CHAPTER III

SOME REACTIONS OF

DIMETHYLOXOSULPHONIUM METHYLIDE
SUMMARY

It is shown that the bicyclic ketone synthesised by Corey by reacting dimethyloxosulphonium methyleide with carvone has the stereochemistry indicated by the structure (XVI) (methylene bridge trans to the isopropenyl group). Sodium-alcohol reduction of the bicyclic ketone (XVI) furnishes, as expected, a mixture of substituted cyclohexanols; subsequent oxidation with Jones' reagent furnishes an equilibrium mixture of two epimeric ketones identified as trans-6-methylidihydrocarvone (XXXIII).

Dimethyloxosulphonium methyleide reacts selectively with the C-11 carbonyl of the diketone (XLIII) to furnish the keto-oxide (XLV). LAH reduction of (XLV) furnishes the crystalline diol (XLVI). Since the oxidation of (XLVI) to carissone is already reported in literature, the above transformation constitutes a convenient route for the synthesis of carissone.

Dimethyloxosulphonium methyleide is also treated with citral but the results are not encouraging.
In the year 1957, Kuhn and Trischmann\(^1\) reported that dimethyl sulphoxide and methyl iodide interacted to produce a new compound which on crystallisation from water gave a white crystalline product. They called this new compound as 'Trimethylsulphoxonium iodide' (A). Later on Corey and Chaykovsky\(^2\) redesignated the same compound as 'Trimethyloxosulphonium iodide'.

\[
(CH_3)_2SO + CH_3I \rightarrow (CH_3)_3SOI
\]

(A)

From the facile exchange of hydrogen in (A) with hydroxylic media, they expected that the compound would undergo a proton-transfer to a strong base and this would result in the formation of a reactive intermediate which would be of considerable utility in the field of synthetic organic chemistry. Actually when the trimethyl compound (A) was treated with sodium hydride in dimethylsulphoxide, it did undergo deprotonation and as anticipated a new active intermediate, dimethyloxosulphonium methyllde (B), was formed\(^3\). This intermediate is also referred to as 'methyllde' or simply as 'ylide'. On the basis of chemical evidence and NMR spectral data, the methyllde has been assigned the structure (C).

\[
(CH_3)_2SOCH_2^+
\]

(B)

\[
\begin{aligned}
\text{H}_3\text{C} & \quad \text{S} \\
\text{H}_3\text{C} & \quad \text{O} \\
\text{CH}_2 & \quad \text{H}_3\text{C}
\end{aligned}
\]

(C)
Although the trimethyl compound (A) is quite stable, the methyldie (B) undergoes appreciable decomposition at room temp. in about a week's time but its solutions in tetrahydrofuran are stable for several weeks, if kept in an inert atmosphere and at 0°C.

In its chemical reactions, the methyldie acts as a nucleophile and transfers a methylene to electrophilic unsaturated linkages including C=O, C=N, C=S, and in certain cases C=C. Although the ylide reacts with reactive carboxylic acid derivatives such as esters, amides, thiono compounds the most characteristic reaction of the ylide is with aldehydes and ketones. Analogous to the action of diazomethane on cyclic carbonyl compounds, the ylide was expected either to enlarge the ring of carbonyl compounds or to form oxiranes. Alternatively, the ylide was considered to act in the manner of Wittig reagents and replace the carbonyl group by a methylene. But neither the ring-expansion nor methylene-oxygen exchange took place, it was only a methylene transfer. This methylene-transfer produces two different types of compounds depending upon the nature of the carbonyl function. In the case of aromatic and non-conjugated aldehydes and ketones, the carbonyl function is directly involved in the reaction and oxiranes or epoxy compounds are produced. But in the case of α,β-unsaturated ketones, which are Michael receptors, the methylene from the ylide is transferred to the conjugated double bond and cyclopropyl compounds are produced.
The general reaction for the aromatic and non-conjugated aldehydes and ketones can be represented as

\[
R_1-C=CH-C-R_2 + (CH_3)_2SOCH_2 \rightarrow R_1-C-H-C-R_2 + (CH_3)_2SO \]

Thus benzophenone (I) reacts with the methyldie to give 1,1-diphenylethylene oxide (II) and benzaldehyde (III) gives styrene oxide (IV). Similarly the general reaction for \(\alpha,\beta\)-unsaturated carbonyl compounds can be given as

\[
R_1-CH=CH-C-R_2 + (CH_3)_2SOCH_2 \rightarrow R_1-C-CH-C-R_2 + (CH_3)_2SO \]

Thus 1-acetyl-cyclohexene (V) gives the cyclopropyl ketone (VI), and benzal acetophenone (chalkone) (VII) gives 1-benzoyl-2-phenyl cyclopropane (VIII).

Some stereochemically interesting results are observed if the carbonyl compound is of a cyclic nature and has no \(\alpha,\beta\)-unsaturation. The methyldie transfers a methylene to the carbonyl of these compounds in such a way that the newly formed C-C bond is equatorially oriented. Thus 4-phenyl cyclohexanone (IX) and 4-t-butyl cyclohexanone (XI) give the epoxides (X) and (XI) respectively where the newly formed C-C bond is equatorial.
I

II

III

IV

V

VI

VII

VIII

IX \( R = -C_6H_5 \)

X \( R = -C_6H_5 \)

XI \( R = -C-C-CH_3 \)

XII \( R = -C-C-CH_3 \)
PRESENT WORK

We carried out the reaction of the methyllde with the following compounds:

Carvone (XIII)
the diketone (XLIII)
Citral (XLVII)

but in each case the objective was quite different.

Reaction with (-)-carvone

The reaction of the methyllde with (-)-carvone (XIII) led to the formation of a bicyclic ketone (XIV). This reaction has been already reported by Corey and we have found the IR spectrum (IR-1) of the product formed to be in good agreement with the values reported by him. The NMR spectrum (NMR-1) of the product also gave the following signals (J values).

9.04 - 9.4 (m, cyclopropyl protons)
8.85 (3H, s, methyl at C)
8.29 (3H, s, vinyl methyl at C)
5.29 (2H, s, olefinic protons at C)

which are in good agreement with the values reported by Corey and they also fully support the structure (XIV) of the bicyclic ketone. Semicarbazone of the bicyclic ketone was also prepared which gave the m.p. 163-64° and its microanalytical results well supported the molecular formula C\textsubscript{11}H\textsubscript{16}O of the bicyclic ketone (XIV).

Although Corey has reported the reaction of the methyllde with carvone, our interest in repeating the reaction was mainly centred around the stereochemistry of the cyclopropane...
ring, which Corey has not discussed. The ring can be either cis to the isopropenyl group as in (XV) or trans as in (XVI) or the reaction product may be a mixture of the cis and trans isomers. As has been mentioned earlier, the action of the methyliide with cyclic carbonyl compounds (having no α-β unsaturation) gives oxiranes by a stereospecific addition of a methylene to the carbonyl group. Extending this logic to α-β-unsaturated cyclic carbonyl compounds, we expected that the transfer of methylene to the conjugated double bond would also proceed stereospecifically and give only the cis bicyclic ketone (XV) or only the trans bicyclic ketone (XVI). Furthermore, the close resemblance between the methyliide reaction and alkaline epoxidation of carvone prompted us to consider that the methyliide reaction must also proceed stereospecifically and give the trans bicyclic compound (XVI). Klein has shown that in the epoxidation of carvone with hydrogen peroxide in alkaline medium the species (D) acts as the nucleophile which attacks β-position of the conjugated double bond by the Michael addition process. The resulting compound is an epoxide very similar to the bicyclic ketone above and Klein has further shown that the epoxide ring is trans to the isopropenyl group, as expressed in the formula (XVII). In the methyliide reaction, the methyliide (B) acts as the nucleophile. It was therefore thought that this nucleophile (B) must also be attacking β-position of the conjugated double bond of carvone by Michael
addition process and produce the bicyclic ketone similar to the epoxide mentioned above. From the close resemblance in the two reactions, the findings of Klein that the epoxy or oxirane ring is unequivocally trans to the isopropenyl group impelled us to consider that the cyclopropane ring in the bicyclic compound (XIV) must also be similarly trans to the isopropenyl group and it can be represented as (XVI).

In order to verify the truth of our contention, we decided to prepare separately the cis bicyclic ketone (XV) and trans bicyclic ketone (XVI) from carvone by an entirely independent and stereospecific method and compare their properties with those of the bicyclic ketone obtained by the methyldie reaction. One such method of preparing stereospecifically oriented cyclopropane ring is the Simmons-Smith reaction which makes use of methylene iodide and active zinc-copper couple as the reagent. In this reaction a methylene adds on to the double bond of the substrate to form a cyclopropane system and if there is already a hydroxy group in allylic position to the double bond, the orientation of the cyclopropane ring is always cis to the hydroxy group. We decided to employ this reaction to prepare cis and trans bicyclic compounds from carvone through some intermediate transformations. However, in carvone there is a double bond in the isopropenyl side-chain and this would also undergo an attack since isolated double-bonds are not excluded from the field of Simmons-Smith reaction. The net result of the reaction
would be probably the formation of tricyclic compounds and that would complicate the matters.

It was therefore decided to hydrogenate the isopropenyl side-chain and get carvotanacetone (XVIII). Use of carvotanacetone in place of carvone in the methyliide reaction would not make any change in the stereochemistry of the cyclopropane ring since the methyliide reaction would be independent of the unsaturation in the side-chain. In fact an advantage was seen in using carvotanacetone that the bicyclic compound obtained through the Simmons-Smith reaction would be quite pure so that it could be easily compared with the bicyclic ketone obtained by the methyliide reaction with carvotanacetone.

With these considerations in mind, we subjected carvone to controlled hydrogenation in ethanol, using platinum oxide as the catalyst (Adams' catalyst) and obtained carvotanacetone. After purification through chromatography and distillation, carvotanacetone was subjected to methyliide reaction when the bicyclic ketone (XIX) was obtained. The NMR spectrum (NMR-2) of the product gave signals at:

9.1 (6H, d, J = 6 cps, methyls on isopropyl)
8.82 (3H, s, methyl on C1)

The above spectral data was in full conformity with the structure (XIX) of the bicyclic ketone. Semicarbazone of the bicyclic ketone was also prepared which gave m.p. 190°-91° and its microanalytical results were found to be in conformity with the molecular formula C11H18O of the bicyclic ketone (XIX).
In order to prepare the cis bicyclic ketone (XXIV) and trans bicyclic ketone (XXV) from carvotanacetone by Simmons-Smith reaction, we planned to

i) reduce carvotanacetone to the epimeric carvotanacetols (XX) and (XXI)

ii) separate the above epimers by some suitable method

iii) subject the epimeric alcohols (XX) and (XXI) separately to Simmons-Smith reaction to furnish the bicyclic alcohols (XXII) and (XXIII) respectively

iv) Oxidise the above bicyclic alcohols (XXII) and (XXIII) to produce cis-bicyclic ketone (XXIV) and trans-bicyclic ketone (XXV) respectively.

By comparing these cis and trans bicyclic ketones with the bicyclic ketone (XIX) obtained by the methyliide reaction, the stereochemistry of (XIX) was to be determined.

The formation of allylic carvotanacetols as proposed in step (1) above could only be conveniently accomplished by the use of sodium borohydride or aluminum isopropoxide as the reducing agents. But in either case, a mixture of axial and equatorial would be obtained in which the latter would predominate. We were however mainly interested in the axial hydroxy conformation since in discussing the mechanism of Simmons-Smith reaction, Dauben and Berezin have suggested that stereospecific methylenation of allylic alcohols in the cyclohexyl series involves reaction
through the axial hydroxy conformation*. The sodium borohydride and aluminum isoproploxide reductions were thus considered to be unsuitable for our work as they would give a low proportion of the axial hydroxy epimer.

In order to prepare pure trans-carvotanacetol we tried the method first reported by Klein and Whloff and then by Schroeter for the preparation of trans-carveol. Following the procedure of this method, (-) carvotanacetone (XVIII) was epoxidised with alkaline hydrogen peroxide to give the oxide (XXVI) which on treatment with hydrazine hydrate furnished (+) trans-carvotanacetol** (XXVII).

The above trans alcohol (XXVII) was then subjected to Simmons-Smith reaction but the reaction-product as revealed by the IR and NMR spectra was found to be only the starting material. The reaction was repeated several times but for some incomprehensible reasons the reaction appeared not to proceed at all and only the starting material was recovered in every case. In a recent communication, Rocquet and co-workers11

*However, towards the end of our work we came across a publication by Chan and Rickborn who have arrived at a different conclusion. They have shown on the basis of relative rate-constants for the methylation of allylic axial and equatorial hydroxy conformers that stereospecific methylation of allylic cyclohexenols occurs through the quasi-equatorial conformation rather than through the quasi-axial one.

**This reaction has been previously carried out in this laboratory by Tadwalkar and Rao and it has only recently appeared in the Indian Journal of Chemistry10. The results of our work were found to be in good agreement with the findings of Tadwalkar and Rao.
have claimed that they have successfully employed the Simmons-Smith reaction to obtain the (+) cis-bicyclic alcohol (XXIX) from (+)-cis-carveol (XXVIII). Oxidation of the bicyclic alcohol (XXIX) gave the cis-bicyclic ketone (XXX) whose physical properties were found to be different from those of the bicyclic ketone obtained by the action of the methylide on (+) carvone. Thus the bicyclic ketone obtained by the methylide reaction has been indirectly shown to have a trans relationship between the cyclopropane ring and isopropenyl side-chain and it can be represented by (XXXI).

With the failure of the Simmons-Smith reaction in our work, we reverted back to the bicyclic compound (XIV) obtained from carvone and changed our approach to the problem. We considered the possibility of suitably opening up the cyclopropane ring to produce 6-methyl dihydrocarvone (XXXII). Comparison of (XXXII) with the trans-6-methyl dihydrocarvone (XXXIII) that had been already prepared in this laboratory would enable us to determine the stereochemistry of (XXXII). Following the procedure of House and co-workers, Siscovic and Rao had already prepared 6-methyl dihydrocarvone by the action of lithium dimethyl copper on carvone. On the basis of Allinger's work on 1,4-addition of Grignard reagent to 2-methyl cyclohex-5-en-1-one, and Djerassi's work on the conjugate addition of cyanide to carvone, Siscovic and Rao have already arrived at the same conclusion but by a direct method and our work has been already published at a much earlier date in 'Chemistry and Industry'.
showed that in 6-methyl dihydrocarvone which they had prepared, the newly introduced methyl group was in trans relationship to the isopropenyl group and that the compound could be represented as (XXXIII). We procured a sample of the trans compound (XXXIII) and its semicarbazone (XXXIV) from Siscovic and Rao and preserved these samples as reference compounds for comparison purpose.

Our attempts were now directed to find out a method that would suitably open up the cyclopropane ring of (XIV), leading to the formation of 6-methyl dihydrocarvone (XXXII). On the basis of analogy of the conversion of (XXXV) to (XXXVI) with BF₃ etherate and hydrochloric acid¹⁷, we attempted the conversion of (XIV) to the corresponding chloroketone (XXXVII) with the same reagent. Further conversion of the chloroketone (XXXVII) to (XXXII) could be brought about by using a suitable reagent. However, the reaction of BF₃ etherate and hydrochloric acid with (XIV) gave a tarry mass from which we could not isolate the required chloro compound and we gave up the method.

In another method of opening of the cyclopropane ring of conjugated cyclopropyl ketones, Norin¹⁸ as well as Dauben and Dewiny¹⁹ have investigated the scope of reductive cleavage with lithium and liquid ammonia. They found that the reaction proceeds in a highly stereospecific manner and the direction of the ring-opening is controlled by stereo-electronic factors. That bond of the cyclopropene system is
cleaved which has the maximum overlap with the \( \pi \)-orbitals of the carbonyl group. Thus \((+)\)-carvone (XXXVIII) gave \((-)\)-carvomenthone (XXXIX) and \((-)\)-sabinaketone (XL) gave \((+)\)-3-methyl-3-isopropyl cyclopentanone (XLI). Later on Bellamy and Whitham showed that the same mode and mechanism of cyclopropane ring-opening is operative if sodium and alcohol are used in place of lithium and liquid ammonia.

We thought that this reaction would be of immense help to us in our work and as the sodium-alcohol reduction appeared to be the simpler to handle, it was employed in the case of the bicyclic compound (XIV). But the reaction product was found to contain a hydroxy compound as was revealed by the IR-spectrum. The product was oxidised with Jones' reagent and injected on a VPC column when it showed two peaks, one major peak corresponding to the starting bicyclic ketone (XIV) and the other minor and slightly broad peak due to some other compound, probably the expected 6-methyl dihydrocarvone. On a second treatment of the product with sodium and alcohol and oxidation with Jones' reagent, the VPC analysis gave the same two peaks as obtained previously but now the proportion of the starting bicyclic ketone (XIV) appeared to be decreased while that of the other compound increased considerably. It appears that only a small portion of the bicyclic compound (XIV) underwent an initial attack at the cyclopropane ring and the carbonyl group was reduced to give an alcohol whereas the major
portion of the bicyclic compound (XIV) suffered an attack at the carbonyl group first, to give a hydroxy compound and the formation of a hydroxy function in allylic position rendered the cyclopropane ring less vulnerable to the attack of sodium and alcohol. When the reduction product was oxidised, the major component gave back the starting bicyclic ketone (XIV) and the minor component gave the other ketone which was in all probability the expected 6-methyl dihydrocarvone (XXXII).

The cycle of alternate reduction with sodium and alcohol and oxidation with Jones’ reagent was repeated several times till the relative proportion of the bicyclic ketone (XIV) in the final product was sufficiently reduced and that of the other component substantially increased as was revealed by the VPC analysis. The oxidation product was finally chromatographed over neutral alumina (Gr. II) and the fraction eluted with pet. ether gave a ketonic compound free from the bicyclic ketone (XIV) as was shown by VPC analysis and IR spectrum. This ketonic compound and the trans-6-methyl dihydrocarvone (XXXIII) which we had procured for comparison, gave superimposable IR-spectra (IR-5), two VPC peaks with the same retention times (8 min, 55 sec. and 9 min., 41 sec.) and identical NMR spectra having J values:

- 8.25 (3H, s, methyl of isopropenyl)
- 5.25 (2H, s, vinyl protons)

The ketonic compound also gave a semicarbazone identical with the semicarbazone (XXXIV) that we had procured for
comparison purpose. The semicarbazones gave m.p. and mixed m.p. 182-84°, superimposable IR spectra (IR-6) and identical NMR spectra (NMR-3) with J values:

9.07 (3H, d, J = 6 cps, methyl on C_6)
8.87 (3H, d, J = 6 cps, methyl on C_1)
8.3 (3H, s, methyl of isopropenyl)

Thus, the complete identity of the ketone (XXXII) with the trans-6-methyl dihydrocarvone (XXXIII), as established by the above comparison studies made it clear that in the former, the methyl group generated at C_6 by opening the cyclopropane ring of (XIV) must be in trans relationship to the isopropenyl group. This evidently led to the conclusion that in the bicyclic ketone (XIV), the cyclopropane ring and the isopropenyl group must be in trans relationship to one another and the compound can be represented as (XVI).

**Carissone (XLII) from the diketone (XLIII)**

In connection with the synthesis of carissone (XLII) from the diketone (XLIII) we were interested in finding reagents which would react selectively with the non-conjugated carbonyl group (vide Chapter 2 where carissone and the diketone are represented by (I) and (XII) respectively). It was anticipated that methyl magnesium iodide would serve the purpose and in order to test the truth of this contention, the reaction was first carried out with the model compound progesterone. The experimental results suggested that if
sufficient care were not exercised, the conjugated ketone would also react with methyl magnesium iodide. This limited success in the use of methyl magnesium iodide as a selective reagent prompted us to look for some other reagent that would be still more selective in its reactions with the non-conjugated carbonyl group.

In studying the reactions of the methylide (B) with carbonyl compounds, Corey and Chaykovasky\textsuperscript{2} came across a conjugated ketone, $\Delta^4$-cholestenone (XLIV) which was recovered completely unreacted even when drastic conditions and prolonged period of reaction were used. They reasoned this inability of the compound to undergo reaction as being probably due to its high tendency towards enolisation. On the basis of a close structural resemblance between the ring 'A' of $\Delta^4$-cholestenone and the ring 'A' of the diketone (XLIII) we expected that the methylide would have no reaction with the ring 'A' of the attached diketone but the non-conjugated carbonyl to ring B would react as usual and the net result would be the formation of the oxide (XLV). If this oxide could really be obtained by the methylide reaction, further steps to getting carisssone would be easy since Pinder\textsuperscript{21} has already obtained this oxide by the epoxidation of cyperone and shown how to reduce the oxide with LAH to the diol (XLVI) and further to oxidise the diol with $\text{MnO}_2$ to carisssone.

In accordance with the above plan, the diketone (XLIII) was subjected to the action of the methylide (B) under the
NMR - 4  3-OXO-EUDESM-4-EN-11,12-OXIDE (XLV)  
(IN CCl₄)
usual conditions when the IR spectrum (IR-7) of the product formed showed prominent absence of a band at 1712 cm$^{-1}$ (non-conj. ketone) but retention of bands at 1664 cm$^{-1}$ (conj. ketone) and 1613 cm$^{-1}$ (conj. C=C). The NMR spectrum (NMR-4) of the product gave signals at J:

- 8.77 (3H, s, methyl at C$_{10}$)
- 8.7 (3H, s, methyl at C$_{11}$)
- 8.29 (3H, s, methyl at C$_{4}$)
- 7.5 (2H, m, oxirane protons)

The above spectral data well supported the structure (XLV) of the epoxide and it was quite in accordance with our expectation.

The epoxide was then reduced with lithium aluminum hydride under the conditions used by Pinder$^{21}$ and a solid product was obtained which showed a prominent band at 3425 cm$^{-1}$ (hydroxyl) but no band for a carbonyl or C=C in the IR spectrum. It gave m.p. 128$^\circ$ and ($\alpha$)$_D^{28}$ +55.1$^\circ$, which were quite consistent with the values (m.p. 129-30$^\circ$, and ($\alpha$)$_D^{20}$ +57.8$^\circ$) reported by Pinder$^{21}$ for the diol (XLVI). It was therefore quite evident that the LAH reduction product that we obtained from the oxide (XLV) was the diol (XLVI) which Pinder had obtained via a different route. Furthermore, the NMR spectrum (NMR-5) of the reduction product gave signals which fully justified the structure (XLVI) of the diol. The signals were at
\[ \text{\textit{J} values:} \]

\[
\begin{align*}
8.92 & \ (3\text{H}, \ s; \ \text{methyl on C}_{10}) \\
8.78 & \ (6\text{H}, \ s; \ \text{methyl on C}_{11}) \\
8.27 & \ (3\text{H}, \ s; \ \text{methyl on C}_{4}) \\
5.02 & \ (1\text{H}, \ \text{broad quasi axial* proton at C}_{9})
\end{align*}
\]

Pinder has brought about the conversion of the diol to carissone by oxidation with manganese dioxide. We however tried a careful oxidation of the diol with Jones' reagent and the oxidation product was identified as carissone (IR spectral evidence).

**Reaction of the methylide with citral (XLVII)**

Corey\(^2\) has discussed the action of the methylide (B) with ketones (conjugated, non-conjugated/aromatic) as well as with aldehydes (non-conjugated, aromatic). We were therefore interested in seeing the reaction with conjugated aldehydes, which Corey has not discussed. On the basis of analogy of the reaction with conjugated ketones, the reaction of the methylide with conjugated aldehydes was expected to proceed on similar lines. A compound like citral (XLVII) could be expected to react with the methylide to produce the cyclopropyl compound (XLVIII). If the reaction would really proceed on this line then the cyclopropane ring of the product could be easily opened up in a selective way with sodium and alcohol\(^{20}\) and methyl citronellol (XLIX) would be produced which on oxidation would give the aldehyde (L). The latter could be confirmed by

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\*Distinction between quasixialial and quasiequatorial protons at C\(_9\) on the basis of NMR spectra has been discussed by Piers and Cheng\(^{22}\) in connection with related allylic alcohols.
comparison with methyl citronellal we have obtained by the action of lithium dimethyl copper on citral (vide Chapter 4).

Actually when the reaction of the methylide (B) was carried out with equimolecular quantities of citral, the IR spectrum of the product showed that the reaction had proceeded somewhat in an unusual way; the carbonyl band had disappeared completely, indicating that the carbonyl group rather than the conjugated double bond was involved in the reaction. Since the reaction did not proceed in the way we had anticipated we abandoned our further plans of work.
EXPERIMENTAL

Carvone was obtained by fractionation of spearmint oil. The fraction b.p. 103-4°/12 mm; (α)\(_D^{26}\) = 56° and giving a single peak in VPC analysis was used for our experimental work.

Similarly citral was obtained by fractionation of lemon-grass oil. The fraction b.p. 117-19°/20 mm was used for our work. The fraction gave two peaks in VPC analysis, corresponding to citral 'a' and citral 'b'.

Trimethylsulphonium iodide

This compound was prepared following the procedure given by Kuhn and Trischmann\(^1\).

A solution of pure dry dimethyl sulphoxide (28.8 g) and methyl iodide (55 ml) was refluxed under nitrogen atmosphere for 24 hrs. during which period a solid precipitated. The solid was filtered off, washed with chloroform, dried and found to weigh (26 g). The crude product was crystallised from hot water to give large colourless prisms (22 g) which were crushed and dried over phosphorus pentoxide in a vacuum desiccator.

Dimethyl oxosulphonium methyldide and its reaction with (-)carvone

Sodium hydride in the form of a 50% mineral oil suspension (2.4 g) was taken in a three-necked conical flask.

\(^2\)Corey has reported the refluxing for 72 hrs. However we found the product to decompose after 24 hrs. refluxing. We therefore discontinued the refluxing and worked up the product after 24 hrs., although it gave a low yield.
and washed three times with dry petroleum ether by suspending and decanting the liquid portion, in order to remove the mineral oil. Powdered trimethylsulphonium iodide (11 g) was added to the above flask in which a continuous current of nitrogen was being passed. Dimethyl sulphoxide (50 ml) (dried over CaH2 and freshly distilled) was added to the above mixture and stirred over a magnetic motor. Vigorous evolution of hydrogen ensued and then ceased after about 25-30 minutes when a milky-white solution containing dimethylsulphonium methyldide was obtained.

The above stirred solution of the ylide under N2 atmosphere was slightly cooled and a solution of freshly distilled carvone (6 g) in dry dimethyl sulphoxide (10 ml) was added to it dropwise. After the addition was over, the stirring was continued at room temperature for 2 hrs. and at 50° for 1 hr. It was then poured on cold water (125 ml) and extracted with ether (3 x 50 ml). The ether extracts were pooled together, twice washed with water, dried over sodium sulphate and ether removed by evaporation to leave behind a pale yellow liquid. On distillation under vacuum (10 mm) the bicyclic compound (XVI) was obtained as a colourless liquid (5.66 g)

b.p. 109-100°/10 mm; (c)29° - 24° (c, 5.1)

IR bands (IR - l): 3021, 1689, 1462, 1383, 1368, 1351, 1302, 1250, 1212, 1174, 1147, 1105, 1065, 917, 862 cm⁻¹.

VPC analysis (6 ft., polyester on fire-brick, 178°, hydrogen flow rate 85 ml/min.) gave only one peak (retention time 5 min. 38 sec.) indicating it to be a single compound.
Semicarbazone of the bicyclic ketone (XVI)

To a solution of semicarbazide hydrochloride (0.5 g) and sodium acetate (0.8 g) in water (4 ml), the bicyclic ketone (XVI) (0.4 g) was added. A slight turbidity appeared which was discharged by adding alcohol (4 ml). The solution was warmed on water-bath for a few minutes and allowed to cool to room temperature when a crystalline solid started separating out. After standing overnight the solid was filtered, washed with water and cold alcohol. The crude solid was recrystallised from alcohol and the pure semicarbazone (0.38 g) was obtained m.p. 163-64°.

Analysis

Found: C, 65.25; H, 8.77; N, 18.61.
Calculated for C₁₂H₁₉N₃O: 65.16; H, 8.60; N, 18.99%.

IR spectral bands (IR-2): 3571, 3195, 2941, 1681, 1661, 1634, 1565, 1449, 1366, 1342, 1149, 1087, 1011, 909, 891, 869, 845 cm⁻¹.

Carvotanacetone (XVIII)

Carvone (15 g, 0.1 mol) dissolved in ethanol (75 ml) was hydrogenated under atmospheric pressure, using platinum oxide (0.075 g) as the catalyst. After the absorption of hydrogen was 0.11 mole (2.464 litres at NTP) the hydrogenation was stopped and the reaction mixture filtered. The filtrate was gently distilled using a fractionating column so as to remove only the solvent alcohol. The residue was diluted with water and extracted with ether (3 x 50 ml). The ether extracts
were pooled together, washed with water and dried over sodium sulphate; ether was removed by distillation and the residue totally distilled under vacuum (10 mm) to give the reaction product (14.1 g). IR spectrum of the product gave bands at 1667 (conjugated C=O), 1706 cm⁻¹ (non-conjugated carbonyl). VPC analysis of the product also gave two peaks, one minor peak corresponding to tetrahydrocarvone and one major peak corresponding to carvotanacetone. The product (13.5 g) was chromatographed, using a high ratio of alumina (675 g, grade II, neutral). The earlier fractions eluted with pet. ether (300 ml in all) contained mainly tetrahydrocarvone together with a small amount of carvotanacetone as revealed by IR spectrum and VPC analysis. Further fractions eluted with pet. ether-benzene (80:20) contained only carvotanacetone (absence of tetrahydrocarvone being indicated by absence of a band near about 1700 cm⁻¹). It was distilled under vacuum (5 mm) to give pure carvotanacetone (11.2 g)

b.p. 90-91°/5 mm (α)D²⁷⁻⁰ = 52°

IR spectrum gave bands at: 2941, 1695, 1667, 1460, 1439, 1418, 1379, 1361, 1325, 1207, 1274, 1242, 1212, 1190, 1143, 1105, 1070, 1042, 1026, 1000, 938, 895, 825, 704 cm⁻¹.

VPC analysis (6 ft., polyester on fire-brick, 190°, hydrogen flow rate 66 ml/min.) gave a single peak (retention time 2 min., 28 sec.).
Bicyclic compound (XXV) from carvotanacetone

To a cooled solution of dimethyloxosulphonium methylide prepared from sodiumhydride suspension (1 g), trimethyloxosulphonium iodide (4.5 g) and dimethylsulphoxide (20 ml), a solution of carvotanacetone (2 g) in dimethylsulphoxide (10 ml) was added and the reaction conducted and the product worked out as explained in an earlier experiment. The product after vacuum distillation gave the pure bicyclic compound (XXV) (1.8 g) b.p. 120-250 (bath)/10 mm. IR bands at (IR-3): 2950, 1675, 1453, 1399, 1376, 1359, 1316, 1229, 1126, 1096, 1031, 1010, 980, 965, 952, 943, 917, 905, 887, 877, 860, 835, 826, 810, 796, 760 cm⁻¹. VPC analysis (6 ft polyester on fire-brick, 1300, hydrogen flow-rate 70 ml/min) gave a single peak (retention time 5 min. 30 sec.).

Semicarbazone of the bicyclic compound XXV

Semicarbazide hydrochloride (0.5 g) and sodium acetate (0.8 g) were dissolved in water (4 ml) and the bicyclic ketone (XXV) (0.44 g) was added to the solution. A slight turbidity appeared which was discharged by addition of alcohol (4 ml). The solution was warmed on water-bath for a few minutes and allowed to cool to room temp. when a crystalline product separated out. After standing overnight, the solid was filtered, washed with cold water, cold alcohol and recrystallised from alcohol to give the pure semicarbazone (0.35 g) m.p. 190-91°.
Analysis

Found: C, 64.33; H, 9.36; N, 18.58.

Calculated for $\text{C}_{12}\text{H}_{21}\text{N}_{0}\text{O}_{3}$: C, 64.59; H, 9.41; N, 18.83%.

IR bands (IR-4): 3425, 3175, 2899, 1661, 1562, 1460, 1439, 1429, 1377, 1319, 1299, 1250, 1238, 1188, 1163, 1144, 1126, 1104, 1083, 1038, 1012, 985, 955, 940, 917, 895, 885, 850, 830, 721, 722 cm$^{-1}$.

(+) -trans-Carvotanacetol (XXI)

This was prepared in accordance with the procedure given by Klein and Ohloff$^4$.

To a cooled (-10°) mixture of (-) carvotanacetone (9 g) and 30% $\text{H}_2\text{O}_2$ (18 ml) in dioxane (60 ml), a solution of 6N NaOH (5 ml) was added dropwise with vigorous stirring of the mixture. The rate of addition was controlled so as not to allow the temp. to rise above 0°. The mixture was stirred at 0° for 2 hrs. and poured into water. It was extracted 4 times with ether, ether extracts washed with water and dried over $\text{Na}_2\text{SO}_4$. Ether was removed by evaporation and residue distilled under vacuum to give the epoxy ketone (7.63 g)

b.p. 82-85°/1 mm ($\omega$)D + 94°

Hydrazine hydrate (80%, 9 g) was added to a solution of the above epoxyketone (7.5 g) in dry methanol (50 ml) maintained at 0° and after addition of glacial acetic acid (0.6 g) the mixture was stirred at 0° for 1/2 hr and 30° for 2 hrs. After dilution with water, it was extracted with ether.
Ether extracts were washed with water and dried over $\text{Na}_2\text{SO}_4$. Ether was removed by distillation and the residue distilled under vacuum (6 mm) to give the pure trans alcohol (3.4 g). b.p. 108-109°/6 mm; ($\alpha$)$_D^0 + 147°$.

IR bands: 3571, 2941, 1626, 1460, 1439, 1374, 1355, 1319, 1309, 1265, 1235, 1163, 1149, 1089, 1044, 1027, 1010, 980, 960, 931, 905, 860, 850, 846, 806, 760 cm$^{-1}$.

**Simmons-Smith reaction with (+)-trans-carvotanacetol (XXI)**

The Zn-Cu couple required for the reaction was prepared according to the method given by Eugene LeGoff$^{23}$.

In a two-necked round bottom flask a solution of cupric acetate monohydrate (0.4 g) in glacial acetic acid (20 ml) was heated to boiling and rapidly stirred. Zn dust (7 g) was added to the solution which was kept hot in order to prevent precipitation of zinc acetate. In about a minute's time copper deposited on the zinc dust and after allowing it to stand for another minute, as much acetic acid as possible was decanted off. The dark reddish grey zinc-copper couple was washed with glacial acetic acid and after the removal of the acid the flask was cooled in ice-water. The couple was washed three times with ether and was then ready for use.

To the above flask containing the zinc-cu couple, were added dry ether (50 ml), a small crystal of iodine and methylene iodide (23 g). The mixture was well stirred and warmed with IR lamp until a spontaneous reaction commenced (as was evidenced by continued refluxing when the IR-lamp was removed). The flask
containing the reaction mixture was immersed in a water-bath maintained at 35° and the mixture stirred for 30 minutes. To this gently refluxing mixture was gradually added a solution of (+)-trans-carvotanacetol (1.5 g) in dry ether (15 ml). The mixture was stirred and refluxed for an additional hour. The mixture was cooled to room temp. and treated with a saturated solution of ammonium chloride until the complex inorganic salts precipitated to the bottom of the flask. The ethereal solution was decanted into a separatory funnel and the decanted inorganic salts were washed with ether (2 x 50 ml). The combined ether extract was washed with saturated K₂CO₃ solution (2 x 50 ml) and then with sodium chloride solution. The ether solution was dried over MgSO₄. Ether was removed by distillation and the residual oil was added in a nitrogen atmosphere to a saturated methanolic solution (50 ml) of sodium methoxide and the resulting solution allowed to stand for 24 hrs. The methanolic solution was diluted with water and extracted with ether (3 x 50 ml) and the ethereal solution washed with saturated sodium chloride solution. The ethereal solution was dried, ether removed by distillation and the residual oil distilled under vacuum to give a product (1.42 g) which was found to be only the starting (+)-trans-carvotanacetol (XXI) as revealed the IR and NMR spectra.

Cleavage of the cyclopropane ring by sodium and alcohol

Sodium (3.9 g) was added in small pieces to a solution of the bicyclic ketone of carvone (1.5 g) in dry refluxing
ethanol (40 ml). After all the sodium had dissolved, the solution was heated under reflux for 30 minutes. The mixture was poured in water and extracted with ether. The ethereal solution was separated and washed with water, dried over Na₂SO₄ and ether removed by evaporation. The IR spectrum of the residue showed the presence of a hydroxy function (3400 cm⁻¹) but no carbonyl absorption (1660-1720 cm⁻¹). The product was oxidised with Jones' reagent and the oxidation product did not show the presence of a hydroxy function but only a carbonyl group. The oxidation product was injected on a VPC column when two peaks were obtained; the major peak corresponding to the starting bicyclic ketone (XIV) and the other peak probably corresponding to the expected monocyclic ketone. This cycle of alternate reduction and oxidation was repeated six times when the mixture was found to be sufficiently enriched in the monocyclic ketone. The mixture (1.2 g) was chromatographed, using a high ratio of alumina (50 g, neutral, grade II). The earlier fraction eluted with pet. ether gave the monocyclic ketone which was distilled under reduced pressure to give the pure monocyclic ketone (XXXIII, 0.83 g) b.p. 110⁰/6 mm.

Analysis

Found: C, 79.32; H, 11.1.
Calculated for C₁₁H₁₆O : C, 79.46; H, 10.92%.

IR bands (IR-5): 3300, 2890, 2810, 1720, 1650, 1458, 1380, 1330, 1270, 1250, 1220, 1170, 1130, 1115, 1085, 1055, 1027, 910 cm⁻¹.
VPC analysis (6 ft., carbowax 171°, hydrogen flow rate 85 ml/min.) gave two very close peaks (retention time 8 min. 55 sec. and 9 min. 41 sec. corresponding to two epimers.

Semicarbazone (XXXIV) of the monocyclic ketone

To a solution of semicarbazide hydrochloride (0.4 g) and sodium acetate (0.65 g) in water (3 ml), the monocyclic ketone (XXXIII) (0.3 g) was added. Alcohol (3 ml) was added, the solution warmed and kept aside when a crystalline solid precipitated. The solid was filtered, washed with water, cold alcohol and then recrystallised from alcohol to give the pure semicarbazone (XXXIV) (0.27 g), m.p. 182-84°.

IR bands (IR-6): 3450, 3200, 2900, 1630, 1560, 1470, 1370, 1105, 1075, 980, 770, 730 cm⁻¹.

Reaction of dimethyloxosulphonium methyldie with the diketone (XLIII)

A solution of the diketone (XLIII, 0.55 g) in dimethyl sulphoxide (10 ml) was gradually added to a cooled solution of dimethyloxosulphonium methyldie prepared from a suspension of sodium hydride (0.16 g), trimethyloxosulphonium iodide (0.6 g) and dimethyl sulphoxide (10 ml). The reaction was carried out and the product worked out as explained in an earlier experiment to give the oxirane compound which on distillation under vacuum (0.3 mm) gave the pure oxirane (XLV, 0.44 g), b.p. 128°/0.3 mm.

IR bands (IR-7) 2910, 1667, 1616, 1450, 1376, 1361, 1319, 1295, 1266, 1247, 1202, 1182, 1152, 1087, 1066, 1020, 975, 961, 941, 925, 900, 885, 877, 858, 847, 833, 820, 793, 757, 740, 729, 680 cm⁻¹.
**LAH reduction of the oxirane (XLV)**

To a stirred and cooled (0°) solution of LAH (0.15 g) in dry ether (30 ml) was gradually added a solution of the oxirane (0.39 g) in dry ether (10 ml). After keeping the mixture at 0° for 24 hrs., the reaction product was decomposed as usual with moist ether, ice-water. The ethereal layer was separated, dried over sodium sulphate and ether removed by evaporation. The residue was totally distilled under vacuum (0.3 mm) to give an oily product which solidified readily. The solid was recrystallised from benzene-pet. ether to give the white solid diol (XLVI, 0.31 g), m.p. 128°; (α)\(^28\)_D + 55.1° (literature values\(^21\), m.p. 129-30°, (α)\(^20\)_D + 57.6°).

**IR bands (IR-8):** 3333, 2907, 1645, 1455, 1374, 1274, 1205, 1136, 1073, 1018, 952, 925, 920, 909, 895, 877, 854, 817, 787, 770 cm\(^{-1}\).

**Oxidation of the diol (XLVI) with Jones' reagent**

The diol (XLVI, 0.2 g) was dissolved in acetone (10 ml) and the solution thoroughly cooled to 0°. Jones' reagent was gradually added to the solution till a persistent brown color was obtained. The mixture was kept at 0° for 20 minutes and excess of the reagent was then consumed by adding methanol. The solution was diluted with water (20 ml) and extracted with ether (3 x 30 ml). The combined ether extracts were thoroughly washed with water, dried over sodium sulphate and ether removed by evaporation. The residue was a colourless liquid (0.14 g)
having IR spectrum almost identical with that of authentic carissone.

The product gave IR bands at: 3570, 2880, 1638, 1595, 1450, 1375, 1350, 1325, 1222, 1164, 1145, 1120, 1085, 1010, 991, 957, 917, 887, 872, 848, 815, 776, 750, 702 cm⁻¹.

Reaction of dimethyl oxosulphonium methyldide with citral (XLVII)

To a cooled solution of dimethyl oxosulphonium methyldide prepared from a suspension of sodium hydride (0.5 g) trimethyloxosulphonium iodide (2.5 g) and dimethyl sulphoxide (20 ml), a solution of citral (1.5 g) in dimethyl sulphoxide (10 ml) was added gradually. The reaction was carried out and the product worked out as explained in a similar earlier experiment and a crude reaction product obtained. The IR spectrum of the product showed complete disappearance of the carbonyl band (1685 cm⁻¹) of the starting material citral and no further work was carried out.
IR-2. SEMICARBAZONE OF XVI
(IN NUJOL)
REFERENCES


