A NEW SYNTHESIS OF Δ^9-1-OCTALONE AND SYNTHESIS OF A NEW UNCONJUGATED 1-OCTALONE[1]

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Of the various possible 1-octalones only the Δ^2 (1), Δ^6 (2), and Δ^9 (3) were reported in the literature at the time this work was initiated. This paper reports a new method of preparing the Δ^9 isomer as well as a new 1-octalone which exists in two isomeric forms, isolated as 2,4-dinitrophenylhydrazones. Also, using a method based on the one reported in this paper, Shoemaker and Dienes (4) have prepared a new octalone which they call $\Delta^{5,6}$ although Dr. Shoemaker reports that he is uncertain of the structure and hopes to make further studies of it.

The basis of our method is to prepare a methoxydecalone and to introduce a double bond by refluxing first with hydrogen iodide and then with a base such as alcoholic KOH or dimethylaniline. The methoxydecalones were prepared by hydrogenation of less saturated derivatives. To make 7-methoxy-1-decalone, we started with the previously known 7-methoxy-1-tetralone (5) which was hydrogenated to 7-methoxy-1-decalol, and the latter was oxidized to the methoxydecalone. To make the 4-methoxy-1-decalone, we started with 5,8-dihydro-1,4-naphthalenediol, (6) which was readily monomethylated to give 4-methoxy-5,8-dihydro-1-naphthol. This was likewise reduced to the decalol and the decalol was oxidized to the decalone. Hydrogenation was accomplished in the presence of W-6 Raney nickel at a pressure of 150 atmospheres and 125–200°. The decalols were oxidized to the decalones by chromic anhydride in acetic acid.

7-Methoxy-1-decalone yields, by treatment with hydrogen iodide and subsequently with alcoholic KOH, two isomers isolated as the dinitrophenylhydrazones and semicarbazones. The labile form was converted into the stable form by a method sometimes used for *cis-trans* isomerizations (7). Shoemaker and Dienes give for their so-called $\Delta^{5,6}$ isomer a m.p. of 230° for the dinitrophenylhydrazone compared to 231° for our $\Delta^7(?)$-octalone 2,4-dinitrophenylhydrazone (stable form). However, a mixture melting point determination proved that they were not identical.

4-Methoxy-1-decalone by similar treatment yields by double bond migration the previously known Δ^9-1-octalone. Absorption spectra measurements of this compound and its derivatives confirm its conjugated structure.

With regard to the problem of deciding which of our isomers to call *cis* and

which to call *trans* it appears that recent theories regarding polar and equatorial groups and the energy considerations involved in the isomerism of decalin (8) may throw some light on the matter.

The polar-equatorial concept would lead to a prediction of greater stability for the *trans* isomer in bicyclic compounds of this type, in view of the fact that in the *cis* form, of carbons 5 and 8 in ring B, one will always be polar and one equatorial with respect to ring A, whereas in the *trans* form, as ordinarily formulated, both are equatorial with respect to A.

Substitution of a keto group in the α-position would produce two isomers of *cis*-1-decalone. Starting with the *cis*-decalin as formulated by Turner and putting the keto group in the 1 and 8 positions respectively, it can be seen from molecular models that, while the numbers of skew and staggered conformations are the same in both structures, they will appear in different positions with respect to the carbonyl. For example, in one *cis* form the staggered conformation would be found in the combinations represented by carbon atoms 1, 9, 8, 7; 3, 4, 10, 5; and 1, 9, 10, 5; in the other by 2, 1, 9, 8; 4, 10, 5, 6; and 4, 10, 9, 8. To state it in another fashion the molecule of the *cis*-decalone may be regarded as having a general contour which is curved. In one of the postulated *cis* forms the oxygen atom would slant toward the concave side and in the other it would slant toward the convex side. There is no indication as to which of these possible structures represents the known *cis*-1-decalone.

Similar considerations would exist in the case of the octalones except as modified by the presence of the double bond. Introduction of a double bond in the 7 or 6 position would replace one of the skew conformations with a double bond having the *cis* configuration, which is analogous to the unstable eclipsed conformation of a single bond. Also it would tend to flatten out one side of this ring and result in some modification of all the conformations associated with the carbons in this ring, twisting them in varying degrees away from the normal skew or staggered conformations. This twisting would be noted in both the *cis*- and *trans*-octalones, and presumably would occur to about the same extent. In view of the lack of thermal data for these intermediate conformations it is impossible to make any quantitative predictions of relative stabilities, but qualitatively it may be stated that the stable isomer is probably the *trans*, and that the unstable isomer has one of the two possible *cis* structures.

It is presumed that in the formation of these octalones, the first step is the formation of the iodo derivative, followed by elimination of hydrogen iodide. In elimination reactions of this kind the structure of the final product is the result of a number of interacting forces (9) and includes: 1. Polarizability of the carbonyl oxygen as transmitted down the chain. 2. Inductive effect of attached carbon in the same ring or in the opposite ring. 3. Hyperconjugation, which in the case of alkyl halides would tend to produce the compound with the greatest number of attached alkyl groups. 4. Base-catalyzed migration of the double bond to the most stable form. Hyperconjugation is an important factor here also in determining stability, but there must be other factors not completely understood at present.

Considering 4-iodo-1-decalone, it appears that the polarizability of the carbonyl group transmitted through two carbon atoms would favor 3 and 10 elimination of hydrogen equally, whereas the inductive effect would tend to neutralize this in 10 to a greater extent than it would in 3. However, it can be seen from the standpoint of hyperconjugation the predicted stability of the various compounds which might be formed would be $\Delta^9 > \Delta^4 > \Delta^3$. It is assumed that in this case elimination took place in the 4 position, followed by base-catalyzed double bond migration to the Δ^9 isomer.

Similar results might be expected from 5-iododecalone, although it is probable that the inductive effects would be somewhat different here due to the substituents being in different rings.

Starting with 7-iodo-1-decalone it may be noted that the polarizability of the carbonyl would lead to the formation of the Δ^7 isomer in preference to the Δ^6, owing to the greater distance of the 6 carbon atom from the electrophilic oxygen. The inductive effects would make no important difference in this instance. On the basis of hyperconjugation, the following stabilities would be predicted for the unsaturated ketones; $\Delta^6 > \Delta^7 > \Delta^8$. In view of the fact that the absorption spectra show our compound to be an unconjugated ketone, it appears that it must be either the Δ^6 or Δ^7. By analogy with the behavior of other compounds it appears unlikely that the double bond would shift more than one place. If the Δ^6 were formed first, it should remain in that form, because both the products formed by bond migration would be predicted to have less stability. Bartlett and Woods (2) have prepared a compound which they call the Δ^6. The semicarbazone of this compound does not agree in melting point with the derivatives of either our stable or unstable isomer. Furthermore, their original ketone, which they assume to be *cis*, is a solid and does not agree in physical properties with our presumed *cis* isomer. In view of the possibility of two *cis* isomers, as outlined above, there is a chance that our products could also have the Δ^6 structure, although it seems more probable that they are Δ^7.

EXPERIMENTAL

7-Methoxy-1-decalone. Approximately 0.1-mole portions of 7-methoxy-tetralone (4) in *tert*-butyl alcohol or isoheptane solution were reduced by catalytic hydrogenation in the presence of W-6 Raney nickel at 1600 p.s.i. After removal of the solvent, the crude 7-methoxy-1-decalol was oxidized directly to the ketone, using Sandborn's procedure (10) for a similar oxidation. The ether extract after washing and drying was fractionally distilled, and the 7-methoxy-1-decalone was collected at 99–103°/4 mm. In a typical experiment, from 16.4 g. of 7-methoxy-1-tetralone there was obtained 7.5 g. of the 7-methoxy-1-decalone, a 44% over-all yield.

The *7-methoxy-1-decalone 2,4-dinitrophenylhydrazone* was prepared, m.p. 138–139°.

Anal. Calc'd for $C_7H_{22}N_4O_5$: C, 56.34; H, 6.12; N, 15.47.

Found: C, 55.79; H, 5.92; N, 15.40.

Preparation of the octalone and derivatives. To 7.5 g. of 7-methoxy-1-decalone, 20 ml. of 57% hydriodic acid and 20 ml. of glacial acetic acid were added and the mixture was refluxed for 15 minutes at 95°. The hydriodic acid solution was separated from the acetic acid layer and the acetic acid was distilled off. To the residue was added an excess of alcoholic potassium hydroxide and the mixture was refluxed for 24 hours. The excess base was neutralized with dilute hydrochloric acid, the product was extracted with ether, and the

ether solution was washed with 5% sodium bicarbonate solution. After removal of the sol-
vent, the octalone distilled at 108–109°/5 mm. Yield 3.5 g. (56.5%); n_D^{25} 1.5446; ultraviolet
absorption maximum at 280 mμ; semicarbazone, m.p. 210–211°.

The *2,4-dinitrophenylhydrazone* was prepared and then purified by chromatography, us-
ing alumina as the adsorbent and ethyl acetate as the solvent and eluant. It had m.p. 219–
220°.

Anal. Calc'd for $C_{16}H_{18}N_4O_4$: C, 58.17; H, 5.49; N, 16.97.

   Found: C, *57.59*; H, *5.65*; N, *17.16*.

The stable isomer of the octalone dinitrophenylhydrazone was obtained by refluxing
the derivative (0.1 g.) of the isomeric form in ethyl acetate with a very small amount of
iodine. The compound was purified in the same manner as above. It has m.p. 231° (dec.).

Anal. Calc'd for $C_{16}H_{18}N_4O_4$: C, 58.17; N, 16.97.

   Found: C, 58.25; N, 17.08.

The semicarbazone was isomerized in the same manner. The product turned dark brown
at *214–215° but did not melt until 230–231°.*

4-Methoxy-5,8-dihydro-1-naphthol. A solution of 16.2 g. of 5,8-dihydro-1,4-naphthalene-
diol (6) and 8.0 g. of sodium hydroxide in 700 ml. of distilled water was placed in a three-
necked flask and cooled to 0–10°, and 18 ml. of dimethyl sulfate was added slowly, with
stirring over a period of about 30 minutes. At the first appearance of the crystals of the
dimethoxy derivative about 15 minutes later, the solution was diluted with distilled water
and immediately filtered to remove the dimethoxy derivative. The filtrate was neutralized
with dilute hydrochloric acid and the resulting crystals were removed by extracting the so-
lution three times with boiling petroleum ether. On cooling the petroleum ether solution,
dark crystals separated out which were further purified by recrystallizing from ethanol,
using Norit for decolorization. Yield 9.8 g. (53%) of white crystals melting at 133°.

Anal. Calc'd for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86.

   Found: C, 75.10; H, 6.92.

4-Methoxy-1-decalone. The above compound (in 0.1-mole portions) was reduced in the
same manner as was done for the 7-methoxy-1-tetralone, except that in this instance ethanol
was used as the solvent and the temperature was not allowed to rise above 125°. After re-
moval of the catalyst and distillation of the solvent there was obtained the crude decalol
mixture, b.p. 120–135°/3 mm. This was not further purified, but was oxidized directly to the
ketone as before. From 17.4 g. (0.1 mole) of the 4-methoxy-5,8-dihydro-1-naphthol there was
obtained 9.3 g. of the decalone (51.5%). This compound gave in virtually quantitative yields
a 2,4-dinitrophenylhydrazone, m.p. 171°.

Anal. Calc'd for $C_{17}H_{22}N_4O_5$: C, *56.34*; H, *6.12.*

   Found: C, 56.05; H, 5.85.

Δ^9-1-Octalone. A solution of 4.2 g. of 4-methoxy-1-decalone and 14 ml. of 57% hydriodic
acid in 15 ml. of acetic acid was boiled under reflux for 30 minutes, followed by the addition
of a large excess of dimethylaniline and continued reflux for a period of 12 hours. Dilute
hydrochloric acid was then added and the insoluble oil was separated and taken up in
ether. The ether layer was washed three times with dilute hydrochloric acid and finally
with sodium bicarbonate solution and with water. After drying over sodium sulfate, the
ether was removed and the residue was distilled under a vacuum. The octalone (1.1 g.) dis-
tilled at 85–92°/3 mm. The melting point of the 2,4-dinitrophenylhydrazone was 263°
(Literature 263°, 264°, 266.5–267°) (3). The melting point of the semicarbazone was 242–243°
(Literature 242–243°).

Measurement of the absorption spectra of this compound gave the shifts in the wave
lengths of the absorption maxima expected for a conjugated ketone (11). For the ketone
λ_{max} 237 mμ, log ϵ 3.90 (in 2,2,4-trimethylpentane); for the semicarbazone, λ_{max} 267 mμ,
log ϵ 4.36; for the 2,4-dinitrophenylhydrazone, λ_{max} 381 mμ, log ϵ 4.4 (approx., in alcohol).

SUMMARY

1. Δ^9-1-Octalone has been prepared by a new method.

2. A new non-conjugated octalone has been prepared by a similar procedure.

It has been shown to exist in two isomeric forms, the 2,4-dinitrophenylhydrazones of which were prepared. It is assumed from its method of preparation and its absorption maximum at λ 280 mμ that it must be either Δ^6- or Δ^7-1-octalone, with a slight preference for the latter due to its apparent non-identity with the previously known Δ^6 isomer.

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