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32. Issei Iwai and Kazuo Tomita : Studies on Acetylenic Compounds. XXVIII. A Synthesis of DL-Arabinose and DL-Ribose.*1

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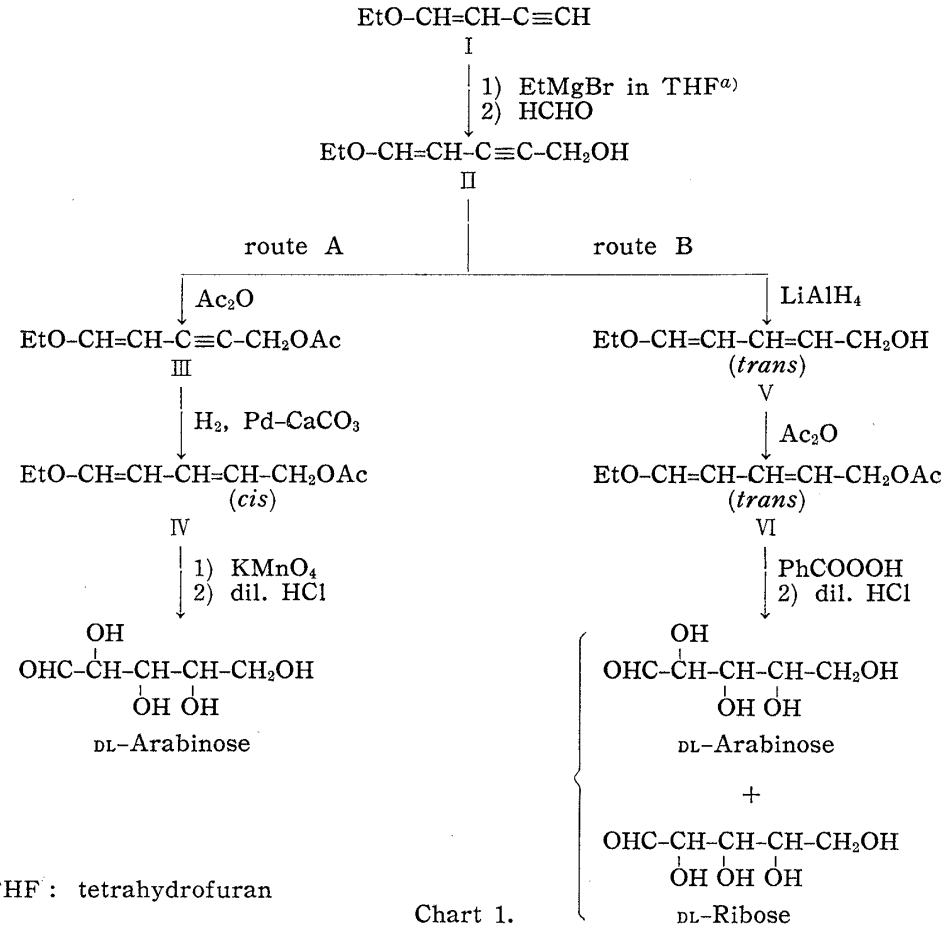
In a previous paper,[1] we reported the stereospecific synthesis of DL-arabinose from 5-ethoxy-4-penten-2-yn-1-ol (II) as shown in Chart 1 (route A). R. C. Hockett, *et al.*[2] prepared D-arabinose by *cis*-hydroxylation of D-arabinal with hydrogen peroxide-osmium tetroxide. On the other hand, M. Gehrke, *et al.*[3] obtained D-ribose as a main product by *trans*-hydroxylation of D-arabinal with perbenzoic acid. Besides these, there appeared numerous reports on a stereospecific hydroxylation of a double bond to give only one glycol derivative. It was anticipated that DL-arabinose and DL-ribose would be obtained as the final products from 2-*cis*-5-ethoxy-2,4-pentadien-1-ol acetate (IV) by *cis*-hydroxylation, but only DL-arabinose was obtained as we had reported earlier. Therefore, it seemed interesting to attempt to synthesize DL-ribose stereospecifically (accompanying no other isomeric pentose) from 2-*trans*-5-ethoxy-2,4-pentadien-1-ol acetate (VI) by *trans*-hydroxylation. However, contrary to our expectation, a mixture of DL-arabinose and DL-ribose was obtained in this case (Chart 1 : route B).



a) THF : tetrahydrofuran

Chart 1.

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1) I. Iwai, K. Tomita : This Bulletin, **9**, 976 (1961).
2) R. C. Hockett, S. R. Millman : J. Am. Chem. Soc., **63**, 2587 (1941).
3) M. Gehrke, F. X. Aichner : Ber., **60**, 918 (1927).

E. L. Pippen and M. Nonaka[4] prepared pentadienal from methoxyvinylacetylene and formaldehyde without isolating 5-methoxy-2,4-pentadien-1-ol which was thought as an intermediate. A similar reaction was now applied to the preparation of 5-ethoxy-4-penten-2-yn-1-ol (II) from 4-ethoxy-3-buten-1-yn-1-yl magnesium bromide and formaldehyde. The resulting reaction mixture was then reduced with added lithium aluminium hydride, and the complex was decomposed under a neutral condition to give 2-*trans*-5-ethoxy-2,4-pentadien-1-ol (V), which showed the infrared absorptions at 3450 (-OH), 1660 and 1623 (-CH=CH-) cm^{-1}, accompanied by a weak absorption band at 1720 cm^{-1} (carbonyl). In view of the fact that Pippen[4] decomposed the reaction complex with diluted sulfuric acid and obtained the corresponding aldehyde by an allylic rearrangement, it was considered that the alcohol (V) might be partially rearranged to the aldehyde, during the isolation procedure. Therefore, the reaction residue was immediately acetylated with acetic anhydride and pyridine to give the acetate (VI) a colorless oil, whose infrared spectrum showed absorptions at 1745 (CH_3COO-), 1658, 1623 (-CH=CH-) and 1110 cm^{-1} (ether), and which was analyzed for VI. When the infrared absorption spectra of IV and VI are compared with those of four isomers of $\Delta^{2,4}$-decadienol reported by L. Crombie, *et al.*,[5] it is seen from Table I that with regard to the absorptions due to the conjugated double bond, IV and VI correspond to 2-*cis*-4-*trans*- and 2-*trans*-4-*trans*-decadienol, respectively, and since the absorptions of the other functional groups of VI coincided with those of IV, so it seems probable that the dienol acetate (VI) should be a geometric isomer of the acetae IV.

Table I. C=C stretching Frequenies of R-CH(4)=CH(3)-CH(2)=CH(1)-CH_2OR' (cm^{-1})

R	R′		$\nu_{I C=C}$	$\nu_{II C=C}$	mean $\nu_{C=C}$	$\Delta\nu_{C=C}$
$CH_3(CH_2)_4$-	H	2-*cis*-4-*trans*[5]	1652	1609	1631	43
$CH_3(CH_2)_4$-	H	2-*trans*-4-*trans*[5]	1660	1626	1643	34
C_2H_5O-	$-COCH_3$	IV (2-*cis*)	1650	1608	1629	42
C_2H_5O-	$-COCH_3$	VI (2-*trans*)	1658	1623	1641	35

Trans-hydroxylation of the acetate VI with a small excess of perbenzoic acid afforded a colorless syrup, from which benzoic acid crystalized out after hydrolysis with diluted hydrochloric acid. This result suggests that dihydroxydibenzoate was produced by this hydroxlation rather than the epoxide as in the case of phenylbutadiene.[6] After benzoic acid was filtered off, the filtrate was successively treated with Amberlite IR-4B and active carbon, and the resulting neutral solution was evaporated to dryness under reduced pressure to give a pale yellow syrupy residue which was strongly positive to Bial reaction, typical for pentose. In paper partition chromatography,*3 it showed two spots at Rf 0.27 and 0.33, which correspond to those of D-arabinose and D-ribose, respectively.

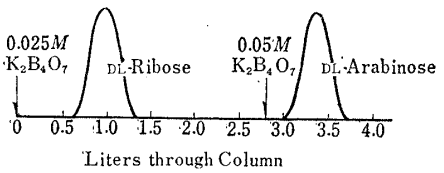

Fig. 1. Separation of Mixture of DL-Ribose and DL-Arabinose

Exchanger : 0.9 $cm^2 \times 12$ cm. Dowex-1 (borate form)
Eluting agent : aq. $K_2B_4O_7$ solution

*3 Toyo Roshi No. 50. Solvent : BuOH-H_2O-AcOH (4:5:1). Temperature 20°. Detection agent : Partridge reagent. Time : 16 hr.

4) E. L. Pippen, M. Nonaka : J. Org. Chem. **23**, 1580 (1958).
5) L. Crombie : J. Chem. Soc., **1955**, 1007; L. Crombie, S. H. Harper, R. J. D. Smith : *ibid.*, **1957**, 2754.
6) I. E. Muskat, M. Herrman : J. Am. Chem. Soc., **54**, 2001 (1932).

By chromatographic purification on Dowex-1 column[7] (borate from)the above residue was separated into two fractions showing a positive orcinol test, as shown in Fig. 1.

The residue obtained from the first fraction (Rf 0.33) was led into a tetrapropionate, as described in the preceding paper,[1] which gave the same infrared spectrum as that of D-ribose tetrapropionate, as shown in Fig. 2.

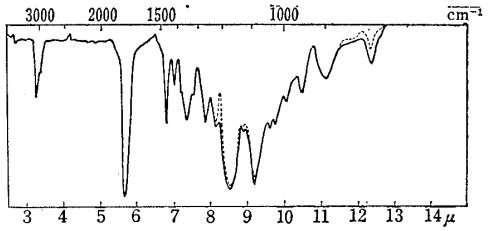

Fig. 2. Infrared Absorption Spectra of DL-Ribose Tetrapropionate and D-Ribose Tetrapropionate (in $CHCl_3$)

—— D-Ribose tetrapropionate
------ DL-Ribose tetrapropionate

The second fraction (Rf 0.27) was likewise propionated to a tetrapropionate whose infrared spectrum was identical with that of D-arabinose tetrapropionate, as shown in Fig. 3.

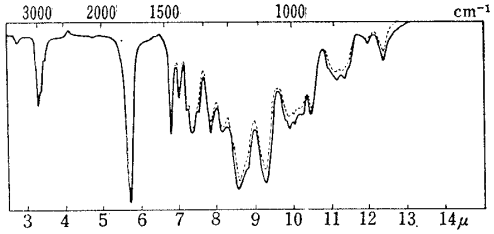

Fig. 3. Infrared Absorption Spectra of DL-Arabinose Tetrapropionate and D-Arabinose Tetrapropionate (in $CHCl_3$)

—— D-Arabinose tetrapropionate
------ DL-Arabinose tetrapropionate

Thus, the residues obtained from the first and the second fraction were confirmed to be DL-ribose and DL-arabinose, respectively. Consequently, it is concluded that *trans*-hydroxylation of *trans*-dienol acetate VI with perbenzoic acid gives two isomeric pentoses of DL-ribose and DL-arabinose, while *cis*-hydroxylation of *cis*-dienol acetate IV with potassium permanganate proceeds stereospecifically, giving only one pentose, DL-arabinose, as reported before.[1]

Experimental

2-*trans*-5-Ethoxy-2,4-pentadien-1-ol (V)——A solution of 1-ethoxy-1-buten-3-yne (48 g.) in dry tetrahydrofuran (250 cc.) was added dropwise with stirring to a Grignard reagent prepared from Mg (12 g.) and EtBr (55 g.) in tetrahydrofuran (300 cc.). After 2 hr's stirring at room temperature, HCHO gas generated from dry paraformaldehyde (24 g.) was introduced into the reaction mixture with a stream of N_2 under ice-cooling, and stirring was continued for an additional 3 hr. at room temperature. The mixture was cooled and treated with abs. EtOH (23 g.). Thirty minutes later, solid $LiAlH_4$ (30.5 g.) was added in small portions over about 30 min. interval. The mixture was stirred for 5 hr. under cooling and then for 12 hr. at room temperature. The reaction mixture was treated successively with Et_2O (water saturated) and AcOEt. The pale yellow mass was filtered off and washed with Et_2O and then water. The organic layer was separated and the aqueous layer was extracted with Et_2O. The combined organic layer was washed, dried over Na_2SO_4, and the solvent was distilled off under reduced pressure to leave a reddish yellow oil (23.0 g.). The residue (6.0 g.) was then fractionally distilled *in vacuo* to give 2.6 g. of 2-*trans*-5-ethoxy-2,4-pentadien-1-ol (V), $b.p_{0.08}$ 78~83° (bath temp.). IR $\nu_{max}^{liq.}$ cm^{-1}: 3450 (-OH), 1660, 1623 (-CH=CH-), 1110 (-O-), together with a weak absorption at 1720 (>C=O).

2-*trans*-5-Ethoxy-2,4-pentadien-1-ol Acetate (VI)——The residue (17.0 g.) containing V was added to a solution of Ac_2O (18 cc.) in dry pyridine (30 cc.), and the mixture was warmed on a steam bath for 30 min., allowed to stand overnight, and poured into ice-water containing HCl. The separated oil was extracted with Et_2O, the extract was washed with 5% $NaHCO_3$ and then water, dried over

7) J.X. Khym, L.P. Zill: J. Am. Chem. Soc., **74**, 2090 (1952).

Na_2SO_4, and evaporated. The residue was distilled *in vacuo* to give 2-*trans*-5-ethoxy-2,4-pentadien-1-ol acetate (VI) as an almost colorless oil, b.$p_{0.1}$ 61~63°(12.7 g.), n_D^{20} 1.4747, IR $\nu_{max}^{liq.}$ cm^{-1}; 1745(CH_3-COO-), 1658, 1623(-CH=CH-), 1110(-O-). *Anal.* Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.39; H, 8.17.

DL-Ribose and DL-Arabinose——A dried $CHCl_3$ solution of perbenzoic acid[8] (3.2 g.) was cooled to 0° and 3.4 g. of the acetate (VI) was added. The mixture was allowed to stand at 4° until oxidation was complete as indicated by iodimetric titration. The time required for this is about 3 days. The $CHCl_3$ was evaporated without warming and the resulting pasty mass was dissolved in Et_2O. The Et_2O solution was shaken with cold $NaHCO_3$ solution to remove completely benzoic acid and then washed with H_2O, dried over Na_2SO_4, and evaporated. To the residue was added abs. EtOH and dry benzene and the solution evaporated *in vacuo* to leave 5.2 g. of a colorless syrup. The syrup (1.0 g.) was treated with 25 cc. of dil. HCl(1:5), and the hydrolysis was effected at room temperature for 4 days, whereupon benzoic acid (0.35 g.) crystallized out as pale yellow plates. After the benzoic acid was filtered off, the filtrate was passed through an anion exchange resin (Amberlite IR-4B), treated with active carbon, and evaporated to dryness at room temperature under reduced pressure to leave a pale yellow syrup (0.17 g.). This substance showed two spots (Rf 0.27 and 0.33) on paper chromatogram, while D-arabinose and D-ribose, used as the control, showed the Rf values (0.27 and 0.32).

The residue (0.12 g.) was dissolved in 0.1*M* $K_2B_4O_7$ (5 cc.), passed through a column (0.9 $cm^2 \times 12$ cm.), filled with an ion-exchange resin (Dowex-1; borate form), and the column was eluted with 0.025*M* $K_2B_4O_7$. After the first fraction showing a positive orcinol test was obtained, the column was eluted with 0.05*M* $K_2B_4O_7$. After a while, the second fraction showing a positive orcinol test was obtained. The distribution of pentoses in the effluent is shown in Fig. 1. In this case, some material, which showed an orange color by orcinol test, came out as a forerun. We considered that the forerun was probably a non-hydrolyzed compound, whose structure was not investigated further.

The first fraction showing a positive orcinol test was treated with Dowex-50 and concentrated *in vacuo* at room temperature. The residse was dissolved in MeOH, and evaporated *in vacuo* at room temperature. An almost colorless syrupy residue (45 mg.) was obtained. The residue was treated with propionic anhydride (0.21 g.) and pyridine (0.30 g.), by the procedure described in the previous paper,[1] and 62 mg. of a viscous oil, b.$p_{0.0005}$ 145~155°(bath temp.) was finally obtained. The IR spectrum of this oil in $CHCl_3$ was identical with that of D-ribose tetrapropionate prepared from D-ribose in like manner. *Anal.* Calcd. for $C_{17}H_{26}O_9$: C, 54.54; H, 7.00. Found: C, 54.51; H, 6.95.

The second fraction was treated likewise to give 43 mg. of a syrupy residue, which was similarly propionated with propionic anhydride (0.21 g.) and pyridine (0.30 g.) to yield 60 mg. of a viscous oil, b.$p_{0.0005}$ 145~155°(bath temp.). The IR spectrum of this oil in $CHCl_3$ was identical with that of D-arabinose tetrapropionate prepared from D-arabinose. *Anal.* Calcd. for $C_{17}H_{26}O_9$: C, 54.54; H, 7.00. Found: C, 54.48; H, 6.90.

The paper partition caromatography of the residue obtained from the first fraction showed only one spot whose Rf value (0.32) was identical with that of D-ribose employed as a control. The residue from the second fraction showed the same Rf value (0.27) as that of D-arabinose (0.27).

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Summary

DL-Arabinose and DL-ribose were synthesized from 2-*trans*-5-ethoxy-2,4-pentadien-1-ol acetate, which was prepared by *trans*-hydrogenation of 5-ethoxy-4-penten-2-yn-1-ol with lithium aluminum hydride.

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8) Org. Synthses, John Wiley and Sons, Inc., New York, 1928, Vol. 8, p. 30.