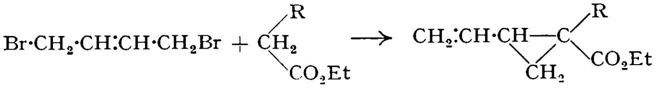
370. cyclo*Propanes. Part III.* The Condensation of 1 : 4-Dibromobut-2-ene with Ethyl Cyano- and Aceto-acetate.*

By R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon.

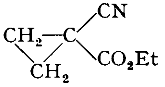
The main products from the condensation of *trans*-1 : 4-dibromobut-2-ene with ethyl sodiocyanoacetate and sodioacetoacetate are ethyl 1-cyano- and 1-aceto-2-vinyl*cyclo*propane-1-carboxylate respectively. From the former reaction a mixture of ethyl 3-cyano-2-imino-4- and -5-vinyl*cyclo*pentane-1-carboxylate is also obtained.

We recently reported (Part I, *J.*, 1952, 3610) that *trans*-1 : 4-dibromobut-2-ene reacts with ethyl sodiomalonate to give ethyl 2-vinyl*cyclo*propane-1 : 1-dicarboxylate (I; $R = CO_2Et$) in good yield :


(I)

This new route to vinyl*cyclo*propanes has now been further exemplified by carrying out analogous reactions with ethyl cyanoacetate and acetoacetate.

When 1 : 4-dibromobut-2-ene was condensed with ethyl cyanoacetate two products were obtained. One, isolated in yields up to 40%, was shown to be the substituted *cyclo*propane (I; $R = CN$). On ozonolysis, followed by oxidative fission of the ozonide and hydrolysis of the resulting nitrile, *cyclo*propane-1 : 1 : 2-tricarboxylic acid was obtained in 24% overall yield and identified by direct comparison with an authentic specimen. Hydrolysis of the ester (I; $R = CN$) gave the corresponding cyano-acid, which melted over a wide range and was obviously a mixture of *cis*- and *trans*-isomers.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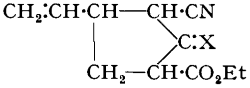
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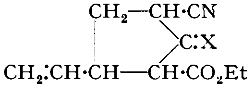
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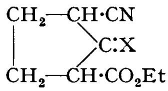
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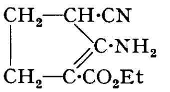
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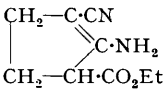
(VII)

Best and Thorpe (*J.*, 1909, **95**, 685) showed that the cyano-ester (II) reacts with ethyl cyanoacetate, in the presence of small amounts of the sodio-derivative of the latter, to give the imino-*cyclo*pentane (III; $X = NH$). It seemed probable that, under the conditions employed for the condensation of dibromobutene with ethyl cyanoacetate, the substituted *cyclo*propane (I; $R = CN$) formed initially would, to some extent, react further with ethyl cyanoacetate to give vinyl derivatives of (III; $X = NH$). The second product from the condensation was therefore regarded as a mixture of (IV; $X = NH$)

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* Part II, *J.*, 1952, 3616.

and (V; X = NH). When this was kept, one of the isomers separated as a crystalline solid. Acid hydrolysis of the mixture gave the corresponding β-keto-esters (IV; X = O) and (V; X = O) in which the presence of a terminal double bond was demonstrated by ozonolysis to formaldehyde (29%). Catalytic reduction of the keto-esters yielded the dihydro-derivatives, which on hydrolysis and decarboxylation were converted into the known 3-ethyl*cyclo*pentanone (Part II), thereby confirming the structures assigned to the isomers in the second fraction from the dibromobutene condensation.

Spectral data (Table 1) for the imino-compounds (III—V; X = NH) indicate that they exist, at least in solution, largely in the amino-forms, *e.g.*, (VI) and/or (VII). The light-absorption properties of the mixture of β-keto-esters (IV; X = O) and (V; X = O), and of their dihydro-derivatives, are in good agreement with those of ethyl 3-cyano-2-keto*cyclo*pentane-1-carboxylate (III; X = O) (Table 2). The maxima recorded with alcoholic solutions must be due to the enolic forms of the keto-esters; the shifts to longer wave-lengths observed with alkaline media result from the conversion of the enols into the corresponding enolates.

TABLE 1.

	$\lambda_{max.}$, Å *	ε	$\lambda_{max.}$, Å *	ε
(IV; X = NH) and (V; X = NH)	2710	17,000	2760 †	16,000
(IV; X = NH) or (V; X = NH)	2690	11,500	2790	10,000
(III; X = NH)	2690	14,000	2800	15,000

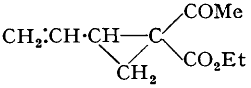
* In chloroform. † Inflexion.

TABLE 2.

	In alcohol.		In 2% aqueous KOH.	
	$\lambda_{max.}$, Å	ε	$\lambda_{max.}$, Å	ε
(IV; X = O) and (V; X = O)	2280	8500	2270	3,500
	2370		2680	12,500
	2420		2760 *	10,500
Dihydro-derivatives of (IV; X = O) and (V; X = O)	2360	8000	2580 *	12,500
	2410		2680	13,000
			2740 *	12,500
(III; X = O) †	2270	6500	2580 *	12,000
	2360	6000	2690	13,000
	2510 *	5000	2790 *	11,000

* Inflexion.
† Prepared from (III; X = NH) by Best and Thorpe's method (*J.*, 1909, **95**, 685).

TABLE 3.

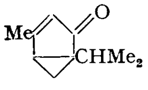
	$\lambda_{max.}$, Å	ε
	2510	1,150
	2570	
	2640	
$CH_2{:}CH{\cdot}C{\vdots}C{\cdot}COMe$ [1]	2510	8,500
	2580 *	8,000
$CH_2{:}CH{\cdot}CH{:}CH{\cdot}CHO$ [2]	2580	29,000
$CHMe{:}CH{\cdot}CH{:}CH{\cdot}COMe$ [3] ...	2700	28,500
Umbellulone (VIII) [4]	2200	5,000
	2650	2,900
Piperitone (IX) [4]	2355	17,780
Carone (X) [4]	<2200	>2,680

* Inflexion.

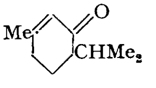
[1] Bowden, Heilbron, Jones, and Weedon, *J.*, 1946, 39. [2] Bader, Weedon, and Woods, *J.*, 1951, 3009. [3] Heilbron, Jones, and Richardson, *J.*, 1949, 287. [4] Gillam and West, *J.*, 1945, 95.

The main product (52%) from the reaction of 1 : 4-dibromobut-2-ene with ethyl sodioacetoacetate was the substituted *cyclo*propane (I; R = COMe). Its structure was established by ozonolysis, followed by hypobromite oxidation and hydrolysis, whereupon *cyclo*propane-1 : 1 : 2-tricarboxylic acid was obtained in 32% overall yield. Catalytic hydrogenation of (I; R = COMe) over platinum at 20° resulted in the rapid absorption of 1·9 mol. of hydrogen, thus affording a further example of the ready reductive fission of a vinyl*cyclo*propane (cf. Part I). Hydrolysis of the saturated keto-ester and decarboxylation yielded methyl pentyl ketone.

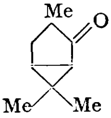
The ultra-violet light absorption spectrum of (I; R = COMe), unlike that of (I; $R = CO_2Et$) or (I; R = CN), exhibits maxima in the 2500—2650 Å region (Table 3). These absorption bands are similar in position to, but of much lower intensity than, those of vinylacetylenic and butadienyl ketones, suggesting that in (I; R = COMe) there is some electronic interaction between the *cyclo*propane ring, the double bond, and the carbonyl group. It has been shown (Part I), by molecular-refractivity measurements, that conjugation in (I; R = CO_2Et) is confined almost exclusively to the vinyl*cyclo*propane system. This difference is in accord with the observations of others on the relative abilities of the *cyclo*propane ring to conjugate with carbonyl and ester groups (for references see Part I). Mutual interaction of the three chromophores under consideration has been noted previously (Gillam and West, *J.*, 1945, 95) in umbellulone (VIII), which has light absorption properties different from those of other αβ-unsaturated ketones, such as piperitone (IX), and of carone (X) (Table 3).



(VIII)



(IX)



(X)

In addition to (I; R = COMe) small amounts of two other products were isolated from the condensation of dibromobutene with ethyl sodioacetoacetate. These have not been examined, but it is probable that one, $C_{16}H_{24}O_6$, was formed by replacement of both bromine atoms in dibromobutene by acetoacetate residues, and the other, $C_{12}H_{20}O_4$, by substitution of the first bromine by acetoacetate and the second by an ethoxyl group. Products of solvolysis have not previously been encountered in the reaction of dibromobutene with active methylene compounds.

EXPERIMENTAL

The 1 : 4-dibromobut-2-ene used was the crystalline, *trans*-isomer, m. p. 54°.

Condensation of 1 : 4-*Dibromobut*-2-*ene with Ethyl Sodiocyanoacetate.*—A warm solution of dibromobutene (53·5 g.) in alcohol (200 c.c.) was added during ½ hr. to a well-stirred, warm suspension of ethyl sodiocyanoacetate (from 56·5 g. of ethyl cyanoacetate and 11·5 g. of sodium) in alcohol (200 c.c.). The mixture was heated under reflux until neutral to litmus (2 hr.), then cooled and filtered. The filtrate was evaporated under reduced pressure, and the residue poured into water. Isolation of the product with ether and distillation gave : (i) *Ethyl* 1-*cyano*-2-*vinyl*cyclo*propane*-1-*carboxylate* (4·4 g., 10%), b. p. 112°/11 mm., n_{D}^{24} 1·4650 (Found : C, 65·3; H, 6·95. $C_9H_{11}O_2N$ requires C, 65·4; H, 6·7%). It showed no light absorption of $E_{1\,\mathrm{cm.}}^{1\%} > 10$ at wave-lengths >2220 Å. (ii) A mixture (16·8 g., 30%) of ethyl 3-cyano-2-imino-4- and -5-vinyl*cyclo*pentane-1-carboxylate, b. p. 107°/0·15 mm., n_{D}^{24} 1·5242 (Found: C, 63·7; H, 6·85%). After 1—2 hr., an alcoholic solution of the mixture gave a violet colour with ferric chloride, probably owing to hydrolysis of the imino-group. On storage at 0° the mixture partly crystallised. The solid was separated and crystallised from benzene–light petroleum (b. p. 40—60°), giving one of the isomeric *esters* (*ca.* 30% of the mixture) as plates, m. p. 86·5—88° (Found : C, 64·25; H, 7·05. $C_{11}H_{14}O_2N_2$ requires C, 64·05; H, 6·85%).

In another experiment, the suspension of ethyl sodiocyanoacetate was added during 1 hr. to a boiling solution of dibromobutene, and the resulting mixture heated under reflux for a further hr. Isolation of the product as described above gave the *cyclo*propane derivative in 40% yield.

cyclo*Propane*-1 : 1 : 2-*tricarboxylic Acid.*—A stream of ozonised oxygen (*ca.* 3% of O_3) was bubbled through a cooled solution of ethyl 1-cyano-2-vinyl*cyclo*propane-1-carboxylate (1·0 g.) in acetic acid (" AnalaR "; 12 c.c.) for 7 hr. Hydrogen peroxide (30 c.c.; 20-vol.) was then added, and the mixture kept at 20° overnight. The resulting solution was evaporated under reduced pressure. The residue (2 c.c.) was heated under reflux with a solution of potassium hydroxide (3·2 g.) in water (3 c.c.) and alcohol (2 c.c.) until the evolution of ammonia ceased (21 hr.). The solution was acidified and extracted thoroughly with ether (constant extractor overnight). Evaporation of the ethereal extract yielded a solid (857 mg.), m. p. 155—157° (decomp.), which was crystallised twice from ether and gave *cyclo*propane-1 : 1 : 2-tricarboxylic acid (250 mg.), m. p. 183° (decomp.), undepressed on admixture with an authentic specimen (Conrad and Gutzeit, *Ber.*, 1884, **17**, 1185, give m. p. 184°, decomp.).

1-*Cyano*-2-*vinyl*cyclo*propane*-1-*carboxylic Acid.*—Ethyl 1-cyano-2-vinyl*cyclo*propane-1-carboxylate (9·0 g.) was shaken for 2 hr. with potassium hydroxide (3·6 g.) in water (10 c.c.). The resulting homogeneous solution was extracted with ether and then acidified with dilute (1 : 5) sulphuric acid. The solution was saturated with ammonium sulphate, and the product isolated by thorough extraction with ether. Evaporation of the extract gave the acid (7·2 g.) as a mixture of isomers which crystallised from benzene–light petroleum (b. p. 40—60°) in prisms, m. p. 67—79° (Found : C, 61·45; H, 5·05%; equiv., 137. Calc. for $C_7H_7O_2N$: C, 61·3; H, 5·15%; equiv., 137). The acid was not decarboxylated when heated to 200°.

*Ethyl 3-Cyano-2-keto-4- and -5-vinyl*cyclo*pentane-1-carboxylate* (cf. Best and Thorpe, *loc. cit.*).—A solution of ethyl 3-cyano-2-imino-4- and -5-vinyl*cyclo*pentane-1-carboxylate (7·3 g.) in concentrated hydrochloric acid (40 c.c.) was kept for 5 min. and then diluted with an equal volume of water and extracted with ether. The ethereal solution was extracted three times with aqueous sodium carbonate (5% w/v). The carbonate extracts were combined and acidified with concentrated hydrochloric acid. Isolation of the oil thus liberated with ether gave the mixture of ketones (5·8 g., 80%), b. p. 123°/0·15 mm., n_D^{24} 1·4755, which gave an intense wine-red colour with ferric chloride but did not react with Brady's reagent (Found : C, 63·95; H, 6·3. Calc. for $C_{11}H_{13}O_3N$: C, 63·75; H, 6·3%).

Ozonolysis. A slow stream of ozonised oxygen was bubbled through a cooled solution of the ketones (500 mg.) in acetic acid ("AnalaR"; 10 c.c.) for 2½ hr. Zinc dust (1·0 g.) was added, and the mixture steam-distilled in an atmosphere of nitrogen. The distillate was treated with an excess of dimedone reagent and yielded the derivative of formaldehyde (204 mg., 29%) as needles, m. p. 185—189°, raised by crystallisation from aqueous methanol to 188—189°, undepressed on admixture with an authentic specimen, m. p. 189°.

*Ethyl 3-Cyano-2-keto-4- and -5-ethyl*cyclo*pentane-1-carboxylate.*—A solution of the preceding isomeric ketones (3·1 g.) in alcohol (25 c.c.) was shaken in hydrogen in the presence of Adams's catalyst. When the rate of absorption became very small, the reaction was interrupted (hydrogen absorbed : 401 c.c. at 23°/741 mm. Calc. for 1 mol., 373 c.c.). Removal of catalyst and solvent, and distillation of the residue, gave the dihydro-derivatives (1·4 g., 44%), b. p. 123°/0·5 mm., n_D^{22} 1·4633, which gave an intense wine-red colour with ferric chloride (Found : C, 62·7; H, 7·5. Calc. for $C_{11}H_{15}O_3N$: C, 63·15; H, 7·25%).

*3-Ethyl*cyclo*pentanone.*—A solution of ethyl 3-cyano-2-keto-4- and -5-ethyl*cyclo*pentane-1-carboxylate (0·65 g.) in concentrated sulphuric acid (1·3 g.) was kept at 20° for 2½ hr. and then diluted with water (6 c.c.). The mixture was heated under reflux for 6 hr. and then kept overnight. Steam-distillation and isolation of the product from the distillate by ether-extraction gave 3-ethyl*cyclo*pentanone (0·3 g.). The 2 : 4-dinitrophenylhydrazone crystallised from methanol in plates, m. p. 78°, undepressed on admixture with the specimen described in Part II (*J.*, 1952, 3616). The di-*m*-nitrobenzylidene derivative crystallised from alcohol–ethyl acetate in needles, m. p. 155—156°, undepressed on admixture with the specimen described in Part II.

*Ethyl 1-Acetyl-2-vinyl*cyclo*propane-1-carboxylate.*—A solution of ethyl sodioacetoacetate (from 65 g. of ethyl acetoacetate and 11·5 g. of sodium) in alcohol (190 c.c.) was added during 1 hr. to a boiling solution of 1 : 4-dibromobut-2-ene (53·5 g.) in alcohol (200 c.c.). The mixture was stirred at 20° overnight and then poured into water. Isolation of the product with ether and distillation gave : (i) *Ethyl 1-acetyl-2-vinyl*cyclo*propane-1-carboxylate* (23·6 g.), b. p. 97°/12 mm., n_D^{19} 1·4630 (Found : C, 65·7; H, 7·8. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·75%. Hydrogen no. : 91·1, equiv. to 2·0 double bonds). It gave no colour with ferric chloride. Light absorption : see Table 3. (ii) A colourless mobile liquid (4·8 g.; 8%), b. p. 103°/0·4 mm., n_D^{24} 1·4471, which gave a blue colour with ferric chloride [Found : C, 63·0; H, 8·6. $C_{12}H_{20}O_4$ requires C, 63·15; H, 8·8%. Hydrogen no. (Adams's catalyst; acetic acid), 119, equiv. to 1·9 double bonds]. (iii) A viscous oil (1·8 g.; 2·3%), b. p. 150° (bath-temp.)/10^{-5} mm., n_D^{22} 1·4621, which gave a blue colour with ferric chloride (Found : C, 61·6; H, 7·75. $C_{16}H_{24}O_6$ requires C, 61·5; H, 7·75%).

cyclo*Propane-1 : 1 : 2-tricarboxylic Acid.*—A slow stream of ozonised oxygen (*ca.* 3% of O_3) was bubbled through a cooled solution of ethyl 1-aceto-2-vinyl*cyclo*propane-1-carboxylate (1·5 g.) in acetic acid ("AnalaR"; 12 c.c.) for 6 hr. Hydrogen peroxide (35 c.c.; 20-vol.) was added, and the solution kept at 20° overnight and then evaporated under reduced pressure. The residue (*ca.* 2 c.c.) was made slightly basic by addition of dilute alkali and cooled to 0°. A solution of sodium hypobromite (from 9·0 g. of sodium hydroxide and 4 c.c. of bromine in 40 c.c. of water) was added slowly, and the mixture kept at 20° for 1 hr. The mixture was extracted with ether and then acidified with concentrated hydrochloric acid. The excess of hypobromite was decomposed by addition of sodium hydrogen sulphite, and the resulting solution was extracted thoroughly with ether (constant ether-extractor, overnight). Evaporation of the extract yielded a solid (630 mg.) which, crystallised twice from ether, gave *cyclo*propane-1 : 1 : 2-tricarboxylic acid (460 mg.), m. p. 184° (decomp.), undepressed on admixture with an authentic specimen.

Methyl Pentyl Ketone.—A solution of ethyl 1-acetyl-2-vinyl*cyclo*propane-1-carboxylate (2·19 g.) in ethyl acetate (15 c.c.) was shaken in hydrogen in the presence of Adams's catalyst until absorption was complete (532 c.c. at 28°/765 mm., equiv. to 1·85 double bonds). The catalyst and solvent were removed and the residue was shaken with aqueous sodium hydroxide (20 c.c., 5% w/v) for 7 hr. at 20°. The mixture was extracted with ether, and the aqueous layer acidified with sulphuric acid (2 c.c.; 50% v/v) and steam-distilled. The distillate was saturated with potassium carbonate and extracted with ether. Distillation of the extract gave methyl pentyl ketone (0·66 g.), b. p. 142°. The 2 : 4-dinitrophenylhydrazone was purified by chromatographic adsorption on alumina from benzene solution and crystallisation from methanol; it had m. p. 72—73°, undepressed on admixture with an authentic specimen.

The investigations described in this and the following paper were performed during the tenure by one of us (R. W. K.) of a Beaverbrook Overseas Scholarship. Analyses and light-absorption measurements were carried out in the microanalytical (Mr. F. H. Oliver) and spectrographic (Mr. A. I. Boston) laboratories of this Department.

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