

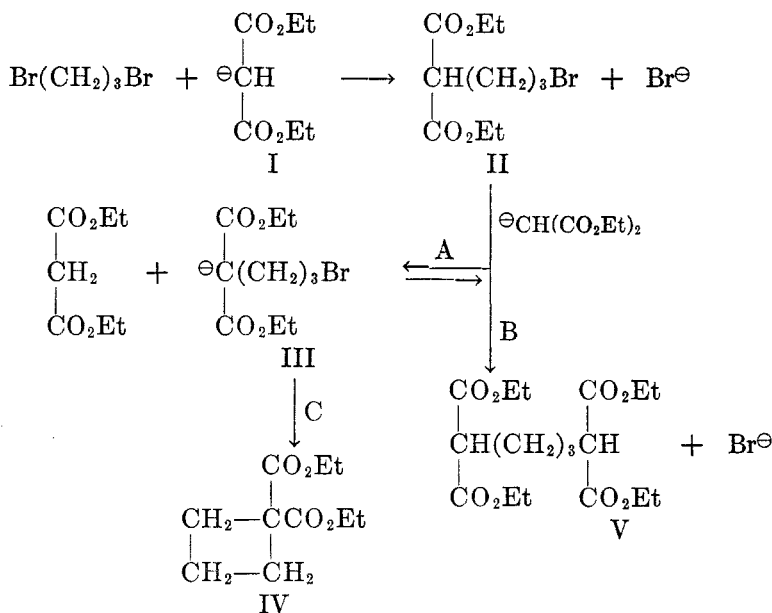
## THE PREPARATION OF CYCLOBUTANECARBOXYLIC ACID

JAMES CASON AND CHARLES F. ALLEN

*Received March 14, 1949*

Cyclobutanecarboxylic acid has been the principal starting material for preparation of monosubstituted cyclobutane derivatives, and in a recent paper (1), there was reported a convenient preparation of cyclobutane from this acid. The hydrolysis and decarboxylation of diethyl cyclobutanedicarboxylate has offered no difficulties; however, low yields have always been reported for the preparation of the diester from condensation of trimethylene dibromide with sodio malonic ester. Heisig (2) has reported that his investigations failed to improve the yield of about 25% reported by previous workers, including Perkin (3) who first carried out the reaction in 1887. The preparation in Organic Syntheses (4) gives a similar yield.

Since considerable quantities of cyclobutanecarboxylic acid were required for preparation of cyclobutane, a study was made of the condensation of trimethylene dibromide with sodio malonic ester, and methods have been developed for obtaining the cyclic diester in yields as high as 60%. The reactions involved in this condensation are presented in the accompanying chart.



It will be noted that the critical feature, which determines whether cyclic ester, IV, or tetraester, V, is obtained, is the mode of reaction of malonic ester ion with the bromoester, II, obtained in the first step. Alkylation of the ion, III, with trimethylene dibromide is not considered since the intramolecular reaction, C, is highly favored. Reaction A is a reversible ion exchange, presum-

ably relatively rapid in comparison with the irreversible reactions B and C. If it be assumed that the rates of reactions B and C are of the same order of magnitude, it follows that the relative yields of esters IV and V depend on the position of equilibrium A. Further, if two moles of sodio malonic ester are used for each mole of trimethylene dibromide, so that the full mole of ion, III, may be obtained as indicated in the chart, a mole of malonic ester is liberated for each mole of cyclic diester formed, and the accumulation of this malonic ester shifts equilibrium A to the right so that formation of tetraester, V, is favored during the latter stages of the reaction. Use of an amount of malonic ester in excess of the sodium, as most previous workers have, is especially unfavorable

TABLE I  
ALKYLATION OF DIETHYL MALONATE WITH TRIMETHYLENE DIBROMIDE

RUN. NO.	RATIO OF REAGENTS			YIELDS, <sup>a</sup> %	
	Dibromide	Na	M.E.	Diester, IV	Tetraester, V
1	1	2	3	24	52
2	1	3	3	53	16.3
3	1 <sup>b</sup>	3	3	49.9	23.9
4	1	2	2	42.8	18.4
5	1	2	1.5	54	12.3
6	1	2 <sup>c</sup>	1.1	52.4	8.1
7	1	2 <sup>d</sup>	1.2	60.8	7.3

<sup>a</sup> All yields based on trimethylene dibromide. <sup>b</sup> Dibromide added during one hour to the refluxing solution. <sup>c</sup> NaOEt (0.9 equivalent) in ethanol added concurrently with the dibromide, during one hour to the refluxing solution. No malonic ester was recovered in this run, but 2 g. of dibromide was recovered. <sup>d</sup> NaOEt (0.8 equivalent) added concurrently as described in <sup>c</sup>. A small amount of unreacted malonic ester was recovered (5.3 g. of fore-run before cyclic ester was collected).

to formation of cyclic ester. It might appear that this difficulty could be avoided by using two moles of sodium ethoxide to one of malonic ester so that the malonic ester and bromoester, II, would be converted to their ions as rapidly as formed. This is a small help; however, only one molecule of sodium ethoxide will react with a molecule of malonic ester, and the second mole of sodium ethoxide destroys considerable trimethylene dibromide during the early stages of the reaction. These are the difficulties which have caused the low yields previously reported<sup>1</sup>, but the dilemma is resolved simply by adding the second mole of sodium ethoxide concurrently with the trimethylene dibromide.

The reality of the principles discussed in the above paragraph is well illustrated by the data in Table I on the yields under various conditions. Runs 1 and 2 are especially striking, since increasing the ratio of sodium (thus converting the third equivalent of malonic ester to its ion) completely reverses the

<sup>1</sup> Since this manuscript was submitted there has appeared a report [Walborsky, *J. Am. Chem. Soc.*, **71**, 2941 (1949)] of preparation of diethyl cyclobutanedicarboxylate by a three-step process from diethyl malonate, the over-all yield being somewhat better than previously reported but considerably less than for the present one-step process.

ratio of cyclic diester to tetraester. Run 3 shows that the relative concentration of trimethylene dibromide has no effect on the ratio of products. It is of interest that the tetraester, V, may be hydrolyzed and decarboxylated to yield pimelic acid, and this would be a favored method of preparing this acid if it were not for its present ready availability from tetrahydropyran (5).

#### EXPERIMENTAL

*Alkylation of diethyl malonate.* The diethyl malonate was a redistilled technical product, and the trimethylene dibromide was washed with sulfuric acid and distilled. The ethanol was dried by distillation from sodium. The data in Table I were obtained in runs using 0.25 mole of trimethylene dibromide, and the indicated equivalencies of the other reagents, and 500 ml. of ethanol per mole of sodium. The products were separated by fractionation through a 65-cm. Podbielniak type column containing a tantalum wire spiral and a partial reflux head. The distillation pattern is illustrated by the following data on distillation of the products from Run 1: (a) diethyl malonate, 52.6 g., b.p. 91–92° (15 mm.); (b) intermediate, 2.7 g.; (c) diester, IV, 12.1 g., b.p. 109–110° (15 mm.); (d) intermediate, 2.4 g.; (e) tetraester, V, 46.8 g., b.p. 182–189° (1.5 mm.); (f) residue, about 3.5 g. The best procedure for preparative purposes is described below.

In a three-necked flask equipped with stirrer, reflux condenser protected by calcium chloride tube, and long-stem dropping-funnel, 23 g. (1 atom) of sodium was allowed to react with 500 ml. of dried ethanol. After cooling, 200 ml. of this solution was drawn into the dropping-funnel by suction and this funnel was placed on top of the condenser. There was then added to the flask 96 g. (0.6 mole) of diethyl malonate, this mixture was heated to boiling with stirring, and there was added concurrently during one hour the sodium ethoxide solution and 101 g. (0.5 mole) of trimethylene dibromide. After addition was complete the mixture was heated an additional ninety minutes, then about 400 ml. of ethanol was distilled with continued stirring. The residue was shaken out with water and benzene, and the aqueous phase was extracted with two additional portions of benzene. After removal of benzene, the residue was distilled in a Claisen flask. After a small fore-run, the *cyclic ester* was collected at 105–112° (15 mm.), yield 60–65 g. (60–65%). The small amount of diethyl malonate in this product does not interfere with its use for the preparation of cyclobutanecarboxylic acid.

*Cyclobutanecarboxylic acid.* The diester was hydrolyzed by heating and stirring under reflux with 1.5 ml. of water and 3 ml. of conc'd hydrochloric acid per gram of ester. The mixture was stirred for one hour after it became homogeneous, usually a total of 3–5 hours. After hydrolysis was complete, water and hydrochloric acid were removed by distillation through a short, indented column and the residue was heated at 160–180° until evolution of carbon dioxide had ceased (usually 1–2 hours). The residue was poured into a distilling flask and distilled at atmospheric pressure, then redistilled at reduced pressure. The yield of colorless *cyclobutanecarboxylic acid*, b.p. 104–106° (21 mm.), is 75–80%. A small additional amount of product may be obtained by ether extraction of the aqueous distillate.

#### SUMMARY

A method has been developed for obtaining diethyl cyclobutanedicarboxylate in 60% yield, from trimethylene dibromide and diethyl malonate.

BERKELEY, CALIFORNIA

#### REFERENCES

- (1) CASON AND WAY, *J. Org. Chem.*, **14**, 31 (1949).
- (2) HEISIG, *J. Am. Chem. Soc.*, **63**, 1698 (1941).
- (3) PERKIN, *J. Chem. Soc.*, **51**, 1 (1887).
- (4) HEISIG AND STODOLA, *Org. Syntheses*, **23**, 16 (1943).
- (5) CASON, WALLCAVE, AND WHITESIDE, *J. Org. Chem.*, **14**, 37 (1949).