Pinacol Rearrangement of 3,4,5,6-Tetramethyl-1,7-octadien-4,5-diol in Formic Acid

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The rearrangement of 3,4,5,6-tetramethyl-1,7-octadien-4,5-diol (I) in 98 % formic acid at 31.7°C has been studied by NMR technique. The two ketones formed, 3,4-dimethyl-3-(1-buten-3-yl)-5-hexene-2-one (Ia) and 3,5,5,6-tetramethyl-1,7-octadien-4-one (Ib), have been identified by their NMR and IR spectra. Only normal pinacol rearrangement has been observed; the butenyl group rearranges without any trace of 1,3-shift.

R ecently the pinacol rearrangement of 4,5-dimethyl-1,7-octadien-4,5-diol (II) in formic acid was investigated.[1] The rearrangement of II was found to be slower than that of the corresponding saturated pinacol and was found to react with 100 % allyl migration. The pinacol II has two possible ways of rearrangement *via* a three or five ring transition state (or intermediate). The pinacol I has been synthesized and rearranged in order to examine whether the rearrangement of an allylic system in the pinacol rearrangement proceeds *via* the expected normal path (Fig. 1, path a) or by the 1,3 shift (Fig. 1, path b). Since I is "marked" with a methyl group in the allylic systems, product analysis can differentiate between the two paths.

KINETICS

The reaction of I was studied by the NMR technique. The rate constant of the first order reaction was computed from the decrease of the methyl peak of I, from the increase of the methyl peaks of Ia and Ib, and from the methine peak of Ib at $\delta = 3.55 - 4.30$. The rate constants thus computed all agree within the experimental accuracy, and were found to be 2.5×10^{-3} min$^{-1} \pm 8$ %. These rate constants are considerably larger than the corresponding rate constant of II which was 0.31×10^{-3} min$^{-1} = 7$ % (all values refer to 31.7°C). The rearrangement of I proceeds with about 20 % methyl migration to give Ib and about 80 % butenyl migration to give Ia. The relative amounts are
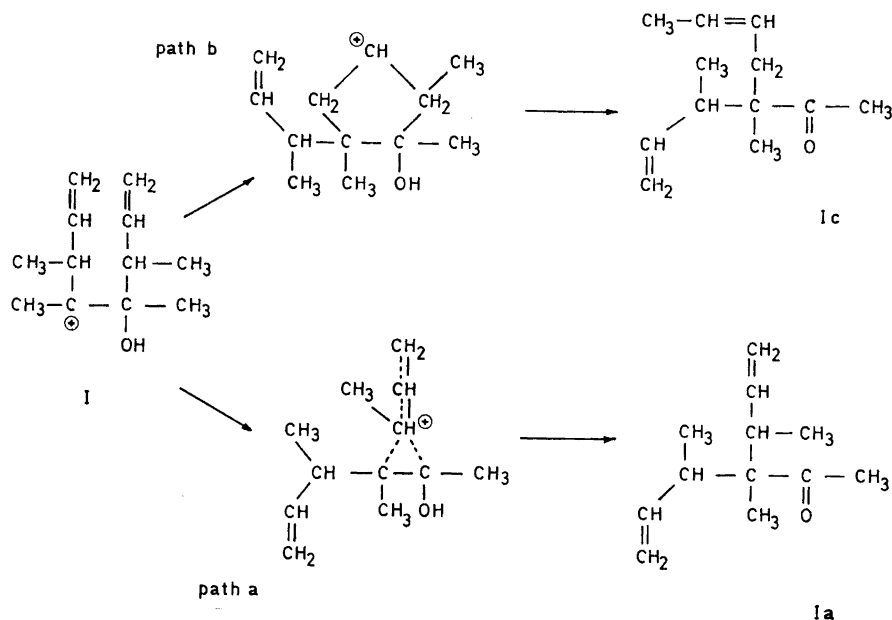
path b

CH₃—CH=CH

[Fig. 1 chemical structures — pinacol rearrangement scheme showing path a and path b, with intermediates and products Ia and Ic]

Ic

I

path a

Ia

Fig. 1.

obtained from the NMR spectrum of rearranged I and gaschromatographic analysis of this mixture. Both methods of analysis give the same results.

[Chemical structures: compound I, Ia, and Ib with numbered carbons]

I

Ia

Ib
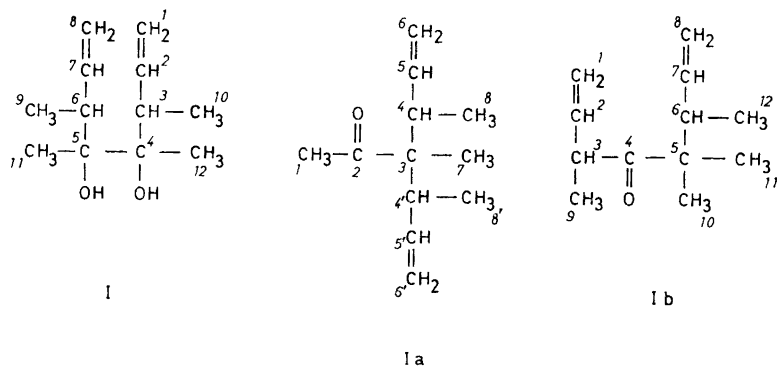
DISCUSSION

The products of the rearrangement of I in formic acid all arise from the normal path (Fig. 1, path a). From the NMR and gaschromatographic analysis of the product mixture, it is seen that the only ketones produced are Ia and Ib. It is thus concluded that allylic systems rearrange *via* three ring transition states in the pinacol rearrangement in formic acid.

The differences in rate and specificity of rearrangement between I and II and the saturated analog of II are interesting since they allow some general conclusions concerning the mechanism of pinacol rearrangement. The introduction of a double bond at β, γ-positions to the hydroxyl groups has two effects. The first is to slow down the total rate of reaction. In some way, the pinacol is stabilized as compared with the carbonium ion like transition state. The other effect is to accelerate the rearrangement of the allylic group as compared with the methyl group. This effect can probably be described as a homoallylic resonance stabilisation of the transition state of the rearrangement step.

The introduction of methyl groups in the allylic systems on going from II to I also has two consequences. Firstly the total rate of reaction is increased. The best explanation for this is in terms of an increased steric strain in the pinacol. This leads to an increased amount of released backstrain on going from the pinacol to the carbonium ion like transition state. The second effect is to decrease the selectivity of rearrangement. II rearranges with 100 % allyl migration and I with 80 % butenyl migration. This can be rationalized as an increased steric strain on the rearrangement terminus making it relatively more difficult for large bulky groups to migrate than for small groups which can more easily sneak into a crowded neighbourhood. This phenomenon has been studied in some detail by Dubois and Bauer [2] who found pronounced effects between the relative migratory aptitudes of ethyl and methyl groups when substitutions were made on the rearrangement terminus. Contrary to the suggestion of Stiles,[4] it can be concluded that the pinacol rearrangement proceeds without any neighbouring group participation by the alkyl groups. Any such acceleration would necessarily lead to a parallelism between reaction rate and specificity of rearrangement. This is found in all earlier investigations of alkyl pinacols,[3,4] but has obviously been due to parallel steric and electronic effects. However, this investigation clearly shows that an acceleration of the total reaction need not lead to increased specificity of rearrangement. Thus, the possibility of neighbouring group participation by the alkyl groups is ruled out. Bartlett and Tidwell [5] have drawn the same conclusions from their investigation of highly branched p-nitrobenzoates.

The above conclusions all support the accepted mechanism of the pinacol rearrangement [3] as being a Wagner-Meerwein like carbonium ion reaction where the total rate of reaction is not primarily affected by the migratory ability of the different alkyl groups.

EXPERIMENTAL

Synthesis. 3,4,5,6-Tetramethyl-1,7-octadien-4,5-diol (I) was synthesised analogously to II [1] from 2,3-butandione and crotyl magnesium bromide, and was distilled twice at reduced pressure. The b.p. was 117—122°C (10 mm Hg). IR and NMR spectra, and quantitative analysis all agree with the structure I. The product is proposed to be the D,I form with respect to atoms 4 and 5 (see IR spectra). This form is also expected from the rule of Cram.[6] The product is a mixture of different diastereomeric isomers differing in configuration on atoms 3 and 6. No attempt has been made to separate these diastereomers.

IR spectra. I. The IR spectrum of I shows two OH peaks at 3615 cm^{-1} (very weak) and at 3550 cm^{-1} (strong). This indicates that the obtained isomer mixture has D,L

configuration with respect to the atoms 4 and 5. These isomers should have strong intramolecular hydrogen bonding which would give a weak free OH peak.[1,7] I also absorbs at 3070 cm^{-1} (unsaturated C—H), 2970, 2925, and 2870 cm^{-1} (saturated C—H), 1630 cm^{-1} (C=C) and at several positions in the finger print region.

Ia. Ia shows the same C—H stretching peaks as I at 3070, 2970, 2930, and 2870 cm^{-1}, and a carbonyl peak (strong) at 1700 and 1697 cm^{-1}. The splitting is probably caused by the different diastereomeric forms differing in configuration in the butenyl groups on atoms 4 and 4'. The C=C stretch is observed at 1632 cm^{-1} and there are several bands at lower frequencies.

Ib. The IR spectrum of Ib is very similar to that of Ia. The C—H stretches appear at 3070, 2965, 2925, and 2865 cm^{-1}, the carbonyl peak at 1702 cm^{-1} and the C=C stretch at 1632 cm^{-1}. The finger print region is also very similar; the peaks are different only in intensity and in a few cm^{-1} in frequency.

All the spectra were taken on solutions in CCl$_4$, 0.1 mm cells on a Perkin Elmer 257 IR-spectrometer.

NMR spectra. In formic acid, I shows a methyl peak at $\delta = 1.28$. This peak shows a narrow splitting into three peaks. This splitting is caused by the different configurations around atoms 3 and 6. The butenyl methyl groups give rise to a doublet centered at $\delta = 1.11$ with a coupling constant of 7 cps. The methine protons appear as a multiplet between $\delta = 2.37$ and $\delta = 3.13$, and the vinyl protons as two complicated multiplets between $\delta = 4.87$ and $\delta = 6.58$. The areas of the peak groups have the expected relative ratios of 3:3:1:3. In CCl$_4$ and benzene the hydroxyl protons show up as a broad, incompletely resolved multiplet between the C—H multiplet and the CH$_3$ peaks.

The NMR spectrum of the ketone Ia in CCl$_4$ shows that Ia is a mixture of meso and D,L forms. The butenyl methyl groups (atoms 8 and 8') give two doublets at $\delta = 0.89$ and $\delta = 0.93$, and they both have a coupling constant of 6.7 cps. The methyl group (atom 7) situated on the same carbon as the butenyl groups (atom 3) gives two peaks at $\delta = 1.07$ and $\delta = 1.09$, and the methyl group (atom 1) on the carbonyl group gives two peaks at $\delta = 1.98$ and $\delta = 2.00$. The methine protons (on atoms 4 and 4') give a multiplet centered at $\delta = 2.53$ and the vinyl protons give an ordinary pattern between $\delta = 4.68$ and $\delta = 6.07$. The peak areas (relative) have the expected ratios 6:3:3:2:6.

The spectrum of Ib in CCl$_4$ also shows that Ib is a mixture of two diastereomers. The methyl groups in the butenyl groups, however, have different chemical shifts. One (number 12) gives two doublets at $\delta = 0.89$ and $\delta = 0.92$ and both have a coupling constant of 6.7 cps; the other (number 9) gives two doublets at $\delta = 1.07$ and $\delta = 1.10$ with coupling constants of 7 cps. The two methyl groups on carbon number 5 (10 and 11) give two peaks situated at $\delta = 1.01$ and $\delta = 1.03$. The methine protons give two multiplets centered at $\delta = 2.50$ and $\delta = 3.58$, and the vinyl protons give the ordinary pattern between $\delta = 4.76$ and $\delta = 6.03$. The peak areas have the relative ratios 3:3:6:1:1:6 in the order mentioned above.

In formic acid, the ketonic methyl group (Ia, atom 1) appears at $\delta = 2.22$, and the corresponding methine group of Ib (atom 3) appears at $\delta = 3.88$. The rate constants can be evaluated from the time dependence of the areas of these peaks.

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

Kinetic method. The method used was the same as in the investigation of II.[1] Thermostated NMR tubes were used and the spectra were recorded at a probe temperature of 31.7°C. The rate contants were calculated from the time dependence of the area of the different NMR peaks. First order behaviour of the concentrations, and proportionality between the NMR integrals and the concentrations of the corresponding molecular species were assumed. The formic acid was purchased from Hopkins and Williams Ltd., London, (purity grade ANALR, 98 %) and was used without further purification.

Isolation of products. 1 g of I was dissolved in formic acid, thermostated at 31.7°C for 48 h, diluted with water and then was extracted with ether. The ether phase was dried and then was subjected to fractional distillation under reduced pressure. The ketonic fraction (b.p. 42—48°C, 0.4 mm Hg) was then 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). Except for the peak of unreacted

pinacol, only three peaks could be seen. The first was very small, and was thought to be due to unsaturated hydrocarbons. The other two peaks, containing more than 99 % of the products were collected in separate cold traps and subjected to NMR, IR, and elementary analysis, which all confirmed the structures Ia and Ib. The retention times for the different peaks were: peak 1 (believed to be elimination product) 2 min 20 sec, peak 2 (ketone Ib) 2 min 55 sec, peak 3 (ketone Ia) 4 min 10 sec, with a column temperature of 180°C.

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