143. *Diels-Alder Reaction of Tropolones with Maleic Anhydride.*¹⁾

By Tetsuo NOZOE, Shûichi SETO, and Toshiaki IKEMI.

Chemical Institute, Faculty of Science, Tôhoku University.

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Some time ago, Erdtman and Gripenberg²⁾ reported that thujic acid (4, 4-dimethylcycloheptatriene-1-carboxylic acid) did not react normally with maleic anhydride. Cook and the others³⁾ also noted that heating of tropolone with maleic anhydride or cyclopentadiene furnished no adduct. However, Sebe⁴⁾ obtained two kinds of dicarboxylic acid of m.p. 184° and 152–153° by heating hinokitiol (m-isopropyltropolone) with maleic anhydride at 150–160° for 5–7 hrs., and their chemical structures are being studied.

The present authors attempted the reaction of tropolone itself and its various derivatives with maleic anhydride and as a result, found that, contrary to the statement of Cook and the others, tropolone itself and some of its derivatives gave normal adducts.

In an experiment carried out by Sebe on hinokitiol, a mixture of the sample and an excess of maleic anhydride was heated without any solvents but the present authors used xylene as a solvent.

In the case of tropolone (I), a mixture of 1 mole of (I) and 2 moles of maleic anhydride was dissolved in approximately 9 times its weight of anhydrous xylene and refluxed for 5–6 hrs. By allowing the mixture to stand for 15–20 hrs. at a room temperature, and recrystallizing from acetone the crystals that separate out, colorless needles (II), m.p. 169–170°, are obtained. Analytical results showed (II) to be an adduct (A or its enol form) of (I) and maleic anhydride, the yield being 40–50% of the theoretical amount (Anal.

Calcd. for $C_{11}H_8O_5$: C, 59.98; H, 3.66. Found: C, 59.53; H, 3.80)⁵⁾. In this case, some oily substance is also obtained. The recovery of (I) was around 12%. (II) does not show the coloration peculiar to tropolones by ferric chloride, is difficultly soluble in ether and benzene, comparatively soluble in alcohol and acetone, and is slightly difficult to dissolve

(A)

in cold water, but by dissolving in boiling water and concentrated, free carboxylic acid (II'), colorless needles, which melt at 183–184° with evolution of gas, separates out. The analytical values of (II') correspond to dicarboxylic acid containing one mole of water of crystallization (Anal. Calcd. for $C_{11}H_{10}O_6 \cdot H_2O$: C, 51.54; H, 4.72.

Found: C, 52.47; H, 4.90). But its molecular weight by titration corresponds to mono carboxylic acid. The solubility behavior of (II') is similar to those of (II) but is slightly more soluble than (II) in acetone, alcohol and water. In this reaction, the ratio of (I) and maleic anhydride was changed in various ways, 1:1 molar ratio furnishing 30-40% of (II) with recovery of 20% of (I), while 1:5 molar ratio gave only 30% or less of (II) although the recovery of (I) was in trace amounts.

In the case of tropolone methyl ether (III), the same reaction as for (I) gave an adduct (IV) of colorless microneedles, m.p. 180.5-181.5° (Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.51; H, 4.30. Found: C, 61.38; H, 4.28). (IV) clearly showed depression of the melting point when fused with (II) but its solubilities were similar to those of (II), solution of (IV) in boiling water with subsequent condensation furnishing the free dicarboxylic acid containing one mole of water of crystallization (V) in quantitative yields. (Anal. Calcd. for $C_{12}H_{12}O_6 \cdot H_2O$: C, 53.32; H, 5.19; mol. wt., 270. Found: C, 52.78; H, 5.00; mol. wt., 262). (V) is dehydrated at around 170° and the melting point rises to 178-179°. The dehydrated (V) melts at 180° when mixed with (IV). (V) is insoluble in ether and benzene, and soluble in acetone, alcohol and warm water. The recovery of (III) was very slight in this reaction.

o-Bromotropolone (VI) does not give any adduct under the similar conditions, (VI) being recovered almost quantitatively.

By the same treatment of m(β)-methyltropolone (VII) as in the case of (I) and (III) gave an adduct of colorless needle crystals of m.p. 175.5-176.5° in 13% yield (Anal. Calcd. for $C_{12}H_{10}O_5$: C, 61.51; H, 4.30. Found: C, 61.30; H, 4.55).

In the case of α -thujaplicin (o-isopropyltropolone) (VIII), the same reactions as in the foregoing failed to give any crystalline adduct. After heated under reduced pressure to remove xylene, maleic anhydride and (VIII), the reaction mixture yielded an oily residue which was warmed with saturated solution of sodium bicarbonate. This alkaline solution, acidified and extracted with ether, yielded 0.8 g. of oil from 0.74 g. of (VIII), became vitreous but failed to give any crystalline product. The oily substance is soluble in water. The recovery of (VIII) was also very slight in this case. Further studies of this oil is being made.

For comparison with the results obtained as above, the same reaction was carried out with hinokitiol (m-isopropyl-tropolone) (IX) under exactly the same conditions. Although the adduct was not obtained as its anhydride in this case, the same treatment as in the case of (VIII) furnished two kinds of dicarboxylic acids. The crys-

tals obtained from a comparatively insoluble portion in ether gave, upon recrystallization from acetone, colorless needles of dec. p. 164–165° which are soluble in water, alcohol and acetone, and insoluble in benzene. The analytical values and molecular weight as calculated from titration values, correspond to those of dicarboxylic acid of the adduct (Anal. Calcd. for $C_{14}H_{16}O_6$: C, 59.98; H, 5.76; mol. wt., 280. Found: C, 59.98; H, 5.84; mol. wt., 278). The crystals obtained from the easily-soluble portion are colorless micro-needles of dec. p. 142–142.5° more easily soluble in acetone and water. The analytical values of these also correspond to those of dicarboxylic acid (Anal. Calcd. for $C_{14}H_{16}O_6$: C, 59.98; H, 5.76; mol. wt., 280. Found: C, 59.75; H, 5.39; mol. wt., 270). The combined yield of the two acids is around 30%, with a very slight recovery of (IX). The reactions were attempted with varying ratio of (IX) and maleic anhydride, as in the case of (I), and the best yield was obtained in the molar ratio of 1:2. The refluxing of the mixture in benzene resulted in almost quantitative recovery of (IX). It should be noted in this case that (IX) gives two kinds of isomers quite different from the case of other tropolone derivatives. Studies are now being made to determine the relationship of these two dicarboxylic acids with those obtained by Sebe.

The same treatment of o'-bromohinokitiol (X), as in the case of (IX), gave one kind of dicarboxylic acid of an adduct in 15% yield, dec. p. 182–184°. In this case, however, approximately 30% of (X) is recovered. It follows, therefore, that (X) is more harder to react than (IX) although more easily than (VI) which is assumed to be due to the effect of the isopropylgroup in the meta position.

The decisive conclusion for steric structures of the adducts of tropolones with maleic anhydride must await further studies.

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References.

- 1) The expenses for the present series of experiment were defrayed by the Grant in Aid for Scientific Research from the Ministry of Education.
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- 5) Analyses were carried out by Messrs. Hirai and Kawamoto of the Sankyô Co., Ltd.