# Pinacol Rearrangement of 4,5-Dimethyl-1,7-octadien-4,5diol, 4,5-Dimethyl-4,5-octanediol, and 2,3-Dimethyl-2,3-butanediol in Formic Acid

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The rearrangement of 4,5-dimethyl-1,7-octadien-4,5-diol (I) in 98 % formic acid at 31.7°C has been studied by NMR technique. The ketone formed, 3-allyl-3-methyl-5-hexen-2-one (Ia), has been identified by its NMR and IR spectra. The rate of rearrangement has been compared with the corresponding rates of 4,5-dimethyl-4,5-octanediol (II) and 2,3-dimethyl-2,3-butanediol (III). Evidence for epoxide intermediates in the pinacol rearrangement of III is presented.
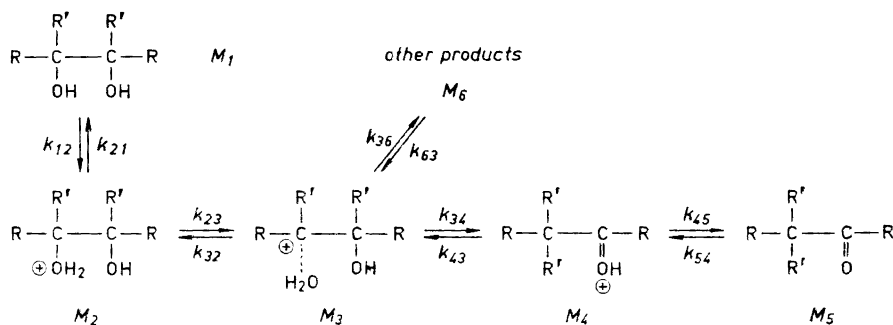
The mechanism of pinacol rearrangement is quite well known [1] (scheme 1), but few studies of the reaction of olefinic glycols in this respect seem to have been made. Glycols with the double bonds situated α, β to the hydroxy

$$I \qquad\qquad Ia \qquad\qquad Ib$$

$$II \qquad\qquad III$$
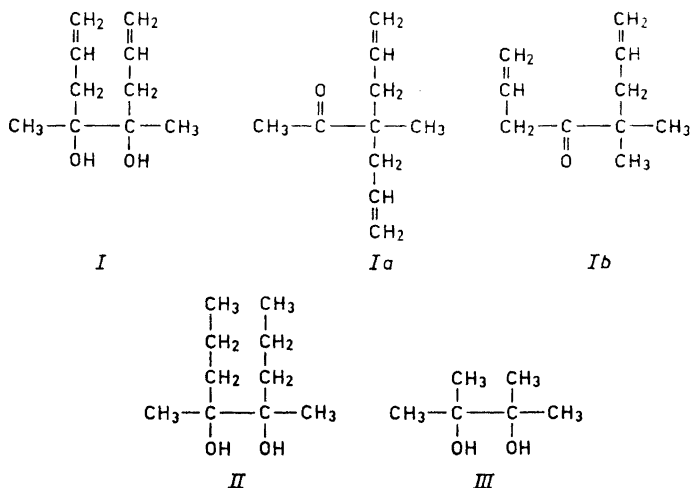
groups have been somewhat investigated, and it has been found that 3,6-substituted 2,6-octadien-4,5-diols rearrange mainly to aldehydes in acidic media.[2,3] The possibility of ring closure of unsaturated carbonium ions has been the subject of many investigations lately,[4-6] however, not in connection with the pinacol rearrangement.

The aim of this investigation has been to study the role of β,γ-double bonds in the pinacol rearrangement, with emphasis on the possibility of homo-allylic participation and carbonium ion cyclization.

The possible ways for 4,5-dimethyl-1,7-octadien-4,5-diol (I) to react in acidic media are:

R—C(R')(OH)—C(R')(OH)—R M_1 other products M_6

k_{12} ⇅ k_{21} k_{36} / k_{63}

R—C(R')(⊕OH_2)—C(R')(OH)—R $\xrightleftharpoons[k_{32}]{k_{23}}$ R—C(R')(⊕:H_2O)—C(R')(OH)—R $\xrightleftharpoons[k_{43}]{k_{34}}$ R—C(R')—C(R')(OH)(⊕)—R $\xrightleftharpoons[k_{54}]{k_{45}}$ R—C(R')(R')—C(O)—R

M_2 M_3 M_4 M_5

Scheme 1. Mechanism of the pinacol rearrangement.

a. Addition of a proton to one of the double bonds, followed by addition, either to a solvent molecule or to another double bond, leading to esters, cyclic compounds or polymers. In this study no addition of protons to the double bonds, or possible consequences thereof, could be detected when formic acid was used as solvent. A good indicium for lack of protonation of the double bonds is that the rate constant for the disapperance of the vinyl protons is the same as the rate constant for the rearrangement, showing that both these reactions probably have a common intermediate, appearing after the rate determining step. See further under kinetics.

b. Addition of a proton to one of the hydroxylic groups, followed by partial elimination of water, leading to the carbonium ion I_+.

c. Other reactions, like esterification of the diol by the solvent. No such reaction could, however, be detected.

The carbonium ion I_+ can then undergo several reactions:

1. Ordinary pinacol rearrangement by shift of (a) an allyl group or (b) a methyl group, leading to the ketones Ia or Ib.

2. Elimination of a proton, leading to a substituted allylalcohol, which should rapidly eliminate another molecule of water and give a conjugated poly-unsaturated hydrocarbon.

3. Ring closure to either a four or a five membered ring, leading to the carbonium ions $I_+{}'$ or $I_+{}''$, which can in their turn undergo several reactions. Investigations made on ring formation by carbonium ions, [5,6] indicate that five membered rings form less easily than four or six membered rings.
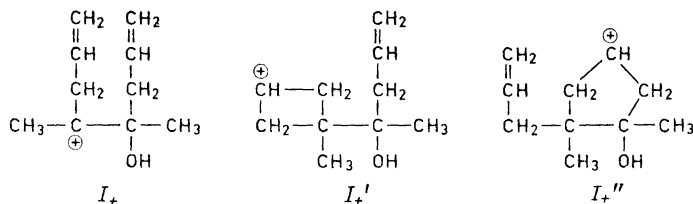
It is interesting to see that the ring in I_+'' can be reopened at the originally unsaturated bond to form the ketone I_a. Analogous reactions of β-hydroxy carbonium ions are known, especially in the rearrangements of terpene derivatives.[7] Thus the allyl shift in this pinacol rearrangement has two possible paths, *via* a three or a five membered ring (scheme 2).

4. Epoxide formation. The eventual epoxide formed, should be reprotonated and converted to a carbonium ion similar to I_+, but without a water molecule associated to the positive charge. Epoxide formation should therefore not affect the rate of disappearance of I directly, since the epoxide would not be in equilibrium with the ion I_+.
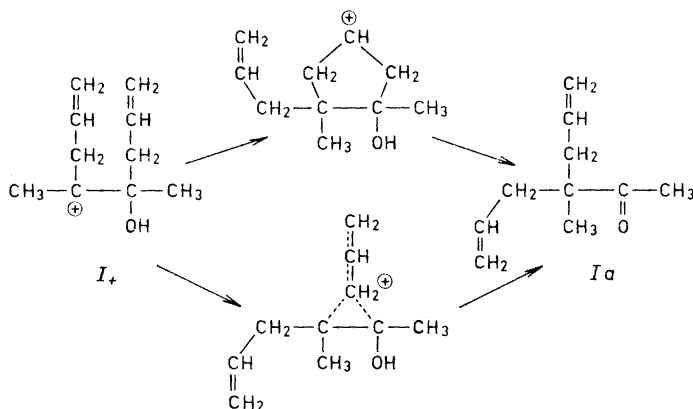
Scheme 2. Possible paths for rearrangement of I.

5. Addition to the double bond of another molecule of type I, Ia, or Ib, leading to different dimers, trimers, *etc.*

In this investigation wo have found products from the reaction paths 1a, 5, and 2. Gas chromatography of the product mixture obtained after a kinetic run gave the ketone Ia (70 %), polymers (25 %), and a minor product (5 %) which probably was an unsaturated hydrocarbon. The ketone was identified by its NMR and IR spectrum, the polymers by their long retention time in the gas chromatograph, smell and colour (brown). While the minor product could not be uniquely classified, its NMR spectrum indicated a highly unsaturated structure and the short retention time in the gas chromatograph

indicated absence of polar groups, making probable that the product was an unsaturated hydrocarbon obtained by dehydratisation of I.

No ketone of the structure Ib could be detected either in NMR during the reaction or in the product mixture separated in gas chromatography. This means that the pinacol rearrangement of the investigated stereo isomer of I (d,l) goes exclusively (more than 95 %) *via* allyl migration, the mechanism of which can be either path (or both) indicated in scheme 2.

Kinetics

a. In the reaction of I, one of the minor products showed absorbance at the same frequency as the original methyl peak ($\delta = 1.29$), which made the kinetics follow the equation $A_t = (A_0 - C) \exp(-kt) + C$, where A_0 and A_t are the areas of the corresponding peak at time zero and t, respectively, and C is the area of the product peak at infinite time.

The reaction itself is not complex, through at least three different products were identified (see above). All these products are formed at the same rate, their concentrations following the above equation with the same rate constant. This fact clearly shows that the only reaction of I is the formation of I_+, and that this step is rate determining for the whole reaction chain of further transformations of I_+. A run with the initial concentration of I at 0.7 M instead of 1.45 M gave the same rate constant, showing that the reaction is first order in pinacol. A run with an additional water concentration of 0.025 g/0.5 ml also gave the same kinetics, which showed that the water produced during the reaction has small influence on the reaction. Fitting of the experimental data to the above kinetic equation gave a rate constant of 0.31×10^{-3} min$^{-1} \pm 7$ %.

b. The reaction of II also followed the above equation, indicating first order behaviour. The NMR spectra recorded during the reaction showed that the pinacol rearrangement was the only reaction, thus no product separation was attempted. It is, however, possible that minor amounts (less than 5 %) of elimination products were masked in NMR by the produced ketones. During the reaction the original methyl groups disappear, and three new methyl and one new saturated methylene group appear at the same rate, again showing the existence of only one rate determining step preceeding the product forming steps. The new peaks are due to the two ketones obtained by propyl and methyl migration, they are formed in the approximate proportion 2:1. No conclusions may be drawn from this quotient since the investigated pinacol II is a mixture of the two forms D,L and *meso*, and it has been shown [8] for related reactions that the two forms give different products. From the first order behaviour of the kinetics it can be seen, however, that the two stereoisomers react at the same effective rates, thus making it possible to make some comparison of the observed reaction rates of I, II, and III. The observed rate constant for the reaction of II is 5.0×10^{-3} min$^{-1} \pm 7$ %.

c. The reaction of III is also a clean pinacol rearrangement as seen from the NMR spectra and the first order disappearance of III. No elimination products could be detected, the only unexpected phenomenon was the gradual appearance of a new broad peak at $\delta = 1.60$, which after one halflife of the reaction began to disappear again. The peak probably is due to small amounts of epoxide (the shift agrees well with the expected value for a methyl group on an epoxide ring [9]). The present author cannot imagine any other possible product or intermediate having only one peak in NMR. The epoxide is then reprotonated and opened to form a carbonium ion similar to M_3, however without the attached water molecule. The mechanism of the reaction of III is summarized in scheme 3. If the epoxide were in a true equilibrium with the ion M_3, the kinetics of the disappearance of III would no longer be first order and the formation of the ketone would follow the same kinetics as the disappearance of III. In this investigation, however, only the disappearance of III followed first order kinetics (with the rate constant 0.73×10^{-3} min$^{-1} \pm 4$ %), while the formation of the ketone followed the more complicated equation $A_i = A_1 \exp(-kt) + A_2 \exp(-k't) + C$. The formation of epoxide follows the same type of equation with the same rate constants but different values for the other parameters. From the parameters A_1, A_2, and C of the epoxide and ketone kinetics it can be estimated that of every three ions M_3, two react to ketone via epoxide and one directly to ketone without any long lived intermediate. The rate constant k of these equations is the same as that of the disappearance of III (0.73×10^{-3} min ± 4 %) while k' (the rate of destruction of the epoxide) is estimated to be 1.70×10^{-3} min$^{-1} \pm 8$ %. A detailed treatment of this type of kinetics is given by Frost and Pearson,[10] the numerical treatment has been made with the method of Gauss.[11,12]
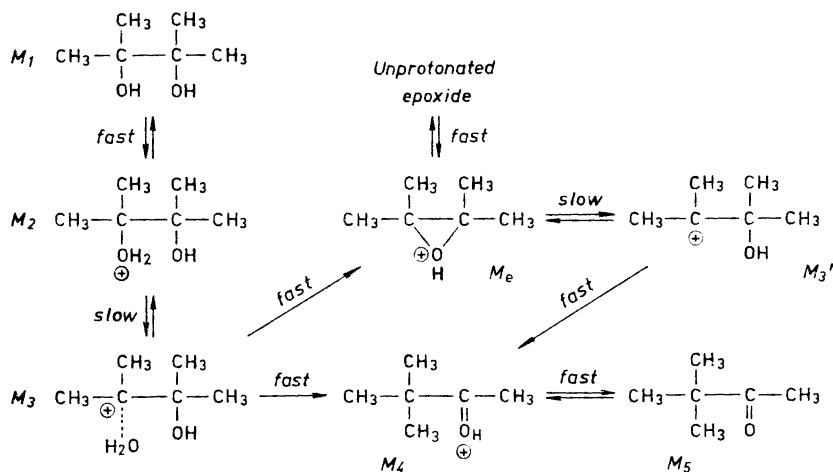
Scheme 3. Rearrangement of pinacol (III) in HCOOH.

DISCUSSION

The pinacol I undergoes pinacol rearrangement at a smaller rate than its saturated analog II. In the reaction, I shows exclusive allyl migration, while II reacts with both propyl and methyl migration. The pinacol I probably is pure D,L (see below), while the pinacol II is a mixture of *meso* and D,L forms. This makes definite explanations of the preferred allyl migration uncertain; it is possible that the reason is purely sterical. It is hoped that future investigations on pure isomers of II and the other isomer of I will clarify this point. The rate difference in the reactions of I and II is also hard to explain, especially since the effective rate constant k_{obs} is a function of considerable complexity:[1]

$$k_{obs} = K\ a_H\ k_{23}(k_{34}+k_{36})/(k_{32}+k_{34}+k_{36})$$

where K is the equilibrium constant for protonated/unprotonated pinacol, a_H is the hydrogen ion activity, the other constants are those of scheme 1.

It is the hope of the author that further investigations, including a study of the effects of substitution on the allyl groups will be of some help in clarifying the role of the double bonds in the pinacol rearrangement.

The formation of epoxide in the reaction of III was not expected; epoxides have been thought to appear only in the pinacol rearrangement of aromatic or highly hindered pinacols.[1,13]. It is possible that epoxides are intermediates also in the reactions of I and II, the uncertainty in the rate constants is, however, too large to distinguish between first order formation of the ketones and formation by the equation with two exponentials. Absorbance by products (in the case of I) and propyl groups (in the case of II) in the region where epoxide absorbance is expected makes direct observance of the eventual epoxide in NMR very difficult for the reactions of I and II. The high proportion of epoxide formation in the reaction of III suggests, however, that the role of epoxides as intermediates in the pinacol rearrangement has been underestimated.

EXPERIMENTAL

Synthesis. 4,5-Dimethyl-1,7-octadien-4,5-diol (I) was synthesized from 2,3-butandione and allyl magnesium bromide,[14] and recrystallized to constant melting point (2−3 times) from light petroleum; m.p. 68−69°C, lit.[14] value: 70.7°C. According to Cram's rule,[15] this route should lead to the D,L isomer, the IR spectrum confirms this assumption (see below).

4,5-Dimethyl-4,5-octanediol (II) and 2,3-dimethyl-2,3-butanediol (III) were made by ordinary pinacol synthesis from 2-pentanon and acetone, respectively, and purified by distillation; b.p. 106−108°C/8 mm Hg, lit.[17] value 116−117°C/15 mm Hg, m.p. 55−70°C, lit.[17] value 62°C and 95°C (II) and b.p. 172−173°C, lit.[18] value 174.3 (III). IR and NMR spectra showed no impurities.

IR spectra. The IR spectrum of I showed two OH peaks at 3610 cm⁻¹ (very weak) and 3555 cm⁻¹ (strong). This agrees with the D,L isomer, which is expected to show strong intramolecular hydrogen bonding and thus give a weak free OH peak.[19] I also gives absorption at 3070 cm⁻¹ (unsaturated C−H), 2970 and 2935 cm⁻¹ (saturated C−H), 1650 cm⁻¹ (C=C), and several peaks in the finger print region.

II gives a similar IR spectrum, though at least three peaks in the OH region can be seen, at 3615 cm^{-1} (medium), 3605 cm^{-1} (weak), and 3555 cm^{-1} (medium). This suggests that II is a mixture of D,L and *meso* forms; neither of the forms would absorb at more than two frequencies in the OH region.[19]

The ketone isolated from the product mixture obtained from a kinetic run starting with I in formic acid gave an IR spectrum fully consistent with the postulated structure Ia. Outside the finger print region absorbance was obtained at 3070, 3060, and 3020 cm^{-1} (unsaturated $C-H$), 2960, 2935, and 2915 cm^{-1} (saturated $C-H$), 1700 cm^{-1} (strong) (carbonyl), and 1660 cm^{-1} ($C=C$).

The small amount of minor product isolated from the kinetic run was not enough to record its IR-spectrum.

All the spectra were taken with solutions in CCl_4, 0.1 mm cells, and IR-spectrometers of type Perkin Elmer 237 and 257.

NMR spectra. In formic acid I shows a singlet (methyl) at $\delta = 1.29$, a multiplet of at least 7 peaks (CH_2) centered at $\delta = 2.45$, and an ordinary vinyl multiplet of high complexity between $\delta = 5.05$ and $\delta = 6.42$. The areas of the peak groups have the expected relative values of 3:2:3. In CCl_4 and benzene the hydroxyl protons can be seen in the CH_2 multiplet, all protons have thus been accounted for.

The NMR spectrum of II is very simple. In formic acid there is a methyl singlet at $\delta = 1.28$, a CH_2 multiplet centered at $\delta = 1.57$ and a methyl multiplet centered at $\delta = 0.95$. The relative areas are 3:4:3, respectively. In CCl_4 and benzene the hydroxyl protons can again be seen.

III in formic acid shows a single methyl peak at $\delta = 1.37$. In CCl_4 or benzene the hydroxyl protons also give a singlet. These NMR spectra agree well with the NMR spectra of III and other pinacols, investigated by Depovere and Devis.[20]

During the reaction of I in formic acid, the NMR spectrum changes in the following way: The methyl peak at $\delta = 1.29$ cps disappears and two new singlets at $\delta = 1.17$ and $\delta = 2.27$ appear. These new peaks obviously are due to the two different methyl groups in the ketone Ia. Other changes in the spectrum are less drastic. The vinyl protons gradually disappear due to polymerization, but $75-80$ % of the unsaturated protons are left unaffected. The saturated CH_2-protons disappear at the same rate as the vinyl-protons. This could, however, be due to difficulties in bookkeeping of the increasing, almost continuous absorption between $\delta = 1.32$ and $\delta = 1.87$, which probably mainly arises from saturated protons in polymer products. This absorption, together with similar complex absorption between $\delta = 0.67$ and $\delta = 1.10$ (due to methyl groups in polymers), never goes over 20 % of the total proton absorption (as counted from the integrated areas).

The NMR spectrum of the main product isolated from the reaction mixture after the kinetic measurements agreed well with the structure of Ia. In CCl_4 there were two singlets at $\delta = 1.07$ and 2.03 corresponding to the methyl groups, a multiplet (octet) at $\delta = 2.21$ corresponding to the saturated CH_2 groups, two multiplets centered at $\delta = 4.88$ and $\delta = 5.10$ corresponding to the CH_2 vinyl protons, and a multiplet situated between $\delta = 5.08$ and $\delta = 6.08$ due to the single CH vinyl proton.

The NMR spectrum of the minor product in pyridine was of low quality, due to low concentration. Expect for a large CH_2=peak and a small $-CH$=multiplet, it showed only one peak at $\delta \approx 4.0$. The approximate relative values of the peaks were 10:2:5 ($CH_2=:-CH=:?$), indicating that the product is highly unsaturated.

The reaction of II in formic acid is easier to follow in NMR. Only two products can be detected. One is the ketone formed by propyl migration, showing two methyl singlets, one at $\delta = 2.26$, the other one at either $\delta = 1.15$ or $\delta = 1.12$. The two latter peaks cannot be assigned to either of the ketones since they have the same area and grow with the same rate all through the reaction. However, the other ketone, formed by methyl migration, shows a triplet centered at $\delta = 2.62$ with a coupling constant of 7 cps. This is due to the methylene group adjacent to the carbonyl group; its methyl singlet should be the one at $\delta = 1.12 - 1.15$ not belonging to the other ketone.

The reaction of III in formic acid shows only one product, pinacolone, with two singlets, one at $\delta = 2.28$ (methyl at carbonyl group) and one at $\delta = 1.18$ (tert. butyl group), in good agreement with the values found by Depovere and Devis.[20]

All δ values are expressed in ppm, and refer to TMS as internal standard. The NMR spectra were recorded on a Varian A 60 A spectrometer.

Kinetic method. The reactions were studied in 98 % formic acid (Hopkin and Williams Ltd., London, purity grade ANALR) at 31.7°C. The pinacols (ca. 0.025 g) were mixed with 0.5 ml formic acid in an NMR tube and thermostated at 31.7°C. After suitable time intervals the NMR spectrum of the reaction mixture was recorded (probe temperature 31.7°C) and the tube put back into the thermostat again.

The rate constants were calculated by Gauss' non-linear least squares method [11,12] from the time dependence of the area of the different peaks in NMR, assuming that these areas are proportional to the concentrations of the corresponding molecular species.

Isolation of products. No attempts were made to isolate products from the reactions of II and III since the NMR spectra taken during the reactions can only be interpreted in one way (see above) and the products are well known.

The products from the reaction of I in formic acid were isolated in the following way. The reaction mixture from a kinetic run was shaken with water and ether. The ether phase was dried with sodium sulphate and run through a preparative gas chromatography column (Perkin Elmer F 21, column length 2.7 m, diameter 8 mm, filling 12.3 % Sulfosoft from Berol AB, Sweden, main constituent sodium dodecyl-benzene-sulfonate, on Chromosorb W,AW, 80 mesh). Three peaks in addition to the ether peak were detected. One was identified as due to polymeric material (retention time 4 min with column temp. 230°C), another to the ketone Ia (retention time 2.5 min, column temp. 180°C). The vapour giving rise to this latter peak was lead through a cold trap; the content in the trap after 20 consecutive runs was washed out with CCl_4 and studied in IR and NMR (see above). The third peak, appearing just before the ketone peak, (retention time 2.1 min, column temp. 180°C) was also collected in a trap. The amount of this product, however, was so small that it could not be uniquely identified.

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