65. Diels-Alder Reaction of Troponoids. I. Reaction of Hinokitiol (*m*-Isopropyltropolone).

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Previously, Erdtman and Gripenberg¹⁾ reported that thujic acid did not undergo diene-addition with maleic anhydride. The present authors²⁾ tried the same reaction with hinokitiol and recognised that tropolone nucleus of hinokitiol acted normally as cyclohepta-1,3-diene-5,6-dione.

Recently, on the one hand, Cook and the others³⁾ noted that tropolone did not give any adduct and, on the other, Nozoe and his co-workers⁴⁾ reported that the several of tropolone series reacted normally in xylene solution, so the authors, report in the present paper their observations regarding hinokitiol's behaviors.

Hinokitiol was heated at 150–170° for 5–7 hours with maleic anhydride and viscous lump of reaction mixture was dissolved in sodium bicarbonate solution, after removing unreacted material by benzene, and the pale yellow solution was acidified with 2N-HCl, then extracted repeatedly with ether, crystalline residue from ether solution was separated by cold acetone into two kinds of dicarboxylic acids, the one less soluble (I) and the other (II) more soluble in cold acetone.

The decomposition points of these acids are not sharp, varying with the method of heating, especially these in open capillary being much higher than those in sealed tube. Decomposition point of (I) 183–184° (in open tube) 162–162.5°, 167–167.5° (in sealed tube). Decomposition point of (II) 152–153° (in open tube) 141–142°, 145–146° (in sealed tube).

The corresponding acids which were obtained by Nozoe and his co-workers⁴⁾ in xylene solution and noted as dec.p. 164–165° (A) and dec.p. 142–142.5° (B) showed the same facts. The Decomposition point of admixtures of (I) and (A), (II) and (B) were observed under various conditions and both groups were proved to be respectively identical (Anal. Calcd. for C₁₄H₁₆O₆: C, 60.00; H, 5.64. mol. wt. 280. Found: (I) C, 59.84; H, 5.58. (II) C, 59.65; H, 5.62. mol. wt. by titration (I) 290.2; (II) 285.7).

Both (I) and (II) reacted easily with diazomethane in ether solution, the dimethyl esters thus obtained were glassy solids having

no definite m.p. and soluble in ether, benzene and in most organic solvents, insoluble in water.

(I), (II) and their dimethyl esters reacted with phenylhydrazine, p-nitrophenylhydrazine, semicarbazide and o-phenylenediamine, but most of carbonyl derivatives obtained could not be purified, only recrystallizable substances being monophenylhydrazones of methyl esters, fine yellow needles, m.p. 213–214° (from I), and 215–216° (from II) (Anal. Calcd. for $C_{22}H_{28}N_2O_5$: N, 7.00. Found: (from I) N, 7.03. (from II) N, 6.92).

Dimethyl esters gave oximes of fine needles, but these were mixture of monoxime and dioxime and difficult to be purified. After repeated recrystallisations from dilute alcohol, the oximes showed m.p. of 140–145° (from I), and 155–160° (from II) (Anal. Calcd. for $C_{16}H_{22}O_6N_2$: N, 8.28. Found: (from II) N, 8.05).

Both of these oxime mixtures give copper- and nickel-complex salts colored reddish brown and yellowish orange, respectively. These facts indicated that these acids still possess α -dioxo-group⁵.

Both (I) and (II) gave anhydrides by warming with acetic anhydride or acetyl chloride and the anhydrides returned to original acids by hydrolysis, by which it was ascertained that both of the acids possessed a cis-configuration.

Anhydride of (I), fine, colorless needles, m.p. 86–88°, soluble in benzene, chloroform and other organic solvents (Anal. Calcd. for $C_{14}H_{14}O_5$: C, 64.12; H, 5.34. Found: C, 64.16; H, 5.93). (II), by acetic anhydride or acetyl chloride, gave viscous oily anhydride, but a small part of acid remained insoluble in benzene, and could not be induced to the anhydride. After purification, it formed colorless fine needles (III), dec.p. 191–192° (Anal. Calcd. for $C_{14}H_{16}O_6$: C, 60.00; H, 5.64. Found: C, 59.38; H, 5.00). Thus it was noticed that a small part of (II) changed to trans-configuration during this dehydration.

(I) and (II) were catalytically hydrogenated, the uptake of hydrogen being 1.4 moles and 1.0 mole, respectively, and yielded fine colorless, needles of dihydrodicarboxylic acids of (I'), dec.p. 161–162°, and (II'), dec.p. 181–182° (Anal. Calcd. for $C_{14}H_{18}O_6$: C, 59.57; H, 6.38. Found: (I') C, 59.36; H, 6.41. (II') C, 59.78; H, 5.66).

(I') and (II') were methylated with diazomethane in ether solution, dimethyl ester of (I') being fine colorless, needles or large plates, m.p. 116–117° (Anal. Calcd. for $C_{16}H_{22}O_6$: C, 61.93; H, 7.09. Found: C, 62.39; H, 7.38). Dimethyl ester of (II') was glassy viscous matter of no definite melting point. Both (I') and (II') were dehydrated to respective anhydrides by acetic anhydride or acetyl chloride.

Anhydride of (I'), obtained by warming with acetic anhydride, was different from that yielded by acetyl chloride, the anhydride (I'a) by acetic anhydride being fine colorless, leaflets m.p. 132–134° (from benzene) (Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.63; H, 6.66. Found: C, 63.12; H, 5.99). By hydrolysis (I'a) returned to (I').

On the other hand, a different anhydride (I'b) was obtained by warming (I') with acetyl chloride and recrystallized from carbon tetrachloride to lustrous, fine needles, m.p. 138–139° (Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.63; H, 6.66. Found: C, 62.90; H, 6.29). By recrystallisation from benzene, (I'b) gave lustrous fine needles containing a half mol. of benzene, m.p. 140–141° (Anal. Calcd. for $C_{14}H_{16}O_5 \cdot \frac{1}{2}C_6H_6$: C, 67.32; H, 6.27. Found: C, 67.23; H, 6.43). This benzene-adduct liberated benzene by heating at 100° for 22 hours (12 mm. over P_2O_5) (Sample taken, 0.2803 g.; decrease of wt. 0.0358 g., 12.77% Calcd. decrease of wt. 12.87%). The residual anhydride was fine needles, m.p. 136–137°, and the mixing test showed it to be identical with (I'b) (Anal. Calcd. for $C_{14}H_{16}O_5$: C, 63.63; H, 6.66. Found: C, 63.38; H, 5.73). Melting point of the admixture of (I'a) and (I'b) was 113–114° (sintered at 106–107°), showing much depression.

The dicarboxylic acid restored from (I'b) was fine needle crystals, dec.p. 130–131° (Anal. Calcd. for $C_{14}H_{18}O_6$: C, 59.57; H, 6.38. Found: C, 60.08; H, 6.45).

It was found that (I'b) was not the normal anhydride of (I'). (II') was dehydrated by acetic anhydride or acetyl chloride yielding viscous oily anhydride which was soluble in benzene and returned to (II') by hydrolysis, and in this case also, a small part of (II') remained as undehydrated fine needles of dihydrodicarboxylic acid (III') dec.p. 210–211°, insoluble in benzene, which could be changed to its own anhydride with neither acetic anhydride nor acetyl chloride (Anal. Calcd. for $C_{14}H_{18}O_6$: C, 59.57; H, 6.37. Found: C, 59.97; H, 5.88). Thus (III') seemed to be of trans-configuration.

From the fact that hinokitiol reacted with maleic anhydride to yield two kinds of dicarboxylic acids (trans-acid seems to be a secondary product), both of which had an α -dioxo group and cis-configuration, it must be concluded that hinokitiol behaved as isopropyl-cyclohepta-1, 3-diene-5, 6-dione during this addition.

The dicarboxylic acids and dihydro acids from (a) and (b) must be (a') (b') and (a'') (b'') respectively.

To ascertain this conception, the authors several times attempted the oxidation of (I') and (II') with alkaline potassium permanganate, but in all cases merely oxalic acid and isobutyric acid (p-toluidide, m.p. 105–107°) were obtained as reaction products and isopropylsuccinic acid, which was expected from (a''), could not be detected in

the reaction mixture, thereupon it was assumed that both (I') and (II') should have the same constitution (b''), and retrospectively, (I) and (II) were (b').

The authors carried out the bromination of (I) and (II) with bromine water following Alder's method⁹. The product from (I) was fine lustrous needles which, after drying at 120°, 12 mm., showed dec.p. 200–201° (Anal. Calcd. for $\text{C}_{14}\text{H}_{17}\text{BrO}_7$: C, 44.56; H, 4.50; Br, 21.22. mol. wt. 377. Found: C, 44.79; H, 4.35; Br, 20.97. mol. wt. by titration, 392.4). Thus it was proved that this acid was a bromohydroxy diacid possessing no ability of lactonisation and therefore, (I) must have an exo-cis-configuration. Bromination product of (II) was also fine lustrous needles, and after drying over H_2SO_4 at 20 mm., it showed dec.p. 185–186° (Anal. Calcd. for bromohydroxy diacid; $\text{C}_{14}\text{H}_{17}\text{BrO}_7$: C, 44.56; H, 4.50; Br, 21.22., for bromolactone monoacid; $\text{C}_{14}\text{H}_{15}\text{BrO}_6$: C, 46.79; H, 4.18; Br, 22.28. Found: C, 45.57; H, 4.08; Br, 20.76., equivalent Calcd. for $\text{C}_{14}\text{H}_{17}\text{BrO}_7$: 0.00530., for $\text{C}_{14}\text{H}_{15}\text{BrO}_6$: 0.00278. Found: 0.00421 eq./1 g.). From these data, it was known that, on this condition, about 40% of this acid was lactonised and the remainder stayed as a bromohydroxy diacid.

By treatment with acetyl chloride, this acid yielded an anhydride as fine needles, m.p. 109–111° (Anal. Calcd. for $\text{C}_{14}\text{H}_{15}\text{BrO}_6$: C, 46.79, H, 4.18. Found: C, 46.20; H, 4.26). This anhydride was easily hydrolysed by dissolving in dilute methanol to the original bromohydroxy diacid, dec.p. 183–184°.

This substance of dec.p. 185–186° which was assumed to be a mixture of bromohydroxy diacid and bromolactone monoacid was dried at 120° (8 mm. over. P_2O_5) for 5 hours and analysed (Anal. Calcd. for $\text{C}_{14}\text{H}_{15}\text{BrO}_6$: C, 46.79; H, 4.18. Found: C, 46.27; H, 4.16., Alkali equivalent; Calcd. for $\text{C}_{14}\text{H}_{15}\text{BrO}_6$: 0.00278. Found: 0.00325). Then it was considered that in this condition, about 75–80% was lactonised.

While heating at 130° for 10 hours, this acid liberated hydrogen bromide (loss of wt. 14–15%) yielding fine needles of an unsaturated acid, m.p. 74–76°, which still had a small amount of bromine, but analytical data coincided with those of lactone monoacid (Anal. Calcd. for $C_{11}H_{16}O_6$: C, 60.43; H, 5.04. Found: C, 60.16; H, 5.20. Alkali equivalent; Calcd. for $C_{11}H_{16}O_6$: 0.00357. Found: 0.00344). These facts indicate that, in spite of the difficulty of lactonization compared with ordinary γ -hydroxyacids, the bromohydroxy diacid and, retrospectively the acid (II) also, had to be in endo-cis-configurations, and the difficulty of lactonization may be due to the steric effect of isopropyl group attached to the β -carbon atom.

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