose isolation from natural oils has since become far less economical. These materials have been produced from heavy organic chemicals (acetylene and acetone) and by transformation of natural monoterpenes which are available in large quantities (α- and β-pinene). There is no counterpart of the versatile monoterpene myrcene in sesquiterpene chemistry and an advancement comparable to monoterpenes may appear to be unlikely in the near future. But it is interesting to note that an increasing number of speciality chemicals are already appearing on the perfumery scene. In our opinion many perfumery houses use sesquiterpene compounds in limited amounts in various formulations which are often closely-guarded commercial secrets.

During the last 15 years the industry has had benefit from the extensive research on monoterpenes and perhaps now it is time to explore the sesquiterpene field with the same seriousness. It is neither the purpose nor the scope of this paper to deal with the systematic description of sesquiterpenes which have been isolated from essential oils and characterized to-date. Instead, we intend to concentrate on the use and chemistry of those sesquiterpenes and their derivatives which occur in commercially important oils and which have already made an impact on the perfumery industry. Many of these sesquiterpenoid compounds are commercially available.

It will be pertinent at this stage to mention that the biogenesis of most sesquiterpenoids in essential oil yielding plants is considered to be based on the cyclization of *trans-trans* and *cis-trans*-farnesyl pyrophosphate isomers which in turn are produced from mevalonic acid (1, 2). These biogenetic transformations give rise to some important sesquiterpene groups which will be discussed here (*Fig. 1*).

The acyclic olefins α- and β-farnesenes possess interesting odours, which are generally not known to perfumers because of commercial non-availability. The latter compound occurs in many essential oils such as lavender, pepper, hops, copaiba, ylang-ylang and ginger oil (3–5). Peyron, Benezet and

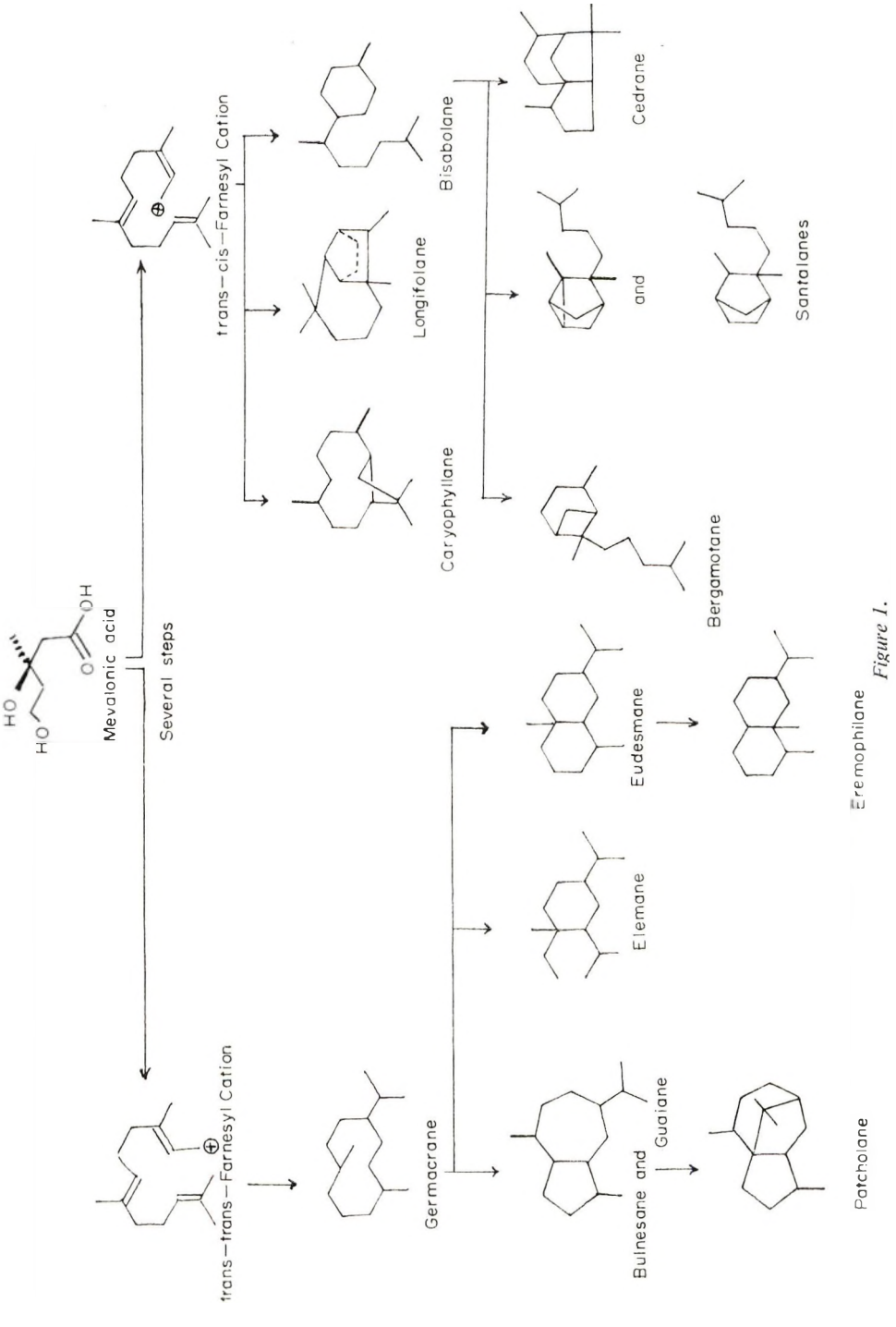

HO
HO
OH
O
Mevalonic acid
Several steps
trans—trans—Farnesyl Cation
trans—cis—Farnesyl Cation
Germacrane
Bulnesane and Guaiane
Elemane
Eudesmane
Caryophyllane
Longifolane
Bisabolane
Bergamotane
and
Cedrane
Santalanes
Eremophilane
Patcholane

Figure 1.

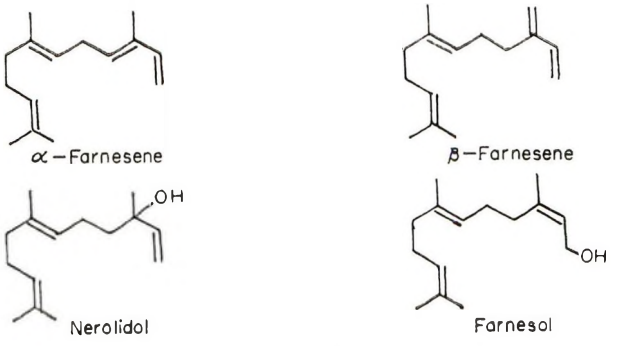


Figure 2.

Garnere (6) found β-farnesene to be one of the most important constituents of lavender oil. The α-isomer has not been reported to occur in nature but has been synthesized by dehydration of nerolidol or farnesol (7, 8).

The isomeric alcohols nerolidol and farnesol are important perfumery chemicals. Nerolidol was first isolated from neroli oil (9) and since has been found to occur in several other essential oils, e.g. jasmine, citronella, pepper and cabreuva oil (10–12). According to Arctander (13) it has a mild and woody-floral, slightly green odour with excellent tenacity, and good blending and fixative properties. With the availability of synthetic nerolidol, a drastic reduction in its price has been observed. The synthesis which is based on cheap raw materials such as acetylene and acetone, makes nerolidol a feasible entry into the sesquiterpene field from a commercial viewpoint (*Fig. 3*).

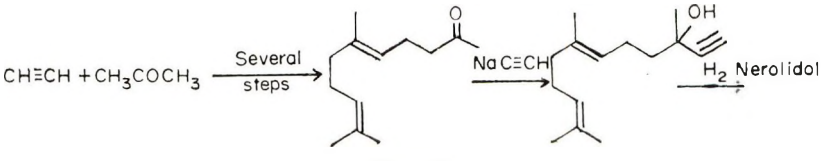


Figure 3.

The chemical possibilities of converting nerolidol into various sesquiterpenes are enormous. Some work has already been carried out on the isomerization to farnesol (15) and cyclization to an interesting range of cyclci terpenes (16). However, unlike nature, the product selectivity in these cyclizations is low, but further research in this area should prove to be extremely useful.

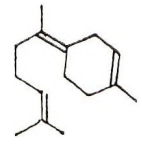
Farnesol occurs in several essential oils, e.g. oils of ambrette seed, neroli, rose, cyclamen, jasmine etc. (17, 18). It has a delicate sweet oily odour developing into a floral fresh-green note and finds uses in floral, oriental and chypre fragrances (13). Biogenetically speaking, this alcohol occupies a very significant position in sesquiterpene chemistry since it has been established that farnesyl pyrophosphate is the *in vivo* precursor of a variety of sesquiterpenes. The acid catalysed cyclization of farnesol, in a manner similar to nerolidol, gives a complex mixture of cyclic products among which bisabolane and cadinane structures are the most prominent (16). Several syntheses of farnesol have been reported in the literature but none of these is commercially attractive. Isomerization of nerolidol to farnesol in acceptable yields should have a significant effect on the usage of this alcohol which is presently restricted because of its high price.

Recently, Stevens, Ludin and Teranishi (19a), isolated and characterized two isomeric aldehydes α- and β-sinesal belonging to the farnesane group which occur in chinese orange oil (19b, c and d). Both aldehydes exist in the all *trans*- form and have attracted the attention of flavourists and perfumers and several commercial syntheses have been accomplished.

Figure 4.

Several members of the bisabolane group of sesquiterpenes occur in many commercially important essential oils. The parent hydrocarbon bisabolene can have several isomers with regard to the position of double bonds, but the γ-bisabolene is the most important one and occurs in oil of bisabol myrrh, lemon, lime, bergamot, cardamom, sandalwood, etc. It is also obtained by dehydration of nerolidol during the cyclization (16). It is interesting perfumery chemical with a pleasant, warm, sweet-spicy-balsamic odour which makes it invaluable in the reconstitution of essential oils and as a perfumery material in its own right. It is a vital part of the oriental, opopanax, chypre and novelty fragrances (13).

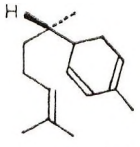
The hydrocarbons zingiberene and ar-curcumene constitute the major part of the sesquiterpene fraction of the oil of *Zingiber officinale* (ginger oil).



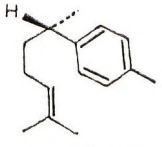
γ- Bisabolene

Figure 5.

Zingiberene has a warm, woody-spicy tenacious odour with deep sweetness. Its structure as shown was assigned by Eischemosher and Schinz and also by Mills (20, 21). Several syntheses of (±) zingiberene have been reported but the most interesting approach is based on citronellal and can lead to the optically active hydrocarbon (22, 23). ar-Curcumene has been synthesized by Honwad and Rao (24, 25) but has an uninteresting odour.



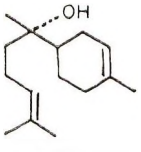
Zingiberene



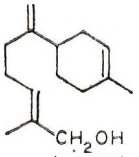
ar-Curcumene

Figure 6.

α-Bisabolol occurs in oil of camomile (26, 27) and the racemic form is prepared by acid-catalysed cyclization of nerolidol (16). It can be used as a fixative and blender in many formulations with interesting results. Another interesting member of the group is a primary allylic alcohol lanceol which occurs in the oil of *Santalum lanceolatum* (21, 28).



α- Bisabolol

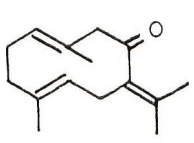


Lanceol

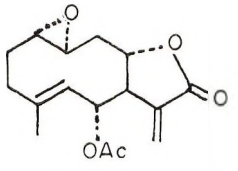
Figure 7.

Germacranes, a group of 10-membered ring compounds, were postulated by Ruzicka, Eschenmoser and Heusser (29) as intermediates of crucial significance in the biogenesis of the elemane-, eudesmane-, and guaiane-type sesquiterpenoids from farnesyl pyrophosphate (29). However, no member of this group was actually isolated and characterized until germacrone and

pyrethrosine were characterized by Ognyanov *et al* and Barton and de Mayo respectively in 1957 (30, 31). Since then several other compounds belonging to this group have been isolated and characterized by careful work-up. Sorm has recently published an excellent review of the chemistry of germacranes (32).



Germacrone

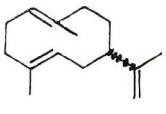


Pyrethrosine

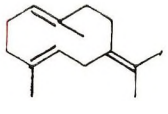
Figure 8.

Germacrone was isolated from oil of *Geranium macrorhizum* in 50% yield (30). It has a faint, sweet-woody, somewhat herbaceous odour of extraordinary tenacity. Although the ketone is not offered as a pure chemical, the oils rich in this material have been suggested to be useful as a modifying fixative in ambre, chypre, and mossy fragrance types. The pure ketone itself blends well with the ionones, geranium, ambergris, vetiver, and cedarwood types (13).

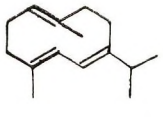
The hydrocarbons germacrene A, B, C and D offer interesting synthetic possibilities of obtaining various well-known sesquiterpenes which are crucially important in simulated essential oils.



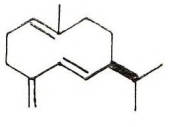
Germacrene – A



Germacrene – B



Germacrene – C



Germacrene – D

Figure 9.

A variety of acid-catalysed and photochemical transformations to systems such as eudesmanes, copaene, ylangane, bourbonane (present in the essential oil of geranium bourbon), cadinane, and muurolane are known and illustrate the biogenetic significance of this group (33).

The elemane group consists of a number of hydrocarbons and oxygenated derivatives including lactones and occur widely in many essential oils. These compounds are closely related to eudesmanes and germacranes, and it is generally supposed that many members are probably artefacts of

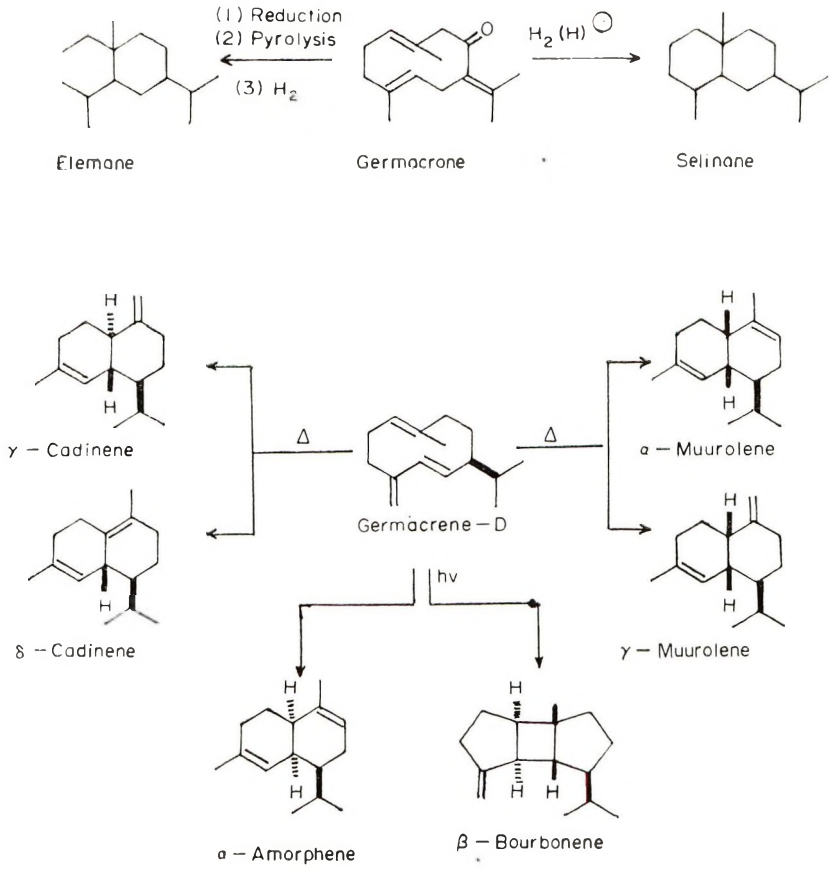


Figure 10.

the latter. The hydrocarbons α- and β-elemene occur in sweet-flag oil (34) and gurjun balsam (35) respectively, but have found no specific use in perfumery so far. The alcohol elemol found in Java citronella oil and elemi oil has the configuration as indicated and affords α-elemene on dehydration (36). Elemol has a faint, sweet-woody odour with an almost floral undertone, and the essential oil fractions rich in this alcohol are used as fixatives, blenders or modifiers in soap perfumery. The total synthesis of elemol was accomplished by Corey and Broger (37).

The eudesmane group is probably the largest of the sesquiterpene groups and can be considered to have been derived from farnesyl pyrophosphate cyclization involving a germacrane skeleton as an intermediate. The hydrocarbons α- and β-selinene are found in Bois de Rose and celery

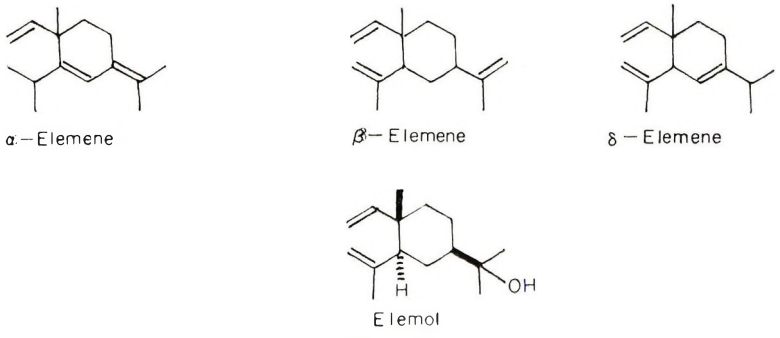


Figure 11.

seed oil (38, 39), whereas the alcohol β-eudesmol occurs in eucalyptus oil (40). α-Selinene has a mild, sweet-woody, and slightly peppery odour, the β-isomer has a similar but warmer and more herbaceous odour (13). β-Eudesmol which finds some use as a fixative offers a delicate, sweet-woody and warm odour. The corresponding acetate ester is also interesting for its linalyl acetate type odour combined with much better tenacity. Both β-

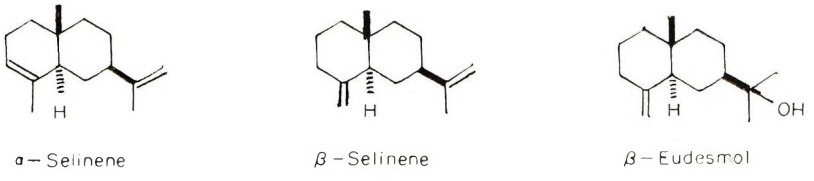


Figure 12.

selinene and β-eudesmol have been synthesized by Marshall, Pike and Carroll (41). Cyperene and α-cyperone also offer interesting structural systems, the latter being the main constituent of the oil of *Cyperus rotandus* (42).

Penfold, Robinson and Simonsen (44) speculated a 1,2-alkyl shift in eudesmanes to generate the commercially important group of compounds known as eremophilanes (44). Eremophilene is present in a number of essential oils and has been a subject of several publications and a recent review by Pinder (43). The ketone Eremophilone is a constituent of *Eremophilla mitchelli* (44).

The most commercially important members of the group are valencene, nootkatene, and nootkatone. Valencene has been isolated from orange juice oil and orange peel oil (45), and its structure and absolute configuration has been related to nootkatene, a *t*-butyl chromate oxidation product of

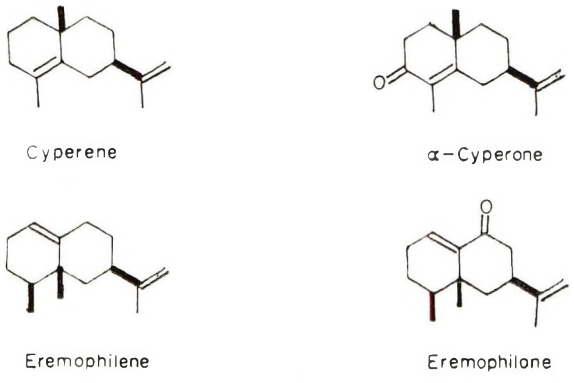


Figure 13.

valencene. Nootkatone itself is an important flavour chemical isolated from grapefruit oil (46). Nootkatene or dehydrovalencene is readily obtainable from wood of *Chamaecyparis nootkatensis* by steam distillation and can be converted in high yield into nootkatone by hydrochlorination followed by oxidation (47). Therefore, the commercial importance of valencene and nootkatene lies in being readily available starting materials for a convenient synthesis of nootkatone. Nootkatone has an extremely powerful, sweet and citrusy odour of good tenacity and hence in addition to its well established use in flavour, it could undoubtedly find use in certain perfume formulations. Its further detection in other oils such as bergamot, lemon, lime, and tangerine emphasizes its importance in flavour and perfumery (45).

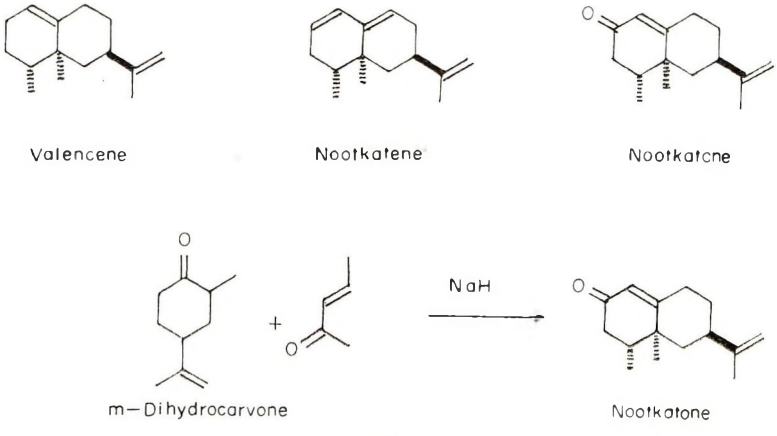


Figure 14.

Several stereospecific syntheses of (±)-nootkatone have been reported in the literature. Pinder and Odom (49) annelated *m*-dihydrocarvone with *trans*-3-pent-en-2-one to obtain nootkatone, which was also synthesized by Marshal and Ruden by a multistep synthesis (50).

A recent patent describes the following synthesis (51).

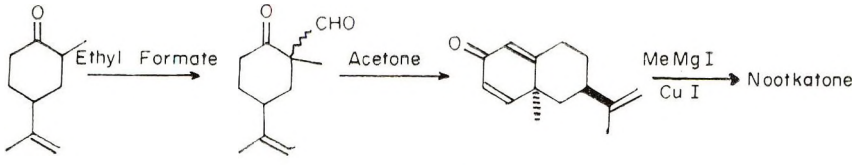
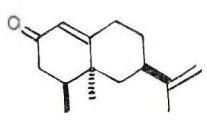


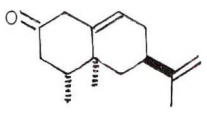
Figure 15.

Nootkatone has also been the subject of detailed sensory properties. Ohloff and Giersch (52) studied the relationship between odour and structure by comparing the odour and taste of various nootkatone isomers and their derivatives. It was found that those compounds with a fruity odour have a bitter taste, whereas those which are devoid of fruity smell have no taste. Furthermore, the double bond remotely situated from the carbonyl function is of special importance in regard to the odour and taste. Stevens, Guadagui and Stern (53) and Teranishi (54) also arrived at similar conclusions, but add that nootkatone isomers have different odour qualities but have only small differences in potencies.

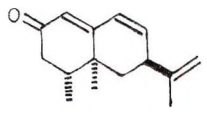
The compounds belonging to vetispirane and tricyclovetivane are derived mainly from the essential oil of *Vetiveria zizanoides*, a perennial grass which grows wild in India, Ceylon, Burma, Reunion Island, and several other countries. The oil, which has been used in perfumery since antiquity, consists mianly of sesquiterpenes. These sesquiterpenes are α-vetivone (55), β-vetivone (56), tricyclovetivenol or khusimol (57), bicyclovetivenol (58), and vetivenyl acetates. Originally these compounds were assigned wrong structures which have been refuted only recently and the revised structures are as shown below. α- and β-Vetivones are used in perfumery as a mixture derived from the ketone fraction of vetiver oil. They possess an odour which is very much reminiscent of the parent oil but more tenacious. These ketones can be a valuable part of oriental type formulations (13). The chemistry of α-vetivone is closely related to that of nootkatone and hence is also known as isonootkatone. Due to this relationship with nootkatone it would be surprising if we do not see a synthetic material commercially available in the near future. Depending upon their origin and



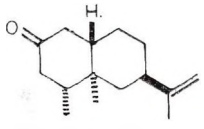
4 - Epinootkatone
Fruity, woody, bitter



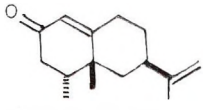
β-γ-Nootkatone
Grapefruity – bitter



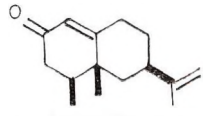
Nardostachone
Fruity – bitter



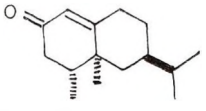
1,10 -Dihydronootkatone
Fruity-bitter



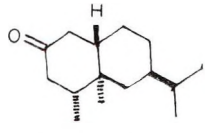
iso - Nootkatone
Woody



4-epi-isonootkatone
Woody

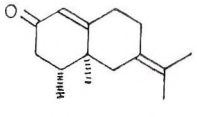


11,12-Dihydronootkatone
floral-woody

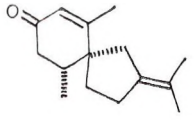


Tetrahydronootkatone
floral-woody

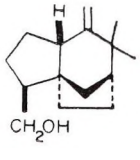
Figure 16.



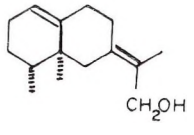
α-Vetivone



β-Vetivone



Tricyclovetivenol (Khusimol)



Bicyclovetivenol

Figure 17.

quality, vetiver oils contain 45–65% free sesquiterpene alcohols bicyclo- and tricyclovetivenols. The commercial product is a mixture of these two vetivenols and has a warm, sweet, mildly earthy-balsamic and extremely tenacious odour. These alcohols blend well with ionones, styrax, sandalwood and various materials for oriental and woody bases or perfumes (13). The corresponding aldehydes are known to have an olibanum type odour. The mixed acetates obtained by the acetylation of the above alcohols or by isolation from essential oil are sold under several trade names. The sweet-dry, fresh-woody odour with excellent tenacity allows its use in all types of perfumes (13).

Longifolene, a hydrocarbon belonging to the longifolane group, is one of the few sesquiterpenes commercially available in quantity. Much interest has been shown by the industry in the new materials that chemical investigation into longifolene chemistry has presented to the perfumer.

Longifolene was first isolated by Simonsen (59) from *Pinus longifolia* and the search for commercial uses for the hydrocarbon extends back 50 years. The structure was established by Moffett (60) and Ourisson (61) and commercial exploitation has followed this breakthrough. The structure of longifolene has been confirmed by a total synthesis (62) but such syntheses are of academic interest only.

Two simple longifolene derivatives are on the perfumer's shelf at the moment: acetyl longifolene and hydroxymethyl longifolene. Acetyl longifolene (63) is prepared by the Friedel–Crafts reaction and has a woody-musky ambergris odour reminiscent of acetyl cedrene.

Figure 18.

The Prins reaction has been of use in the production of perfumery chemicals from monoterpenes (*Nopol*, *Patchenol*) and application of this reaction to longifolene produces ω-hydroxymethyl longifolene (64, 65). This alcohol is of use in perfumery.

The simple methods of longifolene oxidation yield complex mixtures with sesquiterpene acids predominating (66). Direct oxidation of longifolene has not been of great commercial interest. Formylation reactions have been

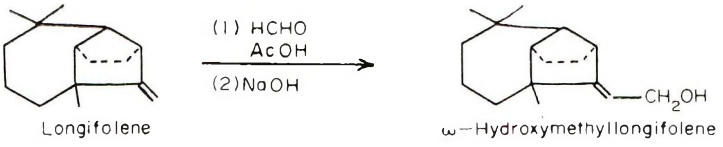


Figure 19.

of recent interest in the production of new monoterpene perfumery chemicals (67–69), e.g. dihydromyrcene cyclic esters. Application of these reaction conditions to longifolene produces longibornan-9-ol formed by rearrangement and transannular hydride shift (70). A recent patent claims this formate to be of value in perfumery (71).

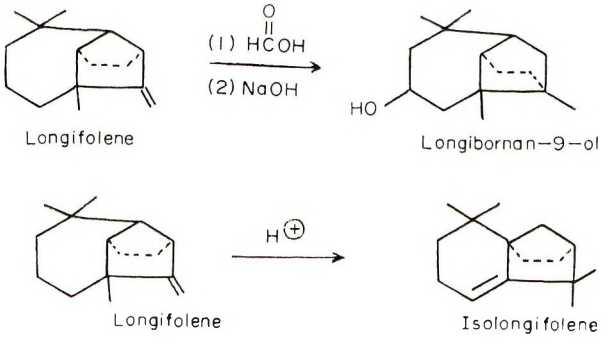


Figure 20.

Early attempts at longifolene acetoxylation did not give good yields of acetates but an isomer of longifolene was produced called isolongifolene (72). The structure of isolongifolene was established by Ranganathan *et al.* (73) who later completed a total synthesis of the hydrocarbon (74). Isolongifolene has proved to be of more commercial interest than longifolene as simple methods of oxidation yield non-acidic products.

If longifolene or isolongifolene are treated with zinc chloride at high temperatures then 1,1-dimethyl-7-isopropyltetralin is formed (75). Acetylation of this tetralin gives the methyl ketones; these are said to have a fine although weak musk odour. The aldehydes have a stronger musk odour but the propionyl compound is odourless (75).

Epoxidation of isolongifolene with peracids yields the α-epoxide (76). This epoxide is of little perfumery interest but rearrangement of the epoxide produces the saturated ketone 8-oxo-7-β-H-isolongifolane which has a desirable woody odour and has found use in perfumery. Epimerization of

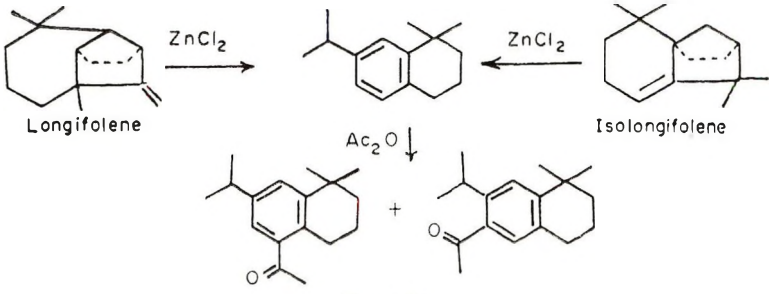


Figure 21.

this ketone to the 7(α)H derivative is simple and this ketone is also of perfumery use as it possesses a sweet-woody odour.

The rearrangement of isolongifolene epoxide has been reported (77–79) to yield two β, γ-unsaturated alcohols. No patents have been published on the rearrangement of the epoxide; under most reaction conditions these alcohols are formed in less than 50% yield, the main product is 8-oxo-7-β-H-isolongifolane (*Fig. 22*).

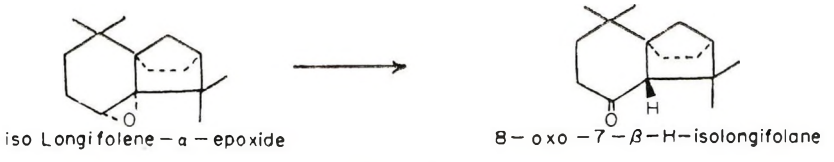


Figure 22.

The sterochemistry of isolongifolene is a subject of academic discussion (76–79) and it is still not known beyond all doubt if the epoxide is, in fact, α- or β. In the author's opinion, the α-structure is the more probable (80).

Sodium dichromate oxidation of isolongifolene yields a complex mixture of ketones with a woody, vetiver type of odour. This mixture has found use in perfumery (81).

Allylic oxidation of isolongifolene with tertiary butyl peracetate gives a mixture of 9α- and β-acetoxy-isolongifolene. This has a woody, vertiveryl acetate odour and has found use in perfumery (82) (*Fig. 23*).

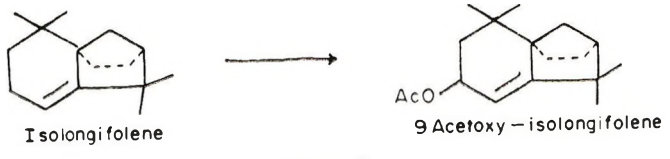


Figure 23.

The rapid commercial exploitation of longifolene in the last few years illustrates the interest shown by perfumers in new sesquiterpene products. With the considerable academic and commercial interest being shown in this hydrocarbon, further developments of interest to perfumers may well be expected.

Sandalwood oil is much used in perfumery and has a large production; its odour is too well known to be described in this paper. The main constituents of the oil are known (83); α-santalene had a sweet-woody odour of excellent tenacity; β-santalene has a similar odour but is said to be less sweet than the α-isomer. α-Santalol is considered to have the refined sweet-woody, tenacious sandalwood odour. Impure α-santalol isolated by distillation from sandalwood oil is the santalol of commerce. β-Santalol is said to have a similar odour but it occurs to a smaller extent in sandalwood oil and samples may have been contaminated with the α-isomer. Perfumery opinion is that the α-isomer is the preferred isomer (*Fig. 24*).

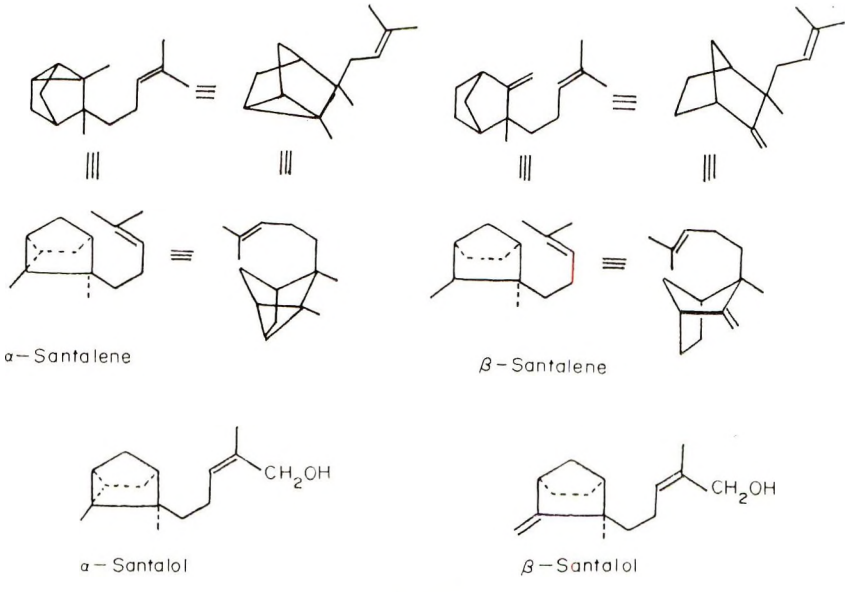


Figure 24.

The santalyl structure is related to the structure of longifolene; if it were possible to open the seven-membered ring of longifolene one would have a santalene structure. The sterochemistry is such that the opposite optical isomer to the natural santalene would be produced (*Fig. 25*).

Figure 25.

Sandalwood is a moderately expensive essential oil and its typical bouquet continues to be favoured by the perfumery industry. The search for sandalwood odours have therefore been intense. A number of chemicals with a sandalwood odour have been made. The so-called terpeno-phenols manufactured by the condensation of phenols with camphene followed by hydrogenation (84) have found application in a number of sandalwood bases. These have found a use in the industry but have not depressed the demand for the natural oil.

The last addition to the sandalwood odours is Osyrol (and its homologs), and although this monoterpene is not a direct replacement for α-santalol, this speciality has a fine sandalwood odour and with its good performance in the middle notes it will be of wide interest in the formulation of perfume compounds where the sandalwood character is desired (85) (*Fig. 26*).

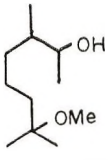


Figure 26.

The commercial synthesis of sesquiterpenes has yet to be achieved but much progress has been made in the academic synthesis of these compounds. Starting from α-bromocamphor French workers were able to synthesize α- and β-santalol in nine steps (86). The reaction sequence is too long for this synthesis to be of commercial interest.

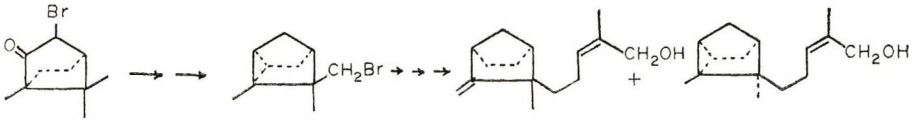


Figure 27.

Canadian workers have devised a route for the synthesis of camphenone. This sesquiterpene is a valuable intermediate for the synthesis of a number of sesquiterpenes and in two steps it may be converted either to α-santalene or β-santalene (87, 88) (*Fig. 28*).

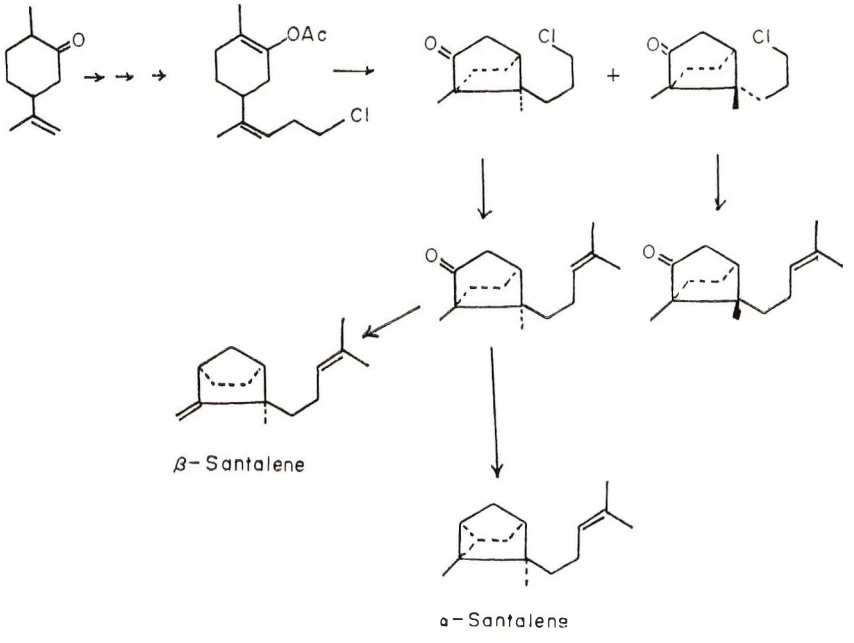


Figure 28.

This synthesis might have been of commercial value but at the key cyclization stage two compounds are produced, one of which gives santalene and the other epi-santalene.

An alternative approach was examined by American workers who synthesized 3-methyl-norcamphor from the Diels–Alder product of methyl cyclopentadiene and ethylene. The construction and addition of the side chain to the camphene structure was more complex and again this synthesis does not offer, at present, any commercial possibility (89).

A more direct synthesis has been described. The key step was the Diels–Alder addition of geraniol to cyclopentadiene; low yields at this stage appear to have discouraged exploitation of this path (90).

The lactonization of camphene-8-carboxylic acid has been reported to yield a lactone with the correct arrangement of functional groups to be a santalene intermediate. Here again the key step produces not only the desired santalene structure but also the epi-santalene structure (91).

As a result of these synthetic studies the odours of a number of santalol derivatives have been reported (89). Dihydro-β-santalol is said to have a sandalwood odour but the α-isomer is said to be much weaker. Tetrahydro-β-santalol has no sandalwood character and has an uninteresting weak woody odour. There is no doubt that the industry would find a synthetic santalol a most welcome addition to the perfumers shelf. It is not possible to say how long it will be before it arrives there.

Cedarwood oil is one of the essential oils whose production exceeds 100 tons/year. The oil is not only of direct use in perfumery; a number of derivatives from the oil have also found a wide use. Although some of these derivatives have been given names in the technical press which would suggest that they are definite chemical entities, many of them are mixtures (e.g. cedrenol) isolated from the oil or the products of reactions on such mixtures (e.g. acetyl cedrene).

Thujopsene and cedrene are the two main sesquiterpene hydrocarbons found in the oil; β-cedrene, β-chamigrene, widdrene, isowiddrene, α-chamigrene, cuprenes and cuparene have been found in smaller quantities (92) (*Fig. 29*).

Cedrol is the main alcohol constituent of the oil; psuedo cedrol, primary cedrol and widderol are also found in the cedarwood oil (92) (*Fig. 30*).

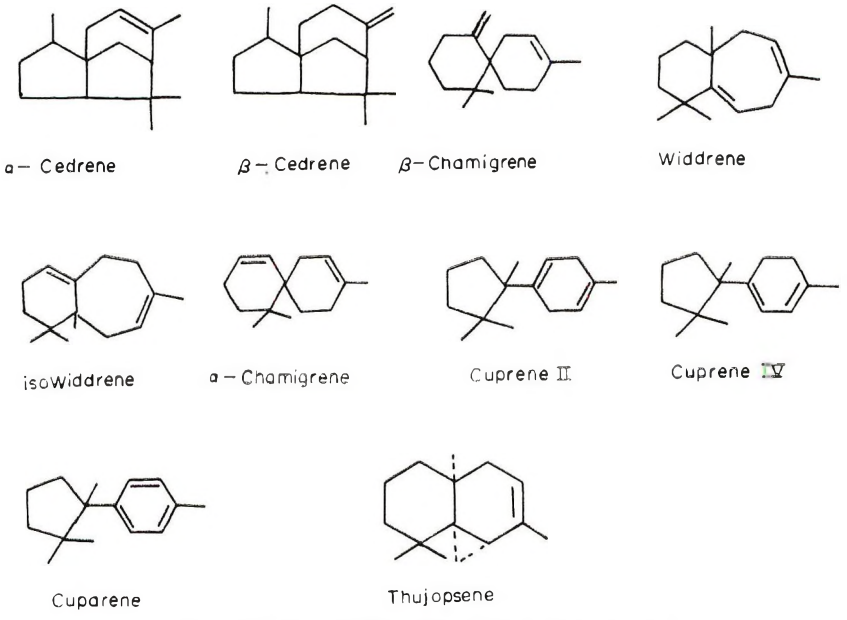
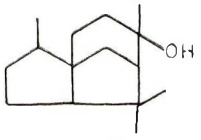
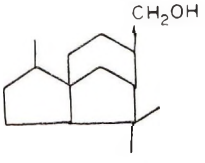


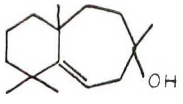
Figure 29. Some hydrocarbons from cedarwood oil.



Cedrol



Primary cedrol



Widderol

Figure 30.

Distillation yields two main fractions, the hydrocarbon fraction is the so-called 'Cedrene' of commerce, impure cedrol is obtained as the alcohol cut. Pure cedrol can be obtained by recrystallization of the alcohol fractions and is used in perfumery. Cedrenol is a mixture of cedrol and its isomers, widdrol and some ketonic compounds. Acetylation of this mixture yields cedrenyl acetate. Cedryl acetate is also made by esterification of the alcohol and a number of qualities are sold; they range from the pure recrystallized acetate to acetate mixtures containing almost 50% hydrocarbons.

Epoxy-cedrene has been manufactured by epoxidation of cedrene-rich hydrocarbon fractions followed by recrystallization (*Fig. 31*).

One of the most interesting cedarwood derivatives is the complex mixture of ketones known as 'acetyl cedrene' obtained by acetylation of the hydrocarbon fraction. This has a woody, warm-ambergris and musky odour (94), and is sold under a number of trade names. A number of investigations have been made to find the odour constituents of the mixture. The hydrocarbon cut used in the manufacture has two main components, cedrene and thujopsene. The acetylation product of the purified cedrene is said to have little odour.

The reaction of thujopsene under these conditions is much more complex. With acid catalysts thujopsene isomerizes into a large number of hydrocarbons and it is thought that this isomerization precedes the acetylation step in the production of acetyl cedrene.

At least seven $C_{17}H_{26}O$ ketones have been observed in the acetylation mixture but the structures of only two are known and these account for

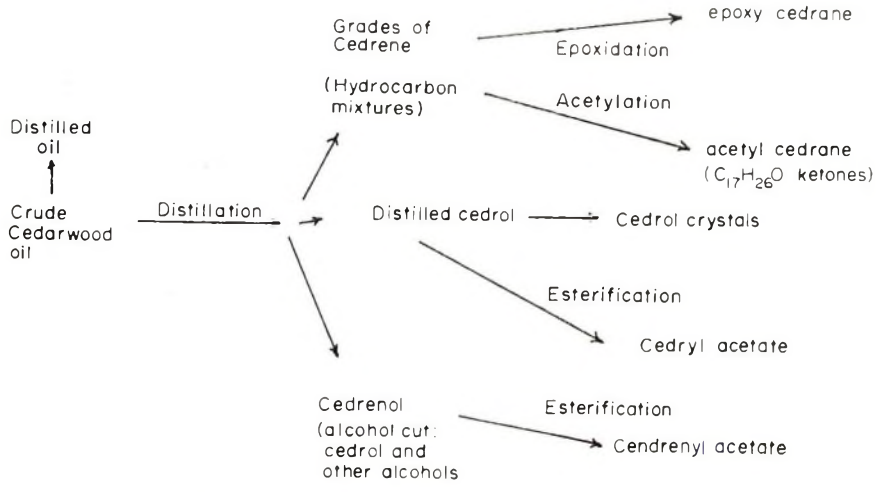


Figure 31. Perfumery materials from cedarwood oil (93).

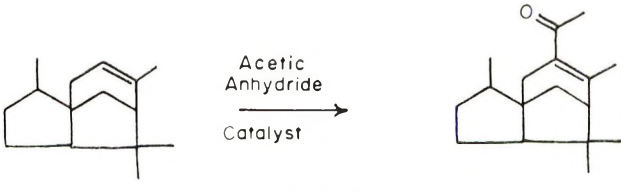


Figure 32.

some 60% of the reaction product. The major ketone is thought to be the active odour constituent of acetyl cedrene. It is said to have a powerful woody, musk-ambergris odour far greater in intensity than any of the other isomers. This acetyl thujopsene isomer has an interesting odour–structure relationship since, although it has a strong musk odour, it has no aromatic ring as have most other tricyclic musks possessing an acetyl group.

Patchouli oil has wide application in the perfumery industry and more extensive use would be made of this essential oil if it were in greater supply. Much effort has been devoted to the analysis of the oil and a number of constituents have been identified. No single compound has the total patchouli odour and any effort to formulate a reconstructed patchouli oil will require the synthesis of a number of sesquiterpene alcohols, ketones and hydrocarbons.

The main alcohol constituent of patchouli oil is patchouli alcohol. A synthesis of this alcohol from homocamphor has been reported (101) but

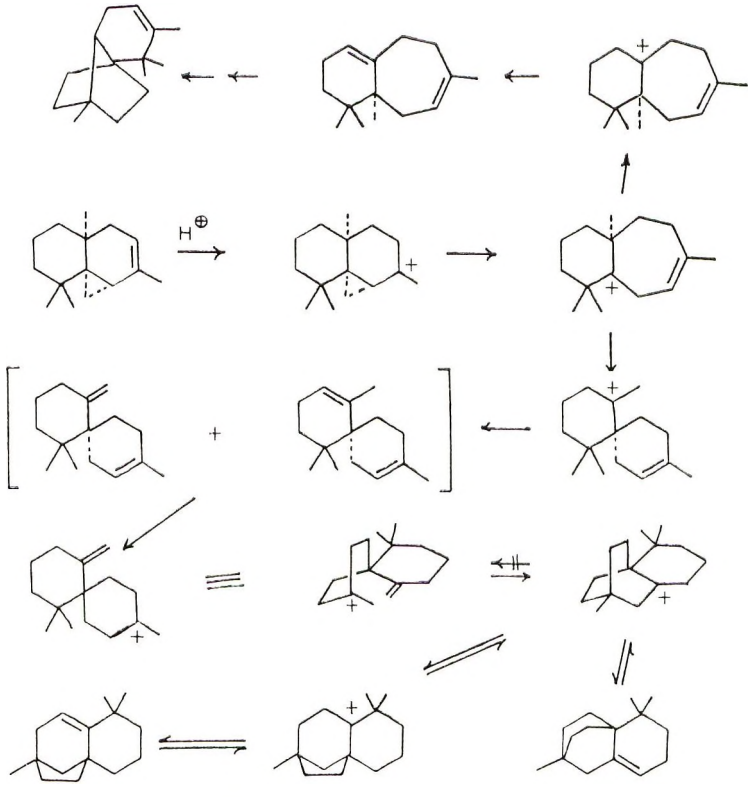


Figure 33. Products of acid isomerization of thujopsene (95).

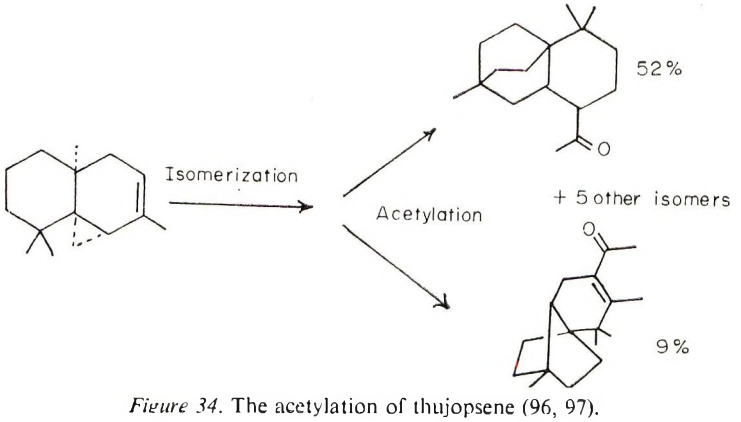


Figure 34. The acetylation of thujopsene (96, 97).

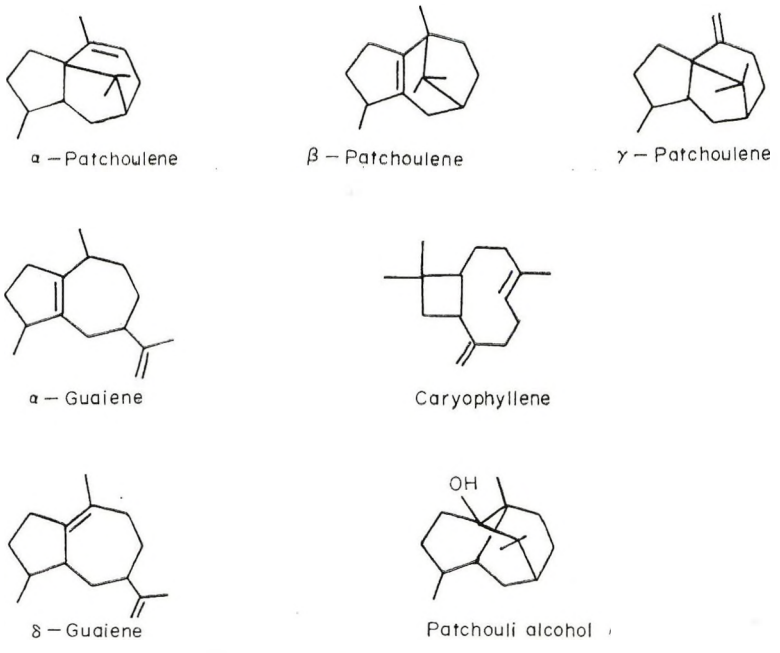


Figure 35. Some constituents of patchouli oil.

the synthesis involves a large number of steps. β-Patchoulene is first synthesized and then converted to the α-patchoulene structure and hence patchouli alcohol. No commercial synthesis of this alcohol appears possible at the present.

Patchouli oil is interesting as it is one of the few oils obtained by steam distillation and is found to contain sesquiterpene alkaloids (102). These alkaloids are formed from the sesquiterpene structures of two hydrocarbons found in patchouli oil, β-patchoulene and α-gauiene; thus they have been called patchoulipyridine and epiguaipyridine. The structures of these products, present in the oil to the extent of 0·1% were determined by physical organic techniques (102) and confirmed by the synthesis of patchoulipyridine and dihydro-epiguaipyridine. Patchoulipyridine was synthesized from β-patchoulene by the action of hydrazoic acid and dehydrogenation of the resulting product. Dihydro-α-guaiene was synthesized (102) from guaiol and subjected to the same reaction steps to yield dihydro-epiguaipyridine.

No odour descriptions have been given for these two alkaloids. An alternative synthesis (103) of patchoulipyridine has been developed by

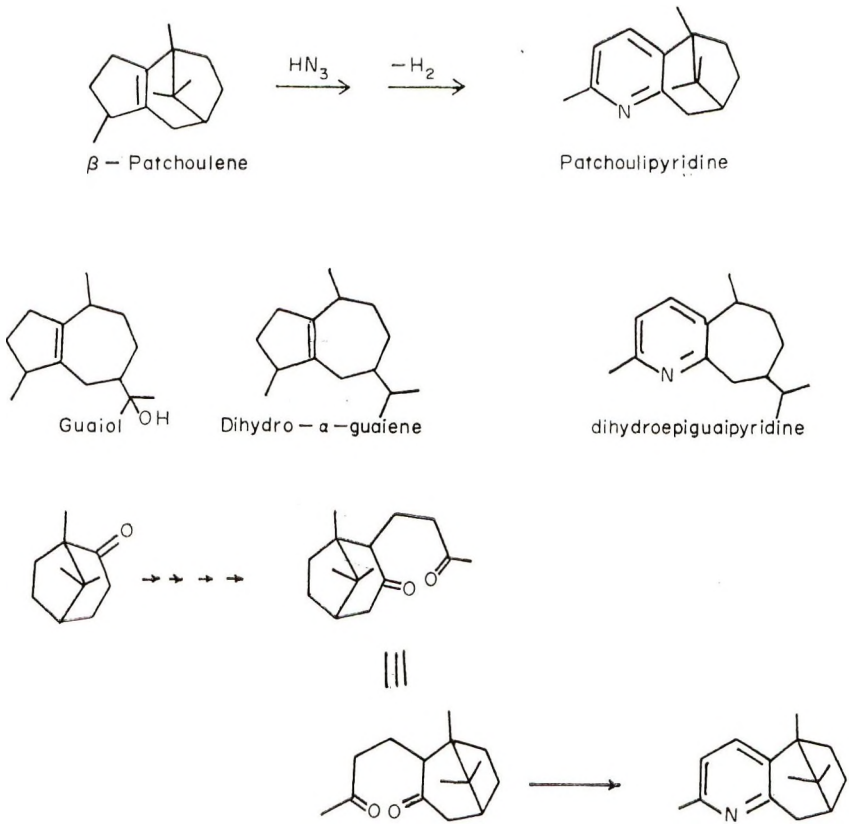


Figure 36

French workers who started from homocamphor. This was converted in a number of steps to a diketone which was then transferred into the pyridine.

Some of the hydrocarbons found in guaiacwood oil have also been found in patchouli oil (104). The main constituents of guaiacwood oil are the two sesquiterpene alcohols guiaol and bulnesol. Treatment of these alcohols with a small quantity (0·01 M) of sulphuric acid produces a number of the hydrocarbons found in patchouli oil. These are obtained as a mixture and isolation of the desired hydrocarbons is difficult (see *Fig. 37*).

A total synthesis (105) of guaiol has been reported but as guaiacwood oil is one of the cheaper sesquiterpene containing essential oils, this work appears to be of academic interest only.

Treatment of guaiol with sulphuric acid, para-toluenesulphonic acid or iodine yields a cyclic ether guaioxide (*Fig. 38*). This ether has been claimed

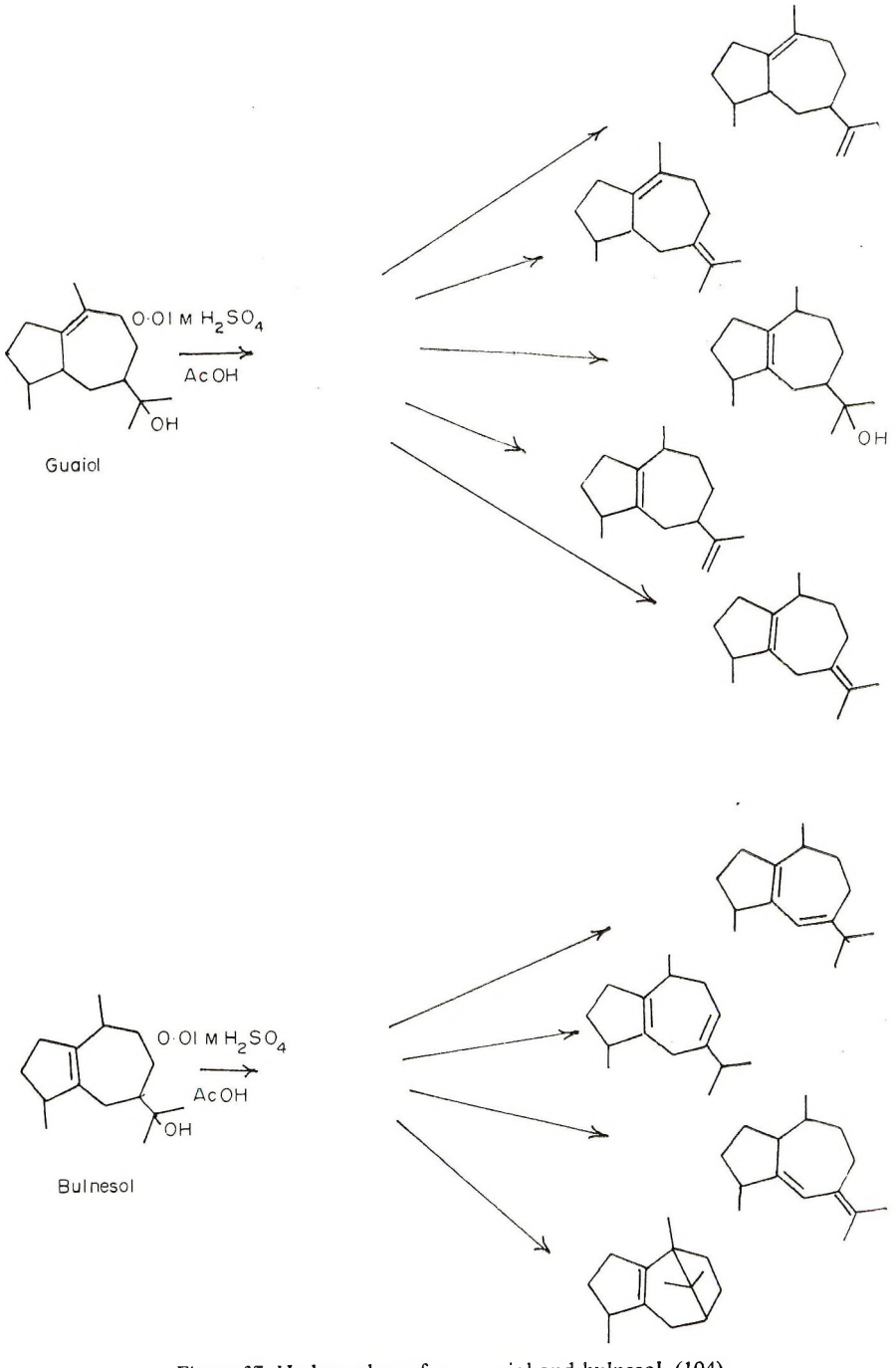
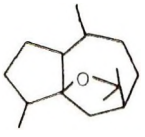
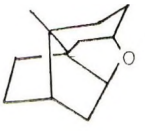


Figure 37. Hydrocarbons from guaiol and bulnesol. (104).

to be of value in perfumery (106). It has a distinctive odour of the warm vetiver type with a warm dry spicy note which is reminiscent of black pepper oil. The cyclic ether has also been reported in guaiacwood oil. A cyclic ether has been isolated from sandalwood oil (107), and it is possible that sesquiterpene ethers will be found to be of some considerable value in perfumery.



Guaioxide



Sandalwood ether

Figure 38

In conclusion it can be said that sesquiterpenes offer a great challenge to the Organic Chemist because of their structural complexity. They are of crucial importance to the perfumery industry as they occur widely in essential oils and individual chemicals offer a wide spectrum of interesting odour types. Therefore, any advancement in the difficult problems of skeletal construction and stereochemical control necessary for such syntheses would have a significant impact on the future of the industry. Undoubtedly during the recent years many new and elegant methods of synthesis have been introduced but unfortunately the majority are of academic interest only. However, one hopes that, in addition to this progress, a better understanding of enzymatic reactions coupled with their commercial exploitation may provide an answer to some of the problems.

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REFERENCES

(1) Parker, W., Roberts, J. S. and Ramage, R. *Quart. Rev.* **21** 331 (1967). and references therein.
(2) Popjak, G. and Cornforth, J. W. *J. Biochem.* **101** 553 (1966).
(3) Sorm, F., Leziva, J. M., Arnold, Z. and Pliva, J. *Collect. Czech. Chem. Commun.* **14** 699 (1950).
(4) Sorm, F. and Arient, J. *Collect. Czech. Chem. Commun.* **15** 175 (1950).
(5) Sorm, F., Zaoral, M. and Herout, V. *Collect. Czech. Chem. Commun.* **16** 626 (1951).
(6) Peyron, L., Benezet, L. and Garnere, J. *Bull. Soc. Chim. Fr.* (8), 3038 (1967).
(7) Naves, Y. *Helv. Chim. Acta,* **49** 1029 (1966).
(8) Brieger, G. *J. Org. Chem.* **32** 3720 (1967).
(9) Hesse, A. and Zeitschel, O. *J. Prakt. Chem.* (ii) **66** 504 (1902).
(10) Katsuragi, H. *Koryo* No. 22 23 (1952).
(11) Calveano, Maria. *Essenz Deriv. Agrum.* **36** (4) 237 (1966).

(12) Lewis, Y. S., Nanbudiri, E. S. and Krishnamurthy, *N. Perfum. Essent. Oil Rec.* **60** 259 (1969).
(13) Arctander, S. *Perfume and flavour chemicals Vols I and II,* (1969) (published by the author, New Jersey, USA).
(14) *British Patent No. 213,250.*
(15) Nazarov, I. N., Gusev, B. P. and Gunar, V. I. *Izv. Akad. Nauk SSSR Otd. Khim. Nauk* 1267 (1957) (CA 52:6150h).
(16) Gutsche, C. D., Maycock, J. R. and Chang, C. T. *Tetrahedron* **24** 859 (1968).
(17) *German Patent No.* 149 603.
(18) Calveano, Maria. *Essenz Deriv. Agrum.* **33** (1) 5 (1963).
(19a) Stevens, K. L., Lundin, R. E. and Teranishi, R. *J. Org. Chem.* **30** 1690 (1965).
(19b) Buechi, G. and Wuest, H. *Helv. Chim. Acta* **50** (8) 2440 (1967).
(19c) Bertele, E. and Schudel, P. *Helv. Chim. Acta* **50** (8) (1967).
(19d) Thomas, A. F. *Chem. Commun.* 947 (1967).
(20) Eischenmoser, A. and Schinz, H. *Helv. Chim. Acta* **33** 171 (1950).
(21) Mills, J. A. *J. Chem. Soc.* 4976 (1952).
(22) Mukherji, S. M. and Bhattacharyya, N. K. *J. Amer. Chem. Soc.* **75** 4698 (1953).
(23) Joshi, G. D. and Kulkarni, S. N. *Indian J. Chem.* **3** 91 (1965).
(24) Honwad, V. K. and Rao, A. S. *Curr. Sci.* **34** (18) 534 (1965).
(25) Honwad, V. K. and Rao, A. S. *Tetrahedron* **21** 2593 (1965).
(26) Sorm, F., Zaoral, M. and Heront, V. *Collect. Czech. Chem. Commun.* **18** 116 (1953).
(27) Tyihak, E., Sarkary-Kiss, I. and Mathe, J. *Pharm. Zeutralhalle* **102** (3), 128 (1963) (CA 59 61956).
(28) Penfold, A. R. *J. Proc. Roy. Soc. N.S.W.,* **62** 60 (1928) and **66** 240 (1932).
Murray, A. R. and Birch, A. J. *J. Chem. Soc.* 1888 (1951).
(29) Ruzicka, L., Eschenmoser, A. and Heusser, H. *Experientia* **9** 357 (1953).
(30) Ognajnov, I., Ivanov Verout, D., Horak, M., Pliva, J. and Sorm, F. *Chem. Ind.* (*London*) 820 (1957).
(31) Barton, D. H. R. and Mayo, P. de. *J. Chem. Soc.* 150 (1957).
(32) Sorm, F. *J. Agr. Food Chem.* **19** (6) 1081 (1971).
(33) Yoshihara, K., Ohta, Y., Sakai, T. and Hirose, Y. *Tetrahedron Lett.* 2263 (1969).
(34a) Sorm, F., Herout, V. and Sykora, V. *Collect. Czech. Chem. Commun.* **21** 267 (1956)
(34b) Rao, A. S. and Patil, L. J. *Tetrahedron Lett.* 2273 (1967)
(34c) Vig, O. P., Matta, K. L., Kapur, J. C. and Vig, B. *J. Indian Chem. Soc.* **45** 973 (1968).
(35) Hirose, Y. and Mosikawa, K. *Tetrahedron Lett.* 1799 (1969).
(36) Paknikar, S. K. and Bhattachayya, S. C. *Tetrahedron* **18** 1509 (1962).
(37) Corey, E. J. and Broger, E. A. *Tetrahedron Lett.* 1779 (1969).
(38) Naves, Y. R. *Bull. Soc. Chim. Fr.* 292 (1956); Klyne, W. *J. Chem. Soc.* 3072 (1953).
(39) Schimmel and Co. News, April, 96 (1910).
(40) McQuillin, F. J. and Parrack, J. D. *J. Chem. Soc.* 2973 (1956).
(41) Marshall, J. A., Pike, M. T. and Carrol, R. D. *J. Org. Chem.* **31** 2933 (1966).
(42) Bradfield, A. E., Hedge, B. H., Rao, B. S., Simonsen, J. L. and Gillam, A. E. *J. Chem. Soc.* 667 (1936).
(43) Pinder, A. R. *Perfum. Essent. Oil Rec.* **59** 280 and 645 (1968) and references therein.
(44) Penfold, A. R., Robinson, R. and Simonsen, J. L. *J. Chem. Soc.* 87 (1939).
(45) MacLeod, W. D. *Tetrahedron Lett.* 4779 (1965).
(46) Hunter, G. L. K. and Brogden, W. B. *J. Food Sci.* **30** (1) 876 (1965).
(47) Ohloff, G. *German Patent* 1,948,033 (*Chem. Abst.* **73** 109933Q).
(48) Van Der Gen, A., Van Der Linde, L. M., Wittleveen, J. G. and Boelens, *H. Recueil* **90** 1034 (1971).
(49) Pinder, A. R. and Odom, H. C. *Chem. Commun.* 26 (1969).

(50) Marshall, J. A. and Ruden, R. A. *J. Org. Chem.* **36** (4) 594 (1971).
(51) Bozzato, G., Pesaro, M. and Schudel, P. *British Patent* 1,236,320.
(52) Ohloff, G. and Giersch, W. *Gustation and olfaction* 184 (1971) (Academic Press, London).
(53) Stevens, K. L., Guadagni, D. G. and Stern, D. J. *J. Sci. Food Agr.* **21** 590 (1970).
(54) Teranishi, R. *Gustation and olfaction,* 165 (1971) (Academic Press, London).
(55) Endo, K. and Mayo, P. de. *Chem. Commun.* 89 (1967); Marshall, J. A., Faubl, H. and Warne, T. M. *Chem. Commun.* 753 (1967).
(56) Marshall, J. A. and Johnson, P. C. *J. Amer. Chem. Soc.* **89** 2750 (1967).
(57) Umarani, D. C., Gore, K. G., and Chakravarti, K. K. *Tetrahedron Lett.* 1255 (1966); Kido, F., Uda, H. and Yoshikoshi, A. *Tetrahedron Lett.* 2815 (1967); MacSweeney, D. F., Ramage, R. and Sattar, A. *Tetrahedron Lett.* 557 (1970).
(58) Ruzicka, L., Capato, E. and Huyser, H. W. *Rec. Trav. Chim.* **47** 370 (1928).
(59) Simonsen, J. L. *J. Chem. Soc.* **123** 2642 (1923).
(60) Moffett, R. H. and Rogers, D. *Chem. Ind.* 916 (1953).
(61) Naffa, P. and Ourisson, G. *Chem. Ind.* 918 (1953).
(62) Corey, E. K., Ohno, M., Mitra, B. and Vitakencherry, P. A. *J. Amer. Chem. Soc.* **86** 478 (1964).
(63) Beyler, R. E. and Ourisson, G. *J. Org. Chem.* **30** 2838 (1965).
(64) Nayak, U. R., Santhanakrishnan, T. and Dev, Sukh. *Tetrahedron* **19** 2281 (1963).
(65) *British Patent No.* 1,225,158.
(66) Ourisson, G. *Recherches* **15** 15 (1966).
(67) Hall, J. B., and Lala, L. K. *J. Org. Chem.* **37** 921 (1972).
(68) *British Patent No.* 1,254,198.
(69) Ansari, H. R. *Tetrahedron* in press.
(70) Prahlad, J. R., Nayak, U. R. and Dev, Sukh. *Tetrahedron* **26** 663 (1970).
(71) *German Patent No.* 2,123,104.
(72) Nayak, U. R. and Dev, Sukh. *Tetrahedron* **8** 42 (1960).
(73) Ranganathan, R., Nayak, U. R., Santhanakrishnan, T. S. and Dev, Sukh, *Tetrahedron* **26** 621 (1970).
(74) Sobti, R. R. and Dev, Sukh. *Tetrahedron* **26** 649 (1970).
(75) Kettenes, D. K., Van Leirop, J. B. H., Van der Wal, B. and Sipma, G. *Recueil* 313 (1969).
(76) Santhanakrishnan, T. S., Sobti, R., Nayak, U. R. and Dev, Sukh. *Tetrahedron* **26** 657 (1970).
(77) Eshinasi, E. H., Shaffer, G. W. and Barteles, A. P. *Tetrahedron Lett.* 3523 (1970).
(78) Lala, L. K. and Hall, J. B. *J. Org. Chem.* 35 (1970).
(79) Santhanakrishnan, T. S., Sobti, R. R., Nayak, U. R. and Dev, Sukh. *Tetrahedron* **26** 657 (1970).
(80) Banthorpe, D. V., Curtis, A. J. and Fordham, W. D. *Tetrahedron Lett.* 3865 (1972).
(81) *British Patent No.* 1,197,579.
(82) *British Patent No.* 1,256,535.
(83) *Die Atherischen Ole Vol. III* 325–9, eds E. Gildemeister and Fr. Hoffman (1960) (Academie-Verlag. Berlin).
(84) Demole, E. *Helv. Chim. Acta* **47** 319 (1964).
(85) *British Patent Application,* 52706/71.
(86) Colonge, J., Descotes, G., Bahurel, Y. and Menet, A. *Bull. Soc. Chim. Fr.* 374 (1966).
(87) Hodgson, C. L., MacSweeney, D. F. and Money, T. *Chem. Commun.* 766 (1971).
(88) Hodgson, G. L., MacSweeney, D. F. and Money, T. *Tetrahedron Lett.* 3683 (1972).
(89) Fanta, W. I. and Erman, W. F. *J. Org. Chem.* **37** 1624 (1972).
(90) Brieger, G. *Tetrahedron Lett.* 1949 (1963).
(91) Vaughan, R., Wolinsky, J., Dueltgen, R. R., Grey, S. and Seichter, F. S. *J. Org. Chem.* **35** 400 (1970).

(92) Kitshens, G. C., Dorsky, J. and Kaiser, K. *Givaudanian* **1** 3 (1971).
(93) Kitshens, G. C., Dorsky, J. and Kaiser, K. *Givaudanian* **2** 9 (1971).
(94) Wood, T. F. *Givaudanian* **1** 3 (1970).
(95) Daeniker, H. U., Hochstetler, A. R., Kaiser, K. and Kitshens, L. C. *J. Org. Chem.* **37** 1 (1972).
(96) Daeniker, H. U., Hochstetler, A. R., Kaiser, K. and Kitshens, L. C. *J. Org. Chem.* **37** 6 (1972).
(97) Dauben, W. L., Freidrich, L. E., Oberhansli, P. and Aoyagi, E. I. *J. Org. Chem.* **37** 9 (1972).
(98) Tsubaki, Naoko, Nishimura, Kiichi and Hirose, Yoshio. *Bull Chem. Soc. Japan* 59 **407** (1967).
(99) Wenninger, J. A., Yates, R. L. and Dolinsky, M. *J. Ass. Offic. Anal. Chem.* **50** 1313 (1967).
(100) Wenninger, J. A., Yates, R. L. and Dolinsky, M. *The Toilet Goods Association,* Proceedings of the Scientific Section 44 (1966).
(101) Buchi, G., MacLeod, W. D. and Padilla, J. *J. Amer. Chem. Soc.* **86** 4438 (1964).
(102) Buchi, G., Goldman, I. M. and Mayo, D. W. *J. Amer. Chem. Soc.* **88** 3109 (1966).
(103) Cren, Marie-Claude, Defaye, G. and Fetizon, M. *Bull. Chim. Soc. Fr.* 3020 (1970).
(104) Bates, R. B. and Slagel, R. C. *Chem. Ind.* 1715 (1962).
(105) Marshall, J. A. and Greene, A. E. *J. Org. Chem.* **37** 982 (1972).
(106) *South African Patent,* 6904,445,07.
(107) Kretschmar, H. C., Barneis, Z. and Erman, W. F. *Tetrahedron Lett.* 37 (1970).

SOCIETY OF COSMETIC CHEMISTS OF GREAT BRITAIN

SYMPOSIUM

COSMETIC SCIENCE AND HUMAN SENSES

Papers are invited for a Symposium dealing with Cosmetic Science and the Human Senses which is due to be held on

7 – 9 April, 1975.

The venue has not yet been decided but will most likely be in the North of England.

Please send titles and synopsis of papers to:-

Mr W. W. F. Scotland
c/o Society of Cosmetic Chemists of Great Britain,
56 Kingsway, London WC2, England.

Book review

STRUCTURE AND BONDING. Vol. 12. Progress in Theory. Springer Verlag, Berlin-Heidelberg-New York.

In comparison with three volumes of the series most recently reviewed this is the largest and almost certainly the least directly useful to practical chemists. It is quite appropriately sub-titled 'Progress in Theory'.

The first of six articles reviews revived interest in quantifying the concept of electron interaction in quantum mechanical calculations, notwithstanding the widespread and frequently adequate use of SCF (self consistent field) models. In a series of examples the author evaluates the sensitivity of correlation energy to structural alternatives, considers other physical properties dependent upon electron correlation (EC), and questions the need for all calculations to start with, and be refined from, SCF functions. In his simple (ammonia 'flip' and ethane rotation) examples EC is of little value but equilibrium distance and one-electron properties offer more scope for it. He selectively examines the application of EC perturbation treatments to molecular properties; but whether EC has any physical reality depends upon the absolute significance of the independent particle models chosen.

The importance and remarkable variety of Cu(II) chelates has prompted exceptional crystallographic and spectroscopic interest. The second article substantiates some theoretical models and represents data compiled by the author hopefully allowing others to construct theoretical spectra for novel Cu complexes.

The third, short, paper offers empirical treatment of cation solvation. Evidence is adduced from donor capacity, polarographic reductions, complex formation, ion pair equilibria and absorption spectroscopy.

Fourth is a most readable account of the so-called 'acid salts' of a variety of carboxylic acids, with special reference to hydrogen bond lengths. The author, an experienced crystallographer, draws heavily on X-ray and neutron diffraction evidence in discussing salts of the $M(HX_2)$ and MX.HX types and more complex examples, giving dimensional data and, in most instances, configurational representations. However, those concerned with partially neutralized soaps will be disappointed by the absence of any reference to the acid salts of C_{12}/C_{18} acids. The review is rounded with a generalized and admittedly tentative discussion of hydrogen bond participation, taking some account of IR and NQR spectroscopic evidence. Interest is maintained by the use of short sections each discussing known carboxylate salts in amiable prose free of jargon and free of mathematical physics.

In contrast, the last two papers are abstruse mathematical contributions, using the technique of irreducible tensorial sets. One is exclusively concerned with deriving coupling coefficients in quantum integrals; and the other analyses harmonic situations potentially of value in calculating spectra of adducts, and which may generate orbitals of pictorial significance in understanding the geometry of the complex.

Of the six articles only the fourth is directly readable—and, with additions, might well merit separate republication; the others are definitely only for consultation on demand. In the first four mathematics is used sparingly although it is necessary to be familiar with quantum mechanical jargon; the last two papers, however, are quite indigestible and would have been more at home in a journal of mathematical physics or spectroscopy

G. F. PHILLIPS

J. Soc. Cosmet. Chem. **25** 235–238 (1974)

VIII I.F.S.C.C. International Congress Grosvenor House Hotel, London August 26–30th 1974

COSMETICS—QUALITY AND SAFETY

TENTATIVE PROGRAMME

The provisional listing of papers which have been accepted for the I.F.S.C.C. VIII International Congress and the arrangements for the Scientific sessions are as follows.

For the three days of the Scientific sessions, the morning sessions will be from 0915 to approximately 1200 with a break for coffee and afternoon sessions will be from 1415 to 1700 with a break for tea.

Preprints of the lectures will be available at the time of registration from Sunday, 25 August onwards. All lectures will be simultaneously translated into English, French, German, Spanish and Japanese. The presenters of papers will be allowed 15 minutes for their presentation and there will be approximately 15 minutes for discussion, although groups of discussions will be taken together where papers are presented on similar topics.

A full social programme has been arranged following the opening plenary session on Monday 26th August.

Registration forms and further details may be obtained from: General Secretary, Society of Cosmetic Chemists of Great Britain, 56 Kingsway, London.

TUESDAY, 27 AUGUST 1974

Morning 0915–1200

QUALITY AND ANALYTICAL METHODS

Chairman: F. SERRA (Spain), IFSCC President 1970/71

Co-chairman: MRS H. BUTLER, SCCofGB President 1972/73

'Effect of Phase Inversion Temperature on Surfactant Location during Emulsification' by T. J. Lin* and H. Ohta† (*Shen, Hsidng, Tang, Chemical Co., Taiwan and† Takasago Perfumery Co. Tk Tokyo, Japan).

'Some Considerations on the Detection Methods of Water-Soluble Polymers for Cosmetics' by S. Togano, E. Kadowaki and I. Matsumoto (Shiseido Laboratories, Yokohama, Japan).

'Analytical Aspects of some Classes of Risk Bearing Substances in Cosmetics' by D. H. Liem (Government Food Control Station, Enschede, Netherlands).

'Analytical Procedures for Chlorhexidine in Oral Products' by E. Cropper and P. Platt (Colgate-Palmolive Ltd, Manchester, England).

'Determination of Allantoin in Dentifrices' by P. Platt and S. Heath (Colgate-Palmolive Ltd, Manchester, England).

Afternoon 1415–1700

EFFECTIVENESS OF COSMETICS 1

Chairman: S. J. Strianse (USA), IFSCC President 1963/64

Co-chairman: J. S. Cannell, SCCofGB President 1971/72

'Effect of some Phosphates on Removal of Dental Plaque' by A. Ishida, T. Amo and F. Tokiwa (Household Products Research Laboratory, Tokyo, Japan).

'New Cosmetic with Unique Appearance and Excellent Stability Formulated without the use of Surfactants' by S. Kubo, I. Hirano and J. Yamada (Shiseido Laboratories, Yokohama, Japan).
'Development of a Skin Cream Designed to Reduce Dry and Flaky Skin' by J. D. Middleton (Unilever Research Laboratory, Colworth/Welwyn, England).

'Studies on Damaged Hairs' by F. Miyazawa, F. Nozaki and T. Tamura (Papilio Cosmetics, Tokyo, Japan).

'Hair Breakage—the Scanning Electron Microscope as a Diagnostic Tool' by A. C. Brown and J. A. Swift (Unilever Research Laboratory, Isleworth, England).

WEDNESDAY, 28 August 1974
Morning 0915–1200

EFFECTIVENESS OF COSMETICS II

Chairman: L. I. Conrad (USA), IFSCC President 1967/68

Co-chairman: K. M. Godfrey, SCCofGB Presdient 1970/71

'So-Called Odor-Eliminators, Part II' by E. Paukner, W. Steiner and V. Hudowenz (DROM, Baierbrunn, Germany).

'The Evaluation of a New Sunscreening Agent for Safety and Activity' by L. I. Conrad (Amerchol, New Jersey, USA).

'Advanced Development of Filters Against Solar Radiation' by J. Lukac, V. Krs, J. Sajvera, K. Licha (Levica Narodni Podnik, Prague, Czechoslovakia).

'The Cleaning Power of Dentifrices' by W B. Davis and D. A. Rees (Beecham Products, Brentford, England).

'Nouvelles Données Concernant L'Etude Analytique et Le Controle de L'Activitie D'Extraits Placentaires Humains' by J. Cotte, B. Guillot, Peyron & Mme. Patet (Hopital Debrousse, Lyon, France).

Afternoon 1415–1530

MICROBIAL PROBLEMS AND MANUFACTURING

Chairman: M. G. deNavarre (USA), IFSCC President 1959/60

Co-chairman: D. E. Butterfield, SCCofGB President 1967/68

'The Incidence of Spoilage Bacteria in Water and the Number Required to Initiate Contamination in Shampoos' by S. A. Malcolm and R. C. S. Woodroffe (Unilever Research Laboratory, Isleworth, England).

'Assimilation of Selected Cosmetic Surfactants by Micro-organisms and Determining the Preservative Activity of Different Antimicrobial Agents' by H. Futagoishi and K. Hasunuma (Kanebo Co. Ltd, Kotobukicho, Japan).

'Some Problems in the Large Scale Manufacture of Topical Products' by J. S. D. Lee (ICI Ltd, Pharmaceutical Division, Macclesfield, England).

Afternoon 1555–1700

COSMETIC LEGISLATION

Chairman: S. D. Gershon (USA), IFSCC President 1972/73

Co-chairman: A. W. Middleton, SCCofGB President 1966/67

'Implications of the Enlarged European Community on the Quality and Safety of Cosmetics and Toiletries' by D. M. Gabriel (Unilever Research Laboratory, Isleworth, England).

'Legislation as Protection for the Good Cosmetic and Toiletry Manufacturer' by H. Butler (D.D.D. Company Ltd, Watford, England).

THURSDAY, 29 August 1974

Morning 0915–1200

COSMETIC SAFETY AND TOXICOLOGY I

Chairman: A. E. Desperrois (France), IFSCC President 1965/66

Co-chairman: C. Pugh, SCCofGB President 1968/69

'Adsorption of Zinc Pyrithione onto Hair and Skin' by T. Okumaura, S. Horin, S. Hayashi and F. Tokiwa (Household Products Research Laboratory, Tokyo, Japan).

'Comparative Study of the Action of Surfactants on Some Proteinic Material. Parallel Connections between such "in vitro" data and the Irritation Potential on Human Skin' by F. Balaguer,* J. J. Garcia Dominguez,† J. L. Parra† and C. Pelejero* (*Antonio Puig, S.A.; †Patronato Juan de la Cierva; Barcelona, Spain).

'Percutaneous Absorption of Irgasan DP 300 from Toilet Preparations' by J. G. Black and D. Howes (Unilever Research Laboratory, Colworth/Welwyn, England).

'Percutaneous Absorption of some Anionic Surfactants' by D. Howes (Unilever Research Laboratory, Colworth/Welwyn, England).

'Factors which Determine the Skin Irritation Potential of Soaps and Detergents' by C. Prottey and T. Ferguson (Unilever Research Laboratory, Colworth/Welywn, England).

'Exaggerated Exposure in Topical Irritancy and Sensitization Testing' by N. J. Van Abbe, P. Nicholas and E. Boon (Beecham Products, Leatherhead, England).

Afternoon 1415–1700

COSMETIC SAFETY AND TOXICOLOGY II

Chairman: P. H. Witjens (Netherlands), IFSCC President 1966/67

Co-chairman: G. A. C. Pitt, SCCofGB President 1973/74 and 1962/63

'The Safety of Fragrances' by D. L. Opdyke (Res. Inst. for Fragrance Materials Inc., New Jersey, USA).

'Studies on the Irritancy of Oils and Synthetic Perfumes to the Skin of Rabbit, Guinea Pig, Rat, Miniature Swine and Man' by K. Motoyoshi, Y. Toyoshima, M. Sato, M. Yoshimura, M. Mochizuka, T. Ishida and K. Yamoato* (Pola Corporation, Yokohama; *Dept of Dermatology, National Childrens Hospital, Tokyo; Japan),

'Eye Irritation Tests. An Assessment of the Maximum Delay Time for Remedial Irrigation' by R. E. Davies, S. R. Kynoch and M. P. Liggett (Huntingdon Research Centre, England).

'Bergaptene Toxicity' by M. A. Cooke* and E. A. Fairburn† (*Albright & Wilson Ltd and the Birmingham Skin Hospital; †University of Birmingham; England).

'Dermatological, Histological and Inhalatory Examination of Aluminium Chlorhydroxide' by K. Rieger (Hoechst A. G., Augsburg, Germany).

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