Diels-Alder Reaction of Troponoids. II[1]*. Adducts of Halotropones and Maleic Anhydride*

By Tetsuo Nozoe and Yasuo Toyooka

(Received on October 17, 1960)

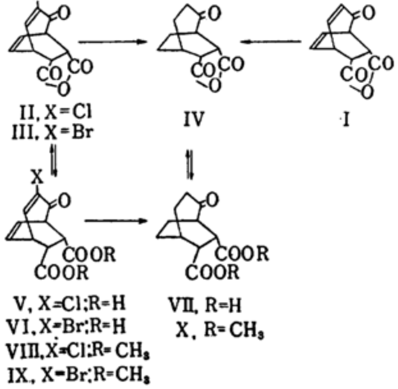
The Diels-Alder reaction of tropone and maleic anhydride has been reported from our laboratory[1]. Tropone gives a normal endo-cis adduct I more readily than tropolone, presumably owing to the property of enhanced unsaturation.

In the present paper the authors wish to report the Diels-Alder reactions of halotropones. It was found that 2-chloro- and 2-bromotropone give normal adducts in good yield, whilst 2, 7-dibromo- and 2, 4, 7-tribromotropone fail to give the adducts resulting in the complete recovery of the materials started with.

Results

The heating of 2-chlorotropone or 2-bromotropone with two molar equivalents of maleic anhydride in dry xylene effected reaction, affording the adduct II or III in a yield of around 65~85%. The ultraviolet absorption spectra of II and III are shown in Fig. 1.

Catalytic hydrogenation of the adduct, II or III, in ethyl acetate with palladium charcoal as a catalyst, results in the absorption of three molar equivalents of hydrogen respectively both forming the same halogen-free tetrahydro compound IV, which showed no depression of the melting point on admixture with each other and with tetrahydro compound obtained from I. These facts not only offer an important clue to the structure of II and III but also prove the configurations of II and III being the same as I. Actually the infrared spectrum of IV obtained from II or III coincides perfectly with the one of tetrahydro compound obtained from I.



II, X=Cl
III, X=Br

IV

I

V, X=Cl; R=H
VI, X=Br; R=H
VIII, X=Cl; R=CH$_3$
IX, X=Br; R=CH$_3$

VII, R=H
X, R=CH$_3$

Treatment of the adduct II or III with hot water results in facile hydrolysis and dibasic acid V or VI is formed. The acids V and VI are known to be dibasic from their analytical value and titration. The decomposition points of V and VI are the same as the melting points of II and III respectively. These are considered to be due to the facial dehydrations of V and VI. Actually the heating of V and VI at 200~220°C under a reduced pressure result in the formations of II and III and such facts naturally indicate that the two carboxyls are in cis configuration.

The halogen-free tetrahydro compound IV is also easily hydrolyzed and forms a dibasic acid VII which undergoes facile dehydration as in the case of V and VI. Catalytic hydrogenation of unsaturated dibasic acids V or VI in water, with palladium charcoal as a catalyst, results in absorption of three molar equivalents of hydrogen to form VII. Methylation of these three dibasic acids, V, VI and VII, with diazomethane affords dimethyl esters, VIII, IX and X. It has been found, however, that the reactions of V and VI with excess diazomethane also afford compounds VIII of $C_{14}H_{15}O_5N_2Cl$ and IX of $C_{14}H_{15}O_5N_2Br$. These compounds seem to be the same ones obtained in the case of dibasic acid of I and to have a pyrazol ring at the double bond of $\alpha\beta$-unsaturated ketone system[1]. All of the dimethyl esters, VIII, IX and X, easily form crystalline 2, 4-dinitrophenylhydrazones.

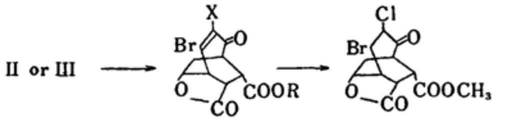
Bromination of the adduct II or III in aqueous solution by the method of Alder-Stein results in addition to the double bond and bromolactone XI or XII is obtained in a good yield. Titration of XI and XII shows them to be a monobasic acid, and the presence of a carboxyl and a γ-lactone is also indicated from the infrared spectral values listed in Table I.

---

[1] Part I of this series: T. Nozoe, T. Mukai, T. Nagase and Y. Toyooka, This Bulletin, 33, 1247 (1960).

TABLE I. INFRARED SPECTRAL VALUES OF SEVERAL ADDUCTS AND THEIR DERIVATIVES (cm^{-1})

		I	II	III	Bromo-γ-lactone of I	XI	XII
5-Membered acid anhydride ($\nu_{C=O}$)		1840 1780	1875 1850 1785	1875 1840 1785			
αβ-Unsaturated ketone ($\nu_{C=O}$)		1665	1690	1680	1675	1685	1685
C=C of αβ-unsaturated ketone ($\nu_{C=C}$)		1625	1630 1605	1630 1595		1655 1615	1610
γ-Lactone ($\nu_{C=O}$)					1770	1780	1780
Carboxylic acid	$\nu_{C=O}$				1745	1710	1735
	ν_{OH}				3320	3300	3350



XI, X=Cl; R=H
XII, X=Br; R=H
XIII, X=Cl; R=CH$_3$
XIV

Methylation of XI with diazomethane afforded monomethyl ester XIII. Catalytic hydrogenation of XIII on palladium charcoal in ethyl acetate results in absorption one molar equivalent of hydrogen and crystalline saturated bromolactone XIV is formed.

Discussion

Bathochromic shifts in the ultraviolet maxima of II and III, 12∼19 mμ, respectively, from that of I, are best explained by the α-substitution of halogen on the αβ-unsaturated carbonyl system, in accordance with Woodwards' rule (calcd. values: 242 mμ for II, 250 mμ. for III).

Similar kinds of shifts are observed in the infrared spectra (cf. Table I). It is safely assumed, therefore, that the addition of maleic anhydride has taken place at C-4 and C-7 of 2-halotropone.

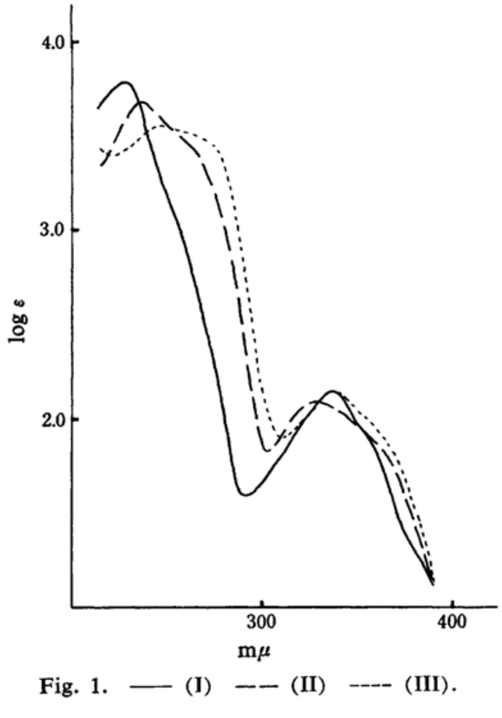


Fig. 1. —— (I) — — (II) ---- (III).

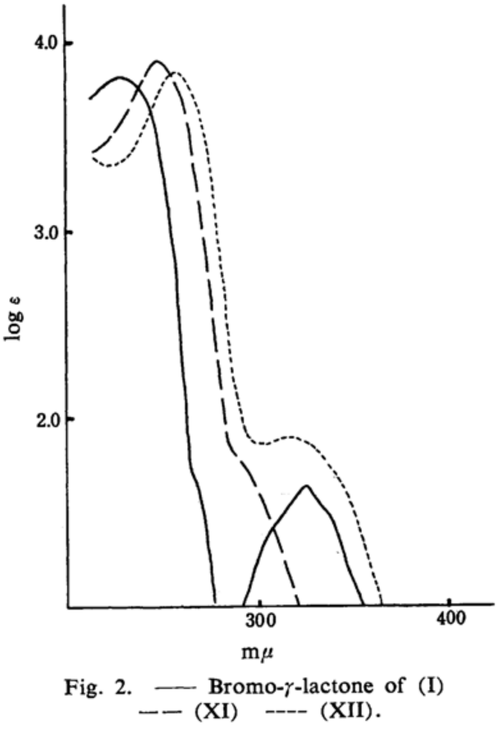


Fig. 2. —— Bromo-γ-lactone of (I) — — (XI) ---- (XII).

It is clear from the foregoing experiments, that both II and III have the endo-cis configuration. Thus tetrahydro compound IV obtained by catalytic hydrogenation II and III is identical with the tetrahydro compound from I.

Products, XI and XII, formed by Alder-Steins' bromination of II and III still have $\alpha\beta$-unsaturated carbonyl system (cf. Fig. 2) indicating that the addition of BrOH occurred on the isolated double bond. This is also supported by the strong band at 1780 cm^{-1} (γ-lactone) in both XI and XIII in their infrared spectra (cf. Table I).

Thus, the structure of bromolactones must be like the ones indicated in the figures.

Experimental

Preparation of Adduct II.—The solution which contained 2.80 g. of 2-chlorotropone and 3.90 g. of maleic anhydride dissolved in 40 cc. of dry xylene was refluxed on an oil bath (175~180°C) for 24 hr. Standing overnight at room temperature, 3.18 g. of pale yellow seeds were separated. Several recrystallizations afforded colorless needles, m. p. 208~209°C.

Found: C, 55.58; H, 2.90. Calcd. for $C_{11}H_7O_4Cl$: C, 55.35; H, 2.09%.

Preparation of IV.—To the solution of 720 mg. of II dissolved in 80 cc. of ethyl acetate, 500 mg. of 5% palladium charcoal was added and was hydrogenated at ordinary temperature and pressure. The absorption of hydrogen was quite slow and 203 cc. of hydrogen (3 mol. equiv.) was absorbed for 2 days. After filtration of the catalyst the solvent was distilled off completely, the residue afforded colorless small needles, m. p. 191~192°C, 320 mg. by several recrystallizations from acetone-ethyl acetate mixture.

Found: C, 63.48; H, 5.63. Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 291 (1.80).

Mixed melting point test with the tetrahydro adduct of I showed no depression.

Preparation of V.—Warming the suspension of 640 mg. of II in 50 cc. water on a boiling water bath, II was gradually dissolved. After evaporation to half volume and cooling in an ice bath, 620 mg. of V, as colorless leaflets separated. Although V has the same melting point to II, it melted in saturated sodium bicarbonate solution with effervescence, and neutralization titration value coincided to the dibasic one.

Found: C, 48.19; H, 3.97. Calcd. for $C_{11}H_{11}\cdot O_6Cl$: 48.09; H, 4.03%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 248 (3.60), 337 (2.19).

Heating of V in phosphorus pentoxide vacuum desiccator for two days, V changed to II.

Preparation of VIII.—To the solution of 550 mg. of V dissolved in 30 cc. of ethyl acetate, two molar equivalents of diazomethane ethereal solution was added dropwise. After several hours the solvent was distilled off completely, the residue afforded colorless fine powders, m. p. 165~169°C, 550 mg. Several recrystallizations gave colorless fine crystals, m. p. 172~173°C, 410 mg.

Found: C, 54.87; H, 4.87. Calcd. for $C_{13}H_{13}\cdot O_5Cl$: C, 58.87; H, 4.60%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 240 (3.74), 330 (1.01).

2,4-Dinitrophenylhydrazone of VIII.—To the solution of 80 mg. of VIII dissolved in 10 cc. of methanol, the mixture of 60 mg. of 2,4-dinitrophenylhydrazine, 0.1 cc. of concentrated sulfuric acid, 0.4 cc. of water and 1.3 cc. of methanol was added, then was refluxed on a water bath for 1.5 hr. Cooling in an ice bath 80 mg. of deep red fine crystals were separated. Several recrystallizations from a small amount of methanol afforded deep red fine crystals, m. p. 154°C, 50 mg.

Found: C, 50.86; H, 3.79; N, 12.38. Calcd. for $C_{19}H_{17}O_8N_4$: C, 49.09; H, 3.69; N, 12.05%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 261 (4.05), 370 (4.42).

Preparation of VII. — (A) *By Catalytic Hydrogenation of V.*—To the solution of 550 mg. of V dissolved in 70 cc. of water, 50 mg. of 5% palladium charcoal was added and the mixture was hydrogenated at ordinary temperature and pressure. The absorption of hydrogen was slow and 139 cc. (3.1 mol. equiv.) of hydrogen was absorbed. After the catalyst was filtered, off the solvent was removed completely, the residue afforded colorless powders (VII), d. p. 172.5°C, 350 mg. by several recrystallizations from small amount of water.

Found: C, 58.39; H, 5.94. Calcd. for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 292 (1.81).

(B) *By Hydrolysis of IV.*—Two hundred milligrams of IV was dissolved in 10 cc. of water, and then the solution was condensed to 1/3 volume on a boiling water bath. Colorless powders (VII), d. p. 173°C, 150 mg. were separated out on cooling.

Either VII obtained by (A) or (B) changed to IV on heating at 150°C in vacuum phosphorus pentoxide desiccator.

Preparation of X.—To the solution of 270 mg. of VII dissolved in 4 cc. of methanol, two molar equivalents of diazomethane ethereal solution was added dropwise. After several hours the solvent was removed completely, the residue afforded pale yellow oil, which failed to crystallize.

2,4-Dinitrophenylhydrazone of X. — The solution which contained 250 mg. of X and 200 mg. of 2,4-dinitrophenyl hydrazine dissolved in 5 cc. of methanol, 0.5 cc. of concentrated sulfuric acid, and 0.5 cc. of water was refluxed on a water bath for 1 hr. Orange crystals were separated. Several washings with hot methanol raised the melting point to 89°.

Found: C, 52.23; H, 4.90; N, 12.94. Calcd. for $C_{19}H_{22}O_8N_4$: C, 52.53; H, 5.10; N, 12.90%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ (log ε): 229 (4.19), 361 (4.33).

Bromination of V: Preparation of XI.—To the solution of 550 mg. of V dissolved in 40 cc. of water, 320mg. of bromine was added dropwise under stirring. The color of the solution changed slowly to pale yellow and then colorless crystals were separated. After standing overnight 160 mg. of XI, d. p. 243°C, in colorless granules were obtained.

Found: C, 39.37; H, 2.27. Calcd. for $C_{11}H_8\cdot O_5BrCl$: C, 39.37; H, 2.41%.

Preparation of XIII.—To the solution of 440 mg. of XI dissolved in 20 cc. of ethyl acetate the calculated amount of diazomethane ethereal solution was added dropwise. After several hours the solvent was removed and residue gave colorless crystals, m. p. 195~198°C, 450 mg. Several recrystallizations from methanol raised the melting point to 201~202°C.

Found: C, 41.40; H, 2.88. Calcd. for $C_{12}H_{10}O_5 \cdot BrCl$: C, 41.23; H, 2.88%.

Preparation of XIV.—To the solution of 250 mg. of XIII dissolved in 60 cc. of ethyl acetate, 100 mg. of 5% palladium charcoal was added and the mixture was hydrogenated at ordinary temperature and pressure. Eighteen cc. of hydrogen was absorbed (1.15 mol. equiv.). After filtration of the catalyst the solvent was distilled off, the residue afforded colorless powders, m. p. 219~222°C, 240 mg. Several recrystallizations from methanol raised the melting point to 230~232°C.

Found: C, 41.25, H, 3.17. Calcd. for $C_{12}H_{12}O_5 \cdot BrCl$: C, 40.99; H, 3.44%.

Preparation of III. — The solution which contained 370 mg. of 2-bromotropone and 400 mg. of maleic anhydride dissolved in 4 cc. of dry xylene was refluxed on an oil bath for 13 hr. Standing overnight in a cool place yellow crystals, m. p. 223~228°C, 410 mg. were separated. Recrystallization from acetone-ethyl acetate mixture raised the melting point to 232~233°C (350 mg.).

Found: C, 46.78; H, 2.40. Calcd. for $C_{11}H_7 \cdot O_4Br$: C, 46.67; H, 2.49%.

Hydrolysis of III.—After dissolving 200 mg. of III in 10 cc. of water, the solution was evaporated to 1/2 volume on a boiling water bath. Colorless scales, d. p. 233°C, 180 mg. were separated on cooling.

Found: C, 44.00; H, 2.86. Calcd. for $C_{11}H_9 \cdot O_5Br$: C, 43.88; H, 3.10%. $\lambda_{\max}^{\mathrm{MeOH}}$ mμ ($\log \varepsilon$): 248 (3.60), 337 (2.16).

Bromination of VI.—To the solution of 570 mg. of VI dissolved in 100 cc. of water, 320 mg. of bromine was added dropwise at room temperature under stirring. After standing overnight colorless granules, d. p. 246°C, 500 mg. were separated. Several recrystallizations from methanol-ethyl acetate mixture afforded colorless crystals, d. p. 257°C, 320 mg.

Found: C, 34.85; H, 2.04. Calcd. for $C_{11}H_8 \cdot O_2Br_2$: C, 34.77; H, 2.12%.

Organic Chemical Laboratory
Chemical Institute
Faculty of Science
Katahira-cho, Sendai