

ISOMERIZATION OF 2,5-DIVINYLTETRAHYDROPYRAN AND ACID-CATALYZED REARRANGEMENTS OF ISOMERIC NOVEL DIHYDROPYRANS

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Abstract—2,5-Divinyltetrahydropyran (1) can be isomerized using a ruthenium trichloride-triphenylphosphine catalyst to give 3,4-dihydro-3-vinyl-6-ethyl-2H-pyran (2) and 3,4-dihydro-3-ethylidene-6-ethyl-2H-pyran (3). These products give a variety of rearranged products on treatment with acid. The course of the reactions can be controlled by reaction conditions to give 4-ethyltoluene (5) or 3-hydroxymethyl-1-octen-6-one (4) from 2, and 3,4-dihydro-2-methyl-3-methylene-6-ethyl-2H-pyran (7), 2,3,4-trimethyl-2-cyclohexen-1-one (8), or 3-hydroxymethyl-2-octen-6-one (6) from 3. All of these products (4-8) can be explained as arising by the initial opening of the dihydropyran to generate an unsaturated hydroxy ketone which then cyclizes to carbocyclic products.

The transition metal catalyzed condensation of butadiene with formaldehyde or acetaldehyde has provided a convenient one-step synthesis of 2,5-divinyltetrahydropyrans in excellent yields.¹⁻³ In view of the ease of preparation of the pyrans, the synthetic utility of 1 was studied with emphasis on rearrangements and transformation.

The double bonds of the tetrahydropyran 1 and other telomerization products of butadiene are highly resistant to isomerization by the palladium-phosphine catalyst used in their formation. We now wish to report isomerizations of 1 with ruthenium catalyst and acid-catalyzed rearrangements of the resulting isomerization products.

RESULTS

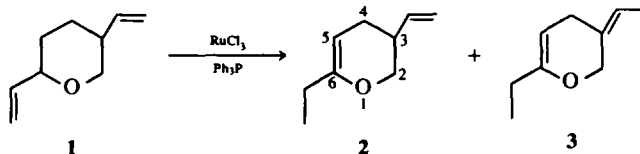
Isomerization. On heating for 1 h with catalytic amounts of ruthenium trichloride and triphenylphosphine (1:4 mole ratio) in refluxing dimethylformamide, the tetrahydropyran 1 was quantitatively converted into an isomeric mixture of 3,4-dihydro-3-vinyl-6-ethyl-2H-pyran (2) and 3,4-dihydro-3-ethylidene-6-ethyl-2H-pyran (3) in 20 and 80 per cent yields,[†] respectively. After heating at reflux

for 3 h, over 90 percent of the product was the thermodynamically more stable isomer 3. The two isomers were separated by fractional distillation and identified by means of IR and NMR techniques.

Compound 2, b.p. 46°/10 mm exhibited peaks at 1656, 1623 and very intense peaks at 995 and 922 cm⁻¹. These are consistent with the presence of double bonds, one being vinylic. This was confirmed from its NMR spectrum which indicated the presence of an ethyl group on an unsaturated carbon and an exocyclic vinylic group. The olefinic hydrogen at C₃ absorbs at δ 4.39, a triplet (*J* = 3.0 Hz). This higher field absorption is typical of β-protons of vinylic ethers. The methylenes at C₂, adjacent to oxygen, exhibit peaks centered at δ 3.55 and δ 3.98 with a geminal coupling of *J*_{AB} = 10.5 Hz. The proton absorbing at a higher field displays an ABX triplet splitting pattern (*J*_{AX} = 9.0 Hz). The lower field proton is a multiplet (*J*_{BX} = 3.5 Hz) with a long range coupling (*J* = 1.0–1.5 Hz). The large coupling *J*_{AX} is indicative of axial-axial coupling.

Compound 3, b.p. 62°/10 mm, also exhibited IR peaks at 1653 and at 890, 925, 960, and 985 cm⁻¹ due to the double bonds. The absence of the vinylic protons in the NMR indicated that the second vinylic group of 2 had also isomerized. A broad quartet (1H) at δ 5.41 in conjunction with the doublet (3H) at δ 1.62 having identical coupling constants (*J* =

[†]The composition of the mixture 2 and 3 was determined by GLC analysis using 6 ft × 1/8 in. 10% UCON W-98 on 8-100 mesh supersupport column.



7.0 Hz), indicates the presence of an exocyclic ethylidene group. A multiplet at δ 4.37 (2H) is assigned to the methylene adjacent to the oxygen. This shift is considerably downfield relative to the corresponding methylene in compound 2, and is attributed to the deshielding effect of the adjacent double bond. The ring olefinic proton absorbs at δ 4.18 as a singlet with some fine splitting. The doubly allylic ring methylene (C₄) absorbs as a multiplet at δ 2.64.

Acid-catalyzed rearrangements of 2 and 3. Unlike compound 1 which is extremely stable to acid treatment, compounds 2 and 3 undergo facile ring opening on treatment with dilute acids—a reaction typical of dihydropyrans. Depending on acid concentration and temperature, the resulting ring-opened hydroxy-ketones can be made to undergo further rearrangements.

When compound 2 was heated with 25 percent sulfuric acid at 100°C for 3 h, it was converted into *p*-ethyltoluene (5) in excellent yield (IR and NMR identical with an authentic sample). Under milder

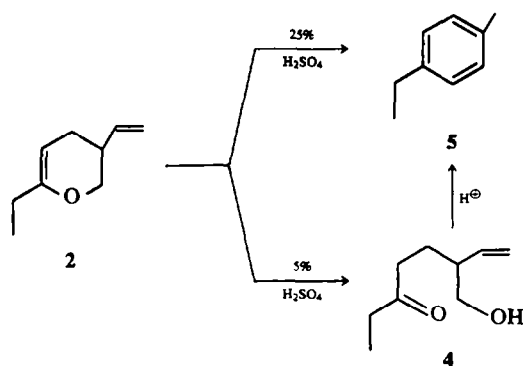
conditions, i.e., heating with 5 percent sulfuric acid, the expected ring-opened hydroxy-ketone (4) was obtained in the crude form. Attempts at purifying by distillation caused it to cyclize and revert to the starting dihydropyran 2. Further treatment of 4 with stronger acid yielded the aromatized product 5. The IR of 4 showed the hydroxyl and carbonyl peaks and the presence of the vinylic protons was confirmed by NMR.

In the presence of 25% sulfuric acid at 100°, 3 rearranged, in excellent yield, to 2,3,4-trimethyl-2-cyclohexen-1-one (8),* while at ambient temperature in 5 percent acid, the open-chain hydroxy ketone 6 was obtained. Upon distillation 6 reverted to the starting dihydropyran 3. When 3 was heated with 5 percent acid for 2 h, to our surprise, yet another intermediate was formed in addition to compound 8. This intermediate, isolated by distillation, was identified as 3,4-dihydro-2-methyl-3-methylene-6-ethyl-2H-pyran (7). The exocyclic methylene absorbed at δ 4.85 as a partially resolved singlet. This value is in agreement with the value of δ 4.90 reported by Ooba⁴ for a compound of similar structure. The secondary methyl appeared as a doublet at δ 1.30, $J = 6.0$ Hz. The rest of the spectrum was consistent with the proposed structure. On further treatment with stronger acid, compound 7 was converted to 8.

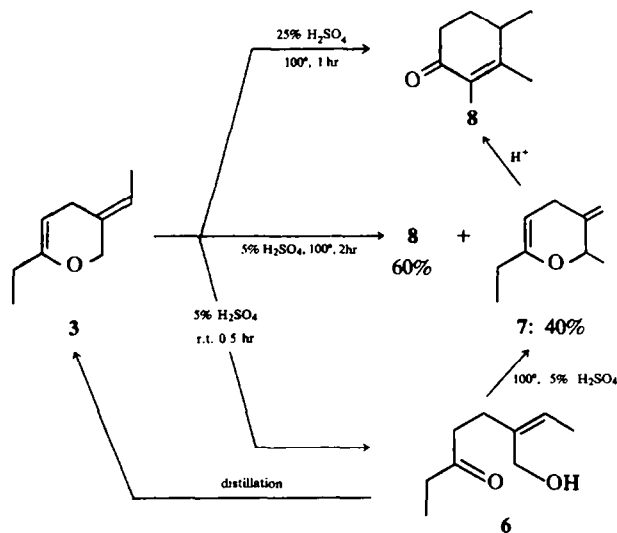
Compound 8 showed the presence of a conjugated carbonyl at 1650 cm⁻¹. The NMR spectrum exhibited a doublet for the secondary methyl at δ 1.17 with $J = 6.5$ Hz. The methyls on the double bond appeared at δ 1.65 and 1.88, with the rest of the protons absorbing as a broad multiplet between δ 1.30 and 2.80, with no absorption below δ 3.0.

DISCUSSION

The facile aromatization of compound 2 to *p*-ethyltoluene (5) can be schematically portrayed by



*Identical with the authentic sample obtained from T. S. Sorenson, *Can. J. Chem.* 50, 3550 (1972).



the sequence of reactions shown in Scheme 1.

The cyclization 4 to 4a leading to 5 bears a close analogy to the cyclization of α -methylheptenone to dihydro-*m*-xylene *via* 1,3-dimethylcyclohexan-1,3-diol reported by Meinwald.³ Protonation of the carbonyl of 4 followed by cationic olefin cyclization and subsequent proton loss would yield the doubly allylic cyclohexene diol 4a. In 25 percent sulfuric 4a would spontaneously dehydrate to yield 5. It is possible that the formation of an intermediary triol may also be involved but this would also rapidly dehydrate to yield the product.

A plausible mechanistic pathway leading to 6, 7, and 8 can be depicted as in Scheme 2. The formation of the dihydropyran 7 from 3 under mild acid treatment reflects the stability of the secondary allylic carbonium ion leading to allylic alcohol 6a *vs* the primary allylic ion obtained from 6.

At this stage it is not possible to ascertain the extent of reaction *via* pathway B. It is unlikely that the secondary allylic alcohol 6a reverts to the primary allylic alcohol 6 to follow exclusively path B, but this cannot be entirely excluded from the limited experimental facts.

Finally, it is mechanistically noteworthy that only six-membered carbocyclic products are

formed in these transformations and that each dihydropyran rearranges specifically to a single final product. The rearrangement of 3 to 8 appears to be a better synthetic route to 8 than the only other known method, *via* the alkylation of Hagemann's ester.

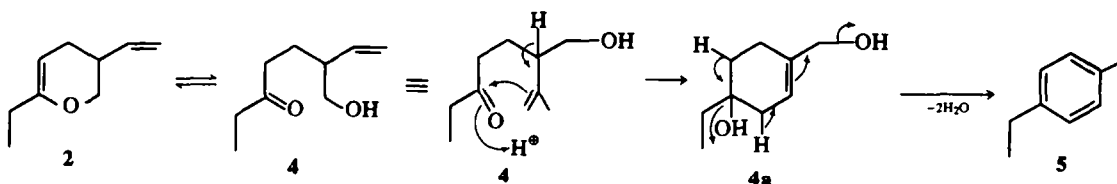
EXPERIMENTAL

M.ps and b.ps are uncorrected. NMR spectra were taken either neat or in CCl₄ on a 60 MHz Varian A-60 spectrometer.

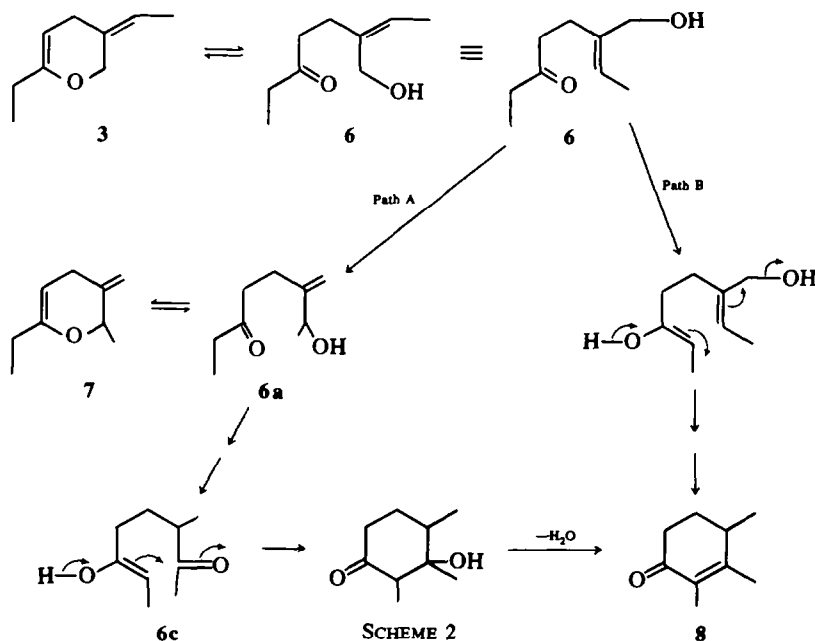
Isomerization of 2,5-divinyltetrahydropyran (1). In an atmosphere of N₂, ruthenium trichloride hydrate (3 mmoles) and triphenylphosphine (12 mmoles) were added to a flask containing 400 ml of DMF. The mixture was heated under reflux (for 10 min) until the solids dissolved. After cooling to 100°, 2,5-divinyltetrahydropyran (300 g) was added. The mixture was again heated under reflux for 1 h. On cooling it was washed with water and dried. GLC analysis indicated complete conversion to 2 and 3 in the ratio of 1:4. Distillation yielded 60 g of 2 b.p. 46°/10 mm and 152 g of 3 b.p. 62°/10 mm.

Compound 2 IR (neat) 3030 ($\text{C}=\text{C}-\text{H}$), 2857, 1656,

1623 ($\text{C}=\text{C}$), 1449, 1235, 1170, 1093, 1067, 1041, 995, 922, 971, 809 and 763 cm^{-1} . NMR (CCl₄) δ 0.99 (t, $J = 7.0$ Hz, 3H); 1.98 (m, 4H); 2.4 (m 1H), 3.55 (q, $J_{AB} = 10.5$ Hz,



SCHEME 1



SCHEME 2

$J_{AX} = 9.0$ Hz), 3.98 (m, $J_{AB} = 10.5$ Hz, $J_{BX} = 3.5$ Hz), 4.39 (t, $J = 3.0$ Hz, 1H), 4.8–6.1 (m, allylic), (Found: C, 78.34; H, 10.20. Calcd for $C_9H_{14}O$: C, 78.25; H, 10.14%).

Compound 3 IR (neat) 2857, 1653 (C=C), 1439, 1366, 1163, 1058, 1022, 985, 960, 925, 890, 820, and 756 cm^{-1} . NMR (CCl₄) δ 0.98 (t, $J = 7.0$ Hz, 3H), 1.62 (d, fine splitting, $J = 7.0$ Hz, 3H), 1.95 (q, $J = 7.0$ Hz, 2H), 2.64 (m, 2H), 4.18 (s, fine splitting, 1H), 4.37 (t, 2H) and 5.41 (q, broad, $J = 7.0$ Hz, 1H). (Found: C, 78.08, H, 10.16. Calcd for $C_9H_{14}O$: C, 78.25, H, 10.14%).

p-Ethyltoluene (5). A mixture of 2 (16.0 g) and 40 ml of 25% H_2SO_4 aq was heated at 100° for 3 h. Usual work-up and distillation yielded 10 g of *p*-ethyltoluene b.p. 46°/10 mm (IR and NMR identical to the authentic sample obtained from Aldrich Chemical Company).

3-Hydroxymethyl-1-octen-6-one (4). Compound 2 (10 g) was heated with 100 ml of 5% H_2SO_4 at 80° for 1 h. Neutralization, extraction in organic solvent and concentration yielded 4 in nearly quantitative yields. (Distillation led to the isolation of starting material.) IR (neat) of crude material, 3413 (OH), 1709 (C=O), 1642 and 913 cm^{-1} (C=C) among other peaks.

3-Hydroxymethyl-2-octen-6-one (6). Compound 3 (10 g) was stirred with 50 ml of 5% H_2SO_4 at room temp for 0.5 h. After work-up as above 9.5 g of crude 6 was obtained. IR (neat) 3390 (OH), 1709 cm^{-1} (C=O) among other peaks. NMR (CDCl₃) δ 1.03 (triplet, $J = 7.5$ Hz, 3 protons), 1.55 and 1.67 (two broad singlets, *cis*- and *trans*-CH₃-C=C, 2.2–2.7 (broad m, 6H), 3.49 (OH), 4.05 (q, 2H) and 5.41 (m, 1H). Distillation led to the isolation of 2.0 g of starting material 3 and polymeric residue.

3,4-Dihydro-2-methyl-3-methylene-6-ethyl-2H-pyran (7). Compound 3 (15.0 g) was heated with 100 ml of 5% H_2SO_4 at 80° for 1 h. (GLC analysis indicated to be a

mixture of predominantly 7 and 8). Usual work-up and distillation yielded 7 in about 40% yield b.p. 49°/10 mm. The higher boiling product b.p. 69°/5 mm was mostly 8. IR (neat) 3058 (C=CH₂), 1678, 1658 (C=C), 1176 and 898 cm^{-1} among other peaks. NMR (neat) δ 0.98 (t, $J = 7.0$ –7.5 Hz, 3H), 1.30 (d, $J = 6.0$ Hz, 3H), 1.95 (q, $J = 7.0$ –7.5 Hz, 2H), 2.70 (m, 2H), 4.19 (m, an s superimposed on a q, $J = 6.0$ Hz, 2H) and 4.85 (broad partially resolved s, 2H), $m/e = 138$ –10540; calculated for $C_9H_{14}O$: 138–10446. (Found: C, 77.30; H, 10.20. Calcd for $C_9H_{14}O$:* C, 78.25; H, 10.14%).

2,3,4-Trimethyl-2-cyclohexen-1-one (8). Compound 3 (20.0 g) was heated with 100 ml of 25% H_2SO_4 100° for 1 h. After usual work-up and distillation 6.0 g of 8 was obtained. (GLC of the crude material showed mostly 8), b.p. 69°/5 mm. NMR (neat) δ 1.17 (d, $J = 6.5$ Hz, 3H), 1.66 (partially resolved broad s, 3H), 1.88 (partially resolved broad s, 3H), broad peaks between 2.1 and 2.7, (2H), and broad peaks between 1.5 to 2.1 superimposed by the Me peaks (Methine 1H); $m/e = 138$. 2,4-Dinitrophenylhydrazone, m.p. 171–173°.

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*The compound contains about 10–15 percent of an impurity having a molecular weight of 154 by mass spectral analysis. Attempts at purification led to polymerization.