The Absolute Configurations of the Carvomenthols

Sir:

We wish to cite an error in the stereochemical configurations assigned by Bose to the isomeric carvomenthols.1 While the evidence for the configurations of carvomenthol (I) and neocarvomenthol (II) leaves no doubt as to the stereochemistry of these isomers, the configurations of isocarvomenthol (III) and neoisocarvomenthol (IV) have never been rigorously determined.

In connection with a study of the stereospecific ring opening of the (+)-limonene 1,2-oxides,8 (+)-cis-limonene 1,2-oxide (V, \(\left[\alpha\right]^{25}_{D} +38.00^\circ\)) was treated with an acetic acid–sodium acetate solution to yield (+)-1-acetoxymethyldihydrocarvone (VI). Pyrolysis of this hydroxy acetate at 370°C afforded a mixture of (+)-dihydrocarvone (VII, \(\left[\alpha\right]^{25}_{D} +21.80^\circ\)), (+)-trans-isocarvomenthol (VIII, \(\left[\alpha\right]^{25}_{D} +82.00^\circ\)), and (-)-trans-carveol (IX, \(\left[\alpha\right]^{25}_{D} -181.80^\circ\)) which were separated by fractional distillation.5

These facts are incompatible with the configurations of isocarvomenthol (IV) and neoisocarvomenthol (III) assigned by Bose.1 There is, however, an obvious


(2) (a) J. T. Gresham, M.S. thesis, Emory University, 1961; (b) H. P. Orloff, Chem. Rev., 64, 375 (1964), and references therein.

(3) (a) J. C. Leffingwell, Ph.D. dissertation, Emory University, August, 1953. The application of the Först–Plattner rule to substituted monocyclic cyclohexene epoxides will be discussed in detail in another paper. See also: (b) J. A. Angyal, Chem. Ind. (London), 1230 (1954); (c) H. C. Brown, E. F. West, J. H. Brewster, J. H. Brewster, J. Am. Chem. Soc., 51, 54 (1954), and references therein.

(4) Preparation of this heretofore unreported isomer was effected by the sequence: (+)-trans-limonene 1,2-oxide (V) \(\rightarrow\) (+)-1-acetoxymethyldihydrocarvone (VI) \(\rightarrow\) (-)-mesityl methyldihydrocarvone (VII) \(\rightarrow\) (+)-cis-limonene 1,2-oxide (VIII).

(5) The purity of each component was in all cases >95% (see v.p.c.);


(7) The hydrogenation experiments were carried out over Pd on ethyl acetate. Analyses were by v.p.c. over a 20% Carbowax on firebrick substrate using authentic samples of the four isomeric carvomenthols as internal standards.

(8) Identical results were obtained from the carvomenthenes, prepared as above from (+)-cis-carvomenthenone oxide.

![Diagram of the configurations of carvomenthol, neocarvomenthol, isocarvomenthol, and neoisocarvomenthol](attachment:diagram.png)
answer to this discrepancy. Assignment of the configurations of cyclohexylamines (and their corresponding alcohols) by analysis of the reactions of the amines with nitrous acid\(^6\) is unreliable when applied to cases in which the conformations are mobile\(^10\) (e.g., iso-carvomenthylamine–iso-carvomenthol\(^11\)). Similarly, configurational assignments on the basis of esterification rates of cyclohexanols must be applied with care in mobile systems.\(^12\)

Based on the evidence presented, and the interrelationships of the carvomenthols with the known structures of the carveols,\(^13\) dihydrocarveols, and sobrerols,\(^14\) the stereochemistry and absolute configurations\(^15\) of the isomeric carvomenthols may be assigned as follows: D-(−)-carvomenthol (I), D-(+)-neocarvomenthol (II), D-(+)-isocarvomenthol (III), and D-(−)-neoisocarvomenthol (IV).

The reversal of Bose’s configurations for iso- and neoisocarvomenthol\(^15\) must of necessity change the configurational assignments which have been based on converting structures of unknown stereochemistry to either of these two carvomenthols.\(^16\) Since completion of the present work, other reports have appeared\(^17\) confirming that iso-carvomenthol has configuration 111.


(10) It has been recognized only recently that the isopropyl group is not as bulky as a i-buty1 group and therefore does not necessarily fix the conformation of a cyclohexane ring as has so often been assumed. For example, A. H. Lewis and S. Weinstein, *J. Am. Chem. Soc.*, 84, 2646 (1962); N. L. Allinger, L. A. Freibel, and S.-E. Hu, *ibid.*, 84, 2886 (1962); N. Mori and F. Sada, *Bull. Chem. Soc. Japan*, 36, 227 (1963).


(13) The reversal of the cis and trans configurations for the carveols (and therefore of all the other related terpenes) as proposed by G. Farges and A. Kergomard (*Bull. soc. chim. France*, 51 (1963)) was rejected on the basis of the above arguments inasmuch as the absolute conformations of the (+)-cis- and (+)-trans-1,2-limonene 1,2-oxides have been established.\(^1\) This confirmed the absolute configurations of the carvomenthols previously postulated. The direct relationships of (+)-limonene with (−)-iso-menthone and (+)-1,2-limonene 1,2-oxides and of (−)-isocarvomenthol (−)-trans-carvone, and (-)-trans- and (-)-cis-carveol have long been known.\(^10\) Johnston and Read have previously found that (+)-cis-carveol (−)-trans-carveol and (−)-neoisocarvomenthol and (−)-trans-carveol (−)-neoisocarvomenthol and (−)-trans-carveol (−)-neoisocarvomenthol.


(15) Brewster’s method for calculating the molecular rotation of saturated cyclic compounds also supports such a reversal of configurational assignments.\(^16\)


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**Received March 6, 1964**

**The Reaction of Methyl Radicals with Dimethylmercury**

Sir:

In a recent publication\(^1\) from this laboratory, aceto-d\(_6\) was photolysed in the presence of dimethylmercury in the gas phase. The following reaction was postulated

\[
\text{CD}_3 + (\text{CH}_3)_2\text{Hg} \rightarrow \text{CD}_3\text{HgCH}_3 + \text{CH}_4 \quad (1)
\]

Evidence for the occurrence of this reaction in the gas phase was based mainly on the appearance of \(\text{CH}_3\) as an important radical specie. In order to verify this interpretation, further experiments have been carried out with mixtures in which the deuteration has been reversed, as \(\text{CH}_3\text{COCH}_3 - \text{CD}_3\text{HgCD}_3\). In this way the rate of formation of \(\text{CD}_3\), which may tentatively be ascribed to the reaction

\[
\text{CH}_3 + \text{CD}_3\text{HgCD}_3 \rightarrow \text{CD}_3\text{HgCH}_3 + \text{CH}_2 \quad (1')
\]

was studied and compared to the rate of formation of \(\text{CH}_3\) which was ascribed to reaction 1 in the previous paper. The values obtained for \(k_1/k_1\) were found to be a factor of three lower than those ascribed previously to \(k_1/k_1\). \(k_2\) and \(k_3\) are the rate constants for the combination reactions

\[
2\text{CD}_3 \rightarrow \text{C}_2\text{D}_6 \quad (6)
\]

\[
2\text{CH}_3 \rightarrow \text{C}_2\text{H}_6 \quad (8)
\]

Because this is an unusually large deuterium isotope effect for this type of process, serious doubts arose as to the correctness of the original interpretation. For this reason attempts were made to determine the actual rate of formation of \(\text{CH}_3\text{HgCD}_3\) produced in these systems. In order to obtain reliable yields of this product, conversions had to be increased from 0.5% in the original work to about 5.0%. Blank runs carried out for long periods of time indicated that in the absence of light, the formation of \(\text{CD}_3\text{HgCH}_3\) in \(\text{CH}_3\text{COCH}_3 - \text{CD}_3\text{HgCD}_3\) mixtures at 453\(^\circ\)K. was negligible. However, \(\text{CD}_3\text{HgCH}_3\) is a product when \(\text{CD}_3\text{COCD}_3\) is photolyzed in the presence of \(\text{CH}_3\text{HgCD}_3\). On the basis of the yield of this product as determined by mass spectrometry a value of \(6.0 \times 10^{-8}\) \(1.7\) mole\(^{-1}\) sec\(^{-1}\) was calculated for the rate constant ratio \(k_1/k_1\). Although the determination of this product does provide a more unambiguous proof for the occurrence of process 1, it should be noted that the rate constant ratio is considerably lower than the value of \(30.0 \times 10^{-8}\) mole\(^{-1}\) sec\(^{-1}\) reported in the previous study. It is clear, therefore, that in the \(\text{CD}_3\text{COCD}_3 - \text{CH}_3\text{HgCD}_3\) system, \(\text{CH}_3\) radicals are also produced by processes other than 1, such as

\[
\text{R} + \text{CH}_3\text{HgCH}_3 \rightarrow \text{RH} + \text{CH}_3 + \text{HgCH}_3 \quad (9)
\]

and/or

\[
\text{CH}_3\text{HgCH}_3 \rightarrow \text{CH}_3 + \text{HgCH}_3 \quad (10)
\]

This is also substantiated in the earlier work in which the ratio (ethane + \(1/2\) methane)/CO is greater than unity at the highest temperature. Reaction 10 was not considered originally as a likely process because the quantum yield of the decomposition of dimethylmercury was reported to be independent of temperature from 26 to 198\(^\circ\).\(^2\) Likewise, it was excluded on the basis of the pyrolytic studies of Gowenlock, et al.,\(^3\) which were carried out in a flow system. However, as pointed out by Srinivasan,\(^4\) the possibility exists that in a static system


