sulting white precipitate was collected to yield 14.6 g. of crude cyclohexylhydroxylamine, m.p. 136–139°.

To a mixture of 20 g. of the crude product in 400 ml. of water and 50 ml. of benzene, 24 g. of benzoyl chloride was added dropwise while 25 g. of solid sodium bicarbonate was added in small portions to neutralize the hydrochloric acid formed. After 2 hr., 50 ml. of ether was added to assist in layer separation, and the aqueous layer was separated and discarded. The benzene layer was extracted with cold 3 *M* sodium hydroxide. Neutralization of the aqueous layer with 3 *M* sulfuric acid and collection and recrystallization of the solid from ethanol–water gave 18.1 g. (46%) of N-benzoylcyclohexylhydroxylamine, m.p. 155–156°.

Anal. Calcd. for $C_9H_9NO_2$: C, 63.56; H, 6.00; N, 9.27; O, 21.17. Found: C, 63.39; H, 5.89; N, 9.21; O, 21.14.

Oxidation Procedure.—The procedures for all of the oxidations cited in Table II were essentially the same except for the variations noted in the table. The procedure is illustrated by the oxidation of N-benzoylphenylhydroxylamine (**2a**).

A solution of 5.0 g. (0.023 mole) of N-benzoylphenylhydroxylamine (N-phenylbenzohydroxamic acid) in 100 ml. of a 1:1 solution of acetic acid–ethanol was cooled to −20°. While this solution was stirred rapidly, 11.5 g. (0.024 mole, based on 94% purity) of lead tetraacetate (Arapahoe Chemical) was added in one portion. In less than 10 sec. (and certainly no more than 15 sec.), when the bright green color which first appeared just *began* to darken, toward tan or brown, 100 ml. of water was added to decompose any unconsumed lead tetraacetate and the then brown to black mixture was steam distilled *as rapidly as possible*, the distillate being collected in a flask filled with ice. The distillate was filtered and the product was pressed dry between filter papers. Generally (because of the alcohol present) no further purification was required; however, the product could be recrystallized from alcohol–water. The yield of nitrosobenzene was 1.4–2.0 g. (56–80%).

The yield was dependent not only on the reaction time (times above 20 sec. often led to a loss of one-third or more of the possible yield) but also on the time required for steam distillation. When steam distillation was completed in 3 min., the yield was 73–80%; in 5 min., the yield was 56–65%.

When the reaction was allowed to proceed too long, the reaction mixture turned deep black. The only steam volatile product was the nitroso compound, albeit in greatly reduced yields. Presumably, the nitroso compounds were attacked by the lead tetraacetate, although more slowly than the N-acyl-N-arylhydroxylamines. The nature of these secondary oxidation products was not determined.

Propionic acid (100 ml.) could be substituted for the 1:1 acetic acid–ethanol; however, the latter not only facilitated the steam distillation (alleviating any tendency toward blockage of the condenser) but also yielded a more nearly pure product (dissolving some of the impurities present in the distillate).

Optimum conditions for large-scale runs were not determined. One run, three times the indicated size, gave a 59% yield, but the mixing time and the time required for steam distillation were obviously too long.

Some recent samples of lead tetraacetate, as received, appeared to give lower yields than older samples. Inasmuch as these samples contained less acetic acid (which tends to stabilize the reagent and lower its activity), these samples were moistened with acetic acid (7 ml./100 g. of lead tetraacetate) and allowed to stand overnight before use. In addition the temperature was brought to −40° before addition of the lead tetraacetate.

The identities of the nitroso compounds were confirmed by comparison of their infrared spectra in potassium bromide disks (*i.e.*, as the nitroso dimers) and of their melting points with those reported by Lüttke[22] (Table III).

TABLE III
PROPERTIES OF NITROSO COMPOUNDS

Compd.	D.M.S. card no.[a]	M.p., °C.	Lit.[a] m.p., °C.
Nitrosobenzene	5363	66–68	68
p-Nitrosotoluene	5365	46–48	47.5–48
p-Nitrosochlorobenzene	5368	86–88	89.5

[a] Reference 22.

Isolation of Benzoic Acid.—Benzoic acid was isolated from the aqueous residue left in still pot from an oxidation of N-benzoylphenylhydroxylamine by extraction with ether. The ether was extracted with 3 *M* sodium hydroxide and the aqueous solution was neutralized with 3 *M* sulfuric acid. The benzoic acid which precipitated melted at 120–121° and had an infrared spectrum identical with that of an authentic sample. Yields of 2.1–2.9 g. (60–85%) were obtained.

(22) W. Lüttke, Documentation of Molecular Spectroscopy, cards no. 5363, 5365, and 5368, Butterworths and Co. (Publishers) Ltd., London.

Stereochemistry of the Decarboxylation of Some 1,1,2-Cycloalkanetricarboxylic Acids[1]

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The stereochemistry of the decarboxylation of the 1,1,2-tricarboxylic acids of the three-, four-, five-, and six-membered carbocyclic rings has been determined in collidine, 5 *N* HCl, and without a solvent. In collidine only the cyclopropyl compound yields any *trans* isomer of the 1,2-dicarboxylic acid; all the others yield exclusively the *cis* isomers. In 5 *N* HCl all four of the acids give mainly *trans* isomers. Decarboxylation without solvent gives largely *cis* isomers. These results are rationalized in terms of steric control of the process depending on the bulk of the proton donor in its approach to the enol intermediate, but modified somewhat by ring strain.

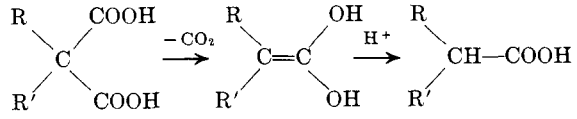
The decarboxylation of α-substituted 1,1-dicarboxylic acids (substituted malonic acids) has been used synthetically for many years, but relatively little attention has been paid to mechanism or stereochemistry. The subject of stereochemistry arose in this laboratory when it was noted that the ratio of *cis*- to *trans*-1,2-cyclobutanedicarboxylic acid varied with conditions of decarboxylation of 1,1,2-cyclobutanetricarboxylic acid. It was deemed of interest to pursue the study of decarboxylation stereochemistry through the three-, four-, five-, and six-membered rings, and note the effect of conditions on the geometry of the product. It was discovered at once that the several reports in the literature[2] on the subject were contra-

(1) Abstracted from the Ph.D. Thesis of D. J. J. Lennon, University of Rhode Island, 1961. Presented in part before the Division of Organic Chemistry, 145th National Meeting of the American Chemical Society, New York, N. Y., Sept. 1963.

(2) (a) E. Buchner, *Ann.*, **284**, 197 (1895); (b) W. H. Perkin, *J. Chem. Soc.*, **65**, 572 (1894); (c) E. Buchman, *J. Am. Chem. Soc.*, **64**, 2696 (1942); (d) A. Kotz and P. Spiess, *J. prakt. Chem.*, [2] **64**, 394 (1901); (e) R. Kuhn and A. Wasserman, *Helv. Chim. Acta*, **11**, 50, 70, 79, 600 (1928); (f) A. Wasserman, *ibid.*, **13**, 207, 223 (1930); (g) R. C. Fuson, C. L. Fleming, P. F. Warfield, and D. E. Wolf, *J. Org. Chem.*, **10**, 121 (1945).

dictory, probably because of equilibration of *cis* and *trans* isomeric products during isolation or purification.

The mechanism of decarboxylation has been studied for a variety of acids.[3] It is presently believed to involve the loss of carbon dioxide as the first step to produce an enol, which then is protonated to yield the



observed acid. The enol has never been isolated, either physically or kinetically. The present study is primarily concerned with the conversion of the enol to the acid. Jacobs and Florsheim[4] were able to demonstrate that the same intermediate, presumably the enol, was involved, because 2^c-carboethoxy-1^c,3^c-dimethylcyclopentane-2^t-carboxylic acid and 2^t-carboethoxy-1^c,3^c-dimethylcyclopentane-2^c-carboxylic acid gave the same mixture of *cis* and *trans* ethyl esters as products. Zimmerman[5] studied the stereochemistry of the ketonization of enols in decarboxylation of two cyclohexyl compounds, the 2-phenyl- and 4-phenyl-1,1-cyclohexanedicarboxylic acids, and came to the conclusion that the side from which the protonating agent approached determined the stereochemistry of the product, with the protonating agent preferentially approaching from the least-hindered side.

The size of the ring also may be expected to have an influence on the protonization process of the enol. Thus the enol will be destabilized by ring strain in the exocyclic double bond so that it may react more readily than an unstrained enol. Furthermore, the geometry of the ring and attached groups will vary among the various ring sizes and possibly block the approach of the proton donor.

The size of the proton donor will also influence the course of the ketonization reaction by varying in its ability to approach the more hindered side of the enol.

The analytical problems were twofold. The decarboxylation conditions had to be adjusted to yield essentially complete reaction, but not yield equilibration of products, and the separation of these chemically very similar *cis* and *trans* dicarboxylic acid isomers had to be effected quantitatively and without equilibration. The first problem was quite simple. Equilibration takes place slowly relative to decarboxylation so that a short, fast decarboxylation was used and was found to give no evidence of variation in product isomer ratios, nor were the products unstable; geometrically under the reaction conditions. The analyses were more difficult, but two methods were eventually worked out. A selective absorption on charcoal gave rough results, and a paper strip chromatographic method yielded good results, concordant with the charcoal method.

Results and Discussion

The 1,2,2-cycloalkanetricarboxylic acids of the three-, four-, five-, and six-membered rings were synthesized by standard methods and purified by fractional crystallization. An interesting note here is that these tricarboxylic acids are considerably more soluble in organic solvents than the dicarboxylic acids, which facilitated purification.

The decarboxylations were carried out by placing a weighed sample of the tricarboxylic acid in a tube of about 5-ml. capacity, together with the solvent, when one was used. The system was swept with dry nitrogen. The reaction tube, connected to a gas buret, was then immersed in an oil bath maintained at 205° for 1 min. The corrected volume of carbon dioxide was measured on a number of typical runs to be sure the reaction was complete. The contents remaining in the reaction tube were then analyzed directly, except, that when collidine was used as a solvent, the bulk of the collidine was first evaporated under high vacuum.

Analyses were made best by descending paper strip chromatography, using 1:7:2 water–ethanol–ammonia in a modification of the method of Cheftel, Munier, and Macheboeuf.[6] Five samples were chromatographed from each decarboxylation. Two were developed with bromocresol green and then lead acetate to locate the position of the two acids. The three remaining chromatograms were cut up, and the individual acids were titrated with standard base. Another analytical method involving selective absorption on charcoal was worked out at first but abandoned in favor of the chromatographic method. In the charcoal absorption method a working curve was derived from known mixtures of the *cis*- and *trans*-1,2-cycloalkanedicarboxylic acids, stirred with an aqueous suspension of activated charcoal, filtered, and titrated. It was possible to obtain isomer distribution results from unknown samples with an accuracy of 5%. Table I compares the two methods. The results of the decarboxylations are given in Table II. Each entry in Table II is the average of two or more decarboxylations, and three paper strip chromatograms per decarboxylation.

TABLE I

COMPARISON OF ANALYTICAL METHODS. DECARBOXYLATION WITHOUT SOLVENT

Ring size	Chromatographic analysis, %	Absorption analysis, %
3	47 ± 2 *trans*	46 ± 5 *trans*
4	29 ± 2 *trans*	30 ± 5 *trans*
5	12 ± 2 *trans*	15 ± 5 *trans*
6	20 ± 2 *trans*	17 ± 5 *trans*

TABLE II

EFFECT OF SOLVENT ON STEREOCHEMISTRY OF DECARBOXYLATION

1,1,2-Tricarboxylic acid	% *cis* isomer formed		
	Collidine	Without solvent	5 *N* HCl
Cyclopropane	83.4 ± 2.0	52.9 ± 2	12.6 ± 2.0
Cyclobutane	100 ± 2.0	70.7 ± 2	11.4 ± 2.0
Cyclopentane	100 ± 2.0	88.4 ± 2	28.9 ± 2.0
Cyclohexane	100 ± 2.0	80.4 ± 2	0.0 ± 2.0

It is apparent from the results given in Table II that the geometry of the decarboxylation can be controlled quite effectively by choice of solvent. Since

(3) L. W. Clark, *J. Phys. Chem.*, **68**, 587 (1964), and previous papers in the series.

(4) T. L. Jacobs and W. H. Florsheim, *J. Am. Chem. Soc.*, **72**, 256 (1950).

(5) (a) H. E. Zimmerman and H. J. Giallombardo, *ibid.*, **78**, 6259 (1956); (b) H. E. Zimmerman and T. W. Cuteshall, *ibid.*, **80**, 2893 (1958).

(6) R. I. Cheftel, R. Munier, and M. Macheboeuf, *Bull. soc. chim. biol.*, **34**, 380 (1952).

the *cis* or *trans* nature of the product is determined entirely by the direction of approach of the protonating agent, steric effects should be of prime importance. The protonating agents in the three systems are presumably the collidinium ion in collidine, molecular acid where no solvent is employed, and hydronium ion in aqueous HCl. Their steric requirements should diminish in that order. The bulky collidinium ion apparently cannot approach the enol from the side blocked by the carboxylic acid group attached to C-2, except in the case of the cyclopropane ring where the approach is least hindered and the enol, because of ring strain, is most reactive. On the other hand, the smaller hydronium ion produces the thermodynamically stable *trans* isomer more readily since it can approach either side of the ring fairly effectively. The decarboxylation without solvent would appear to involve a proton donor of intermediate bulk. One cannot totally rule out intramolecular protonization, but the almost exclusive *cis* isomer formation in the collidine experiments would indicate that this route is unlikely.

The extreme sensitivity of the six-membered ring tricarboxylic acid to reaction conditions in the decarboxylation is especially noteworthy. Zimmerman[5] found only a moderate sensitivity toward solvent in the decarboxylation of 2-phenyl-1,1-cyclohexanedicarboxylic acid (73.5–76.0% *cis* product in collidine, 65.5% *cis* without solvent). The more polar character of the 2-carboxyl group may provide a better shield against protonization than the phenyl.

The over-all pattern demonstrates steric control of the reaction by steric bulk of the proton donor, and only secondarily a rough correlation with ring strain is readily apparent. Their results illustrate a remarkable sensitivity to steric control in the reaction mechanism. Continued research on stereochemistry and reaction kinetics is in progress.

Experimental

1,1,2-Cycloalkanetricarboxylic Acids.—The tricarboxylic acids of the four-, five-, and six-membered rings were synthesized by the method of Fuson and Kao[7] in which adipic, pimelic, and suberic acids, respectively, were converted by thionyl chloride and bromine, followed by ethyl alcohol, to the α,α'-dibromo esters. These were treated with sodium cyanide in absolute alcohol, and the resulting 1-cyano-1,2-carbethoxycycloalkanes were hydrolyzed with barium hydroxide. The precipitated barium salts were decomposed with slightly less than the theoretical amount of sulfuric acid, the barium sulfate was filtered off, and the filtrate was concentrated under vacuum to yield crystals of the tricarboxylic acids. Recrystallizations were from benzene or ether; 1,1,2-cyclobutanetricarboxylic acid, m.p. 91–92° dec.; 1,1,2-cyclopentanetricarboxylic acid, m.p. 129° dec.; 1,1,2-cyclohexanetricarboxylic acid, m.p. 193° dec.

1,1,2-Cyclopropanetricarboxylic acid was prepared by the method of Conrad and Guthzeit[8] and Michael[9] in which sodium diethylmalonate was treated with ethyl 2,3-dibromopropanoate. The triethyl ester (82%) was hydrolyzed with barium hydroxide and the tricarboxylic acid was recovered as with the other tricarboxylic acids above; m.p. 186° dec.; yield from ester, 71%.

***cis*- and *trans*-1,2-Cycloalkanedicarboxylic Acids.**—These acids were needed for reference purposes and in working out the analytical procedures. The *cis* isomers were prepared by decarboxylation of the tricarboxylic acids thermally, and the mixed isomers thus obtained were sealed in a tube and heated at 300° overnight. The resulting *cis* anhydrides were recrystallized and hydrolyzed. The *cis*-cyclohexanedicarboxylic anhydride was prepared from the commercially available *trans* isomer by refluxing with acetic anhydride for 24 hr. followed by hydrolysis of the anhydride so formed. The *trans* isomers were prepared by refluxing the mixed isomers formed by thermal decarboxylation of the tricarboxylic acids with alcoholic potassium hydroxide for 24 hr. followed by acidification and continuous ether extraction. The *trans*-1,2-cyclopropanedicarboxylic acid was made by treating α-bromoglutaric ester with alcoholic potassium hydroxide.

Decarboxylation.—The decarboxylations were carried out under a nitrogen atmosphere at atmospheric pressure in a 5-ml. tube connected to a gas buret. A reaction time of 1 min. at an oil bath temperature of 205° was found sufficient to yield the theoretical amount of carbon dioxide. Control experiments were run to show that *cis–trans* isomerization of products was negligible under these conditions. Sample size was about 0.2 g. About 2–3 ml. of collidine or 5 *N* HCl was used as solvent. In the case of the HCl or when no solvent was employed, the reaction product of the decarboxylation was analyzed directly. In these cases where collidine was employed, the bulk of the collidine was evaporated under high vacuum at 50°, and the residue was mixed with a few milliliters of 0.1 *N* maleic acid solution and chromatographed. The maleic acid was effective in overcoming "tailing" in the chromatography.

Analyses. A. Selective Absorption.—This method was used until the more satisfactory paper chromatographic process was found. A series of mixtures of known composition of *cis* and *trans* isomeric acids of one of the ring sizes was prepared and dissolved to give a solution 0.100 *M* in dicarboxylic acid. A 20-ml. aliquot was stirred for 6 hr. with 0.100 g. of activated charcoal. The solution was filtered and a 10-ml. sample of the filtrate was titrated and compared with a 10-ml. sample of the untreated acid solution. A working curve was prepared of per cent acid absorbed *vs.* per cent isomer composition. The *trans* acids were absorbed less strongly than the *cis* acids, so that the filtrate ranged from, for example, 67–70% of cyclobutanedicarboxylic acid in going from 0–100% *cis* isomer composition of the original solution. Unknowns handled in exactly the same way gave isomer distributions estimable to ±5% (see Table I).

B. Paper Strip Chromatography.—The method of Cheftel, Munier, and Macheboeuf[6] was very successful as descending paper strip chromatography. Reproducibility of R_f values was not very good, however, so that five strips of the same mixture were run simultaneously, two of them developed with bromocresol green and lead acetate, and the remaining three cut up and titrated to determine acid content of the bands. Three decarboxylations for each ring size were run and three analyses were performed for 5 *N* HCl and no solvent, and two decarboxylations for each ring size in the collidine solvent. Isomer separations were very satisfactory. Reproducibility was better than ±2%. The results are summarized in Table II.

(7) R. C. Fuson and T. Y. Kao, *J. Am. Chem. Soc.*, **51**, 1536 (1929).

(8) M. Conrad and M. Guthzeit, *Ber.*, **17**, 1187 (1884).

(9) A. Michael, *J. prakt. Chem.*, **35**, 132, 349 (1887).