the required time the reaction was quenched by immersion in cold water. Analysis for *syn* content was then carried out in the fashion described.

Isomerization in Solution.—A 50.00-ml. sample of cyclohexanol was heated in the top compartment of a constant temperature apparatus maintained (±1°) at the desired temperature by boiling cyclohexanol (161°) or *o*-xylene (144°) in the lower compartment. When constant temperature was attained, 60.0 mg. of the desired isomer of pure amine oxime was added. At measured intervals, 5-ml. samples were withdrawn, quenched in cold water, and analyzed for *syn* content. The presence of cyclohexanol did not interfere with the spectral analysis.

In basic or acidic regions in water, samples containing 6.00 mg. of the amine oxime were removed at measured intervals, neutralized with either acid or base to a pH of 7 using a Beckman Model GS pH meter and analyzed for *syn* content.

Three-membered Rings. V. The Formation of Cyclopropanes Substituted at All Three Ring Carbons. A Steric Analysis

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The reaction of some α,β-unsaturated esters and α-chloro esters in the presence of sodium hydride to form cyclopropanes substituted on all three of the ring carbons has been examined. The yields of diesters and the isomer ratios for each set of reactants has been determined in both polar and nonpolar media. Solvent effects, although present, are masked to a large extent by other effects, mainly steric in origin. The combination of effects in most cases leads to mixtures of isomers, but with certain patterns of substitution a fairly high degree of stereoselectivity may be observed in the nonpolar solvents. One β-substituent in the α,β-unsaturated ester produces no appreciable effect on the yield of the substituted cyclopropane, but an α,β-disubstituted acrylic ester results in decreased yields, and a β,β-disubstituted ester does not result in any isolable product.

In previous papers of this series the formation of cyclopropanes substituted on only two of the ring carbons has been examined.[2a,b] A major reason for this choice was that the products could exist in only two stereoisomeric forms, one *cis* isomer and one *trans* isomer. The present report concerns the extension of these studies to some examples of the more general case in which all three carbon atoms of the cyclopropane nucleus are substituted. We have limited our examples to esters, but on the basis of the earlier work we expect that the conclusions presented here can be extended to similar compounds in which ester groups are replaced by nitrile or related functional groups.[2a,b]

These more general cases are more complex than those previously studied for three reasons: (1) As many as four stereoisomeric products may be formed; (2) The intermediate anion may exist in two diastereomeric forms; and (3) The starting olefinic component may exist in either *cis* or *trans* form. These points are illustrated by the following equations which also summarize the compounds studied in this work.

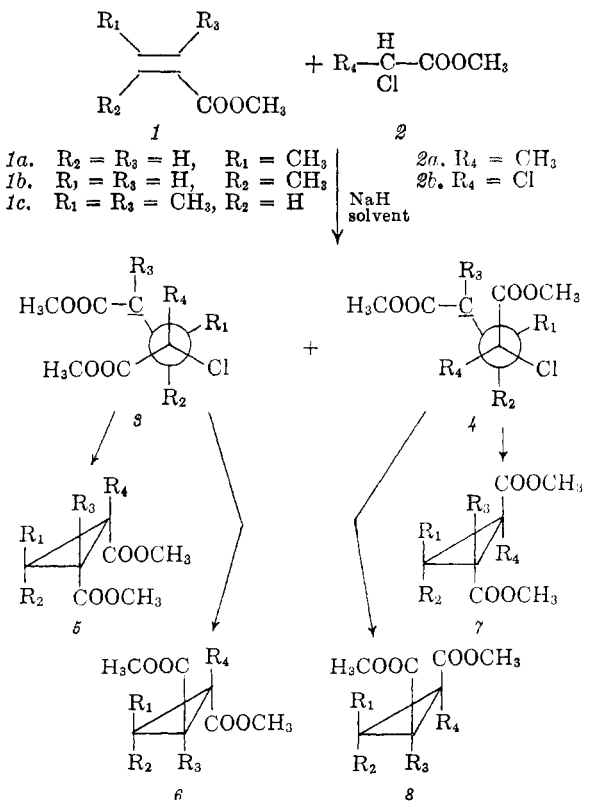

Chart I

Results

Yields of Ester Mixtures.—The products, mixtures of stereoisomeric esters, are generally obtained in satisfactory yield from monosubstituted acrylic esters, the substituent being in either the α-[2a,b] or β-position. With a disubstituted acrylic ester the yield of product drops markedly. This decrease is almost certainly due to hindrance in the initial Michael addition (Chart I). For reactions with α,β- or β,β-dimethyl acrylates much starting material was recovered. If this recovered ester is taken into account in the α,β-

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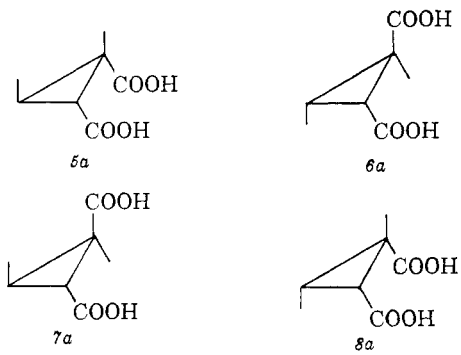
(2)(a) L. L. McCoy, *J. Org. Chem.*, **25**, 2078 (1960); (b) L. L. McCoy, *J. Am. Chem. Soc.*, **84**, 2246 (1962).

dimethyl derivative (methyl tiglate), the conversion to cyclopropane product is only slightly lower than for monosubstituted acrylates. This suggests that once the anion is formed by Michael addition it will close normally to the cyclopropane. Consequently, it is expected that heavily and suitably substituted glutaric esters would react satisfactorily to produce cyclopropanes.[2b] No satisfactory yields have been obtained from the β,β-dimethyl acrylate, indicating that this system offers more hindrance to Michael addition than the α,β-dimethyl arrangement.[3] The small amounts of "products" isolated were shown by gas chromatography to be complex mixtures consisting of at least five components. These were not identified or investigated.

Assignment of Configuration.—The compounds obtained in the present study are new. In order to draw any conclusions about the steric course of the reactions, it was necessary to assign configurations to the isomers isolated.

It is clear that in all isomeric sets the *cis* isomers will form monomeric cyclic anhydrides, thus readily differentiating them from the *trans* isomers. For the isomeric 1,3-dimethyl-1,2-cyclopropanedicarboxylic acids it is also clear that each isomer has only one



($R_1 = R_4 = CH_3$, $R_2 = R_3 = H$, for Chart I)

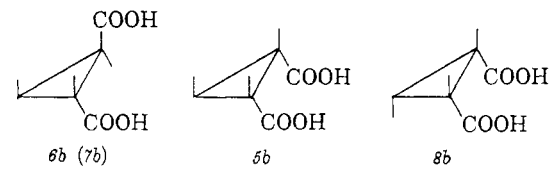
α-hydrogen next to a carboxyl group and, therefore, only one carboxyl group which may be isomerized. Consequently, *5a* and *6a* and *7a* and *8a* may be related in pairs by isomerization procedures (see Experimental). It is necessary, then, only to determine the structure of any one of the four isomers and the structures of the remaining three will be defined as a consequence of the established relationships. Actually, three of the isomers, *5a*, *6a*, and *7a*, can be assigned specific configurations on the basis of the n.m.r. spectra of their dimethyl esters, and consequently, the configuration of *8a* will also be determined.[4] The observed coupling constants for the ring protons are *5a*, 6.1 c.p.s., *6a*, 9.6 c.p.s., *7a*, 6.4 c.p.s. That is, the *cis* ring hydrogens of *6a* have a larger coupling constant than the *trans* ring hydrogens of *5a* and *7a*.[4b]

(3) No product was reported for the attempted reaction between *t*-butyl chloroacetate and ethyl β,β-dimethylacrylate with potassium *t*-butoxide as the condensing agent. R. Fraisse and M. Guitard, *Bull. soc. chim. France*, 418 (1960).

Thus, for the four isomeric acids isolated (see Experimental), the assignment of configuration is: *5a*, m.p. 129.8–130.4°; *6a*, m.p. 205–206°; *7a*, m.p. 199–200°; and *8a*, m.p. 157–158°. These n.m.r. configurational assignments are consistent with the previously established isomerization relationships.

The acid dissociation constants of the acids produced in the present work were also determined in aqueous solution at 20°.[5] The values of the *trans* isomers are of no value in assigning configurations, but the values for the *cis* isomers in conjunction with the assignments for the 1,3-dimethyl derivatives determined by n.m.r. spectra are of value. For *5a*, pK_1 is 3.69, pK_2 is 6.82, and ΔpK is 3.13, while for *8a*, pK_1 is 3.09, pK_2 is 7.91, and ΔpK is 4.82. These results are consistent with the reported values for *cis*-1,2-cyclopropanedicarboxylic acid (at 25°), pK_1 is 3.33, pK_2 is 6.47, and ΔpK is 3.14, and *cis*-caronic acid (at 25°; the 3,3-dimethyl derivative), pK_1 is 2.34, pK_2 is 8.31, and ΔpK is 5.97.[6] That is, for the *cis* diacid having a third *cis* substituent, ΔpK is quite large, ~4.5–6.0, much larger than with no substituent or a *trans* substituent on the third carbon in which cases ΔpK is ~2.0–3.5.

For the 1,2,3-trimethyl derivatives no difficulty arises with the single *trans* isomer. However,



($R_1 = R_3 = R_4 = CH_3$, $R_2 = H$, Chart I)

only one of the *cis* diacids was isolated. The acid dissociation constants, pK_1 4.23, pK_2 6.74, ΔpK 2.51, suggest that this *cis* acid is *5b*, m.p. 143.0–143.8°.

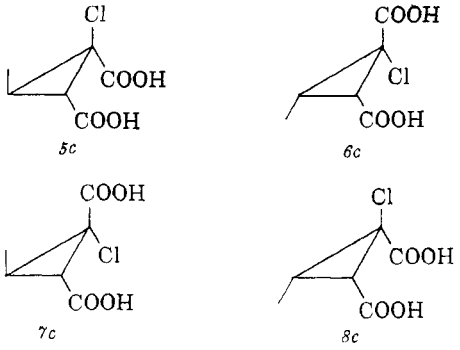
Methyl dichloroacetate is a unique type of halogen compound for this reaction. Thus, with R_4 = Cl, *3* and *4* become equivalent, *i.e.*, there is only one anionic intermediate (Chart I). In spite of this, four stereoisomeric products are possible in

(4)(a) These n.m.r. spectra were obtained and analyzed by Dr. W. C. Neikam, Sun Oil Co., Basic Research Division, Marcus Hook, Pennsylvania; the work was done at Columbia University. The spectra were obtained from dilute carbon tetrachloride solutions with internal tetramethylsilane standard at 60 Mc. The spectra are rather complex and a complete analysis was not attempted, but the coupling constants assigned to the ring protons for *5a*, *6a*, and *7a* are unambiguously established; (b) The assignment of configuration from these coupling constants are based on the values determined by Hutton and Schaeffer [*Can. J. Chem.*, **40**, 875 (1962)] for the ring hydrogens of *cis*-chrysanthemumic acid (8.7 c.p.s.) and *trans*-chrysanthemumic acid (5.4 c.p.s.). The paper by Hutton and Schaeffer contains a discussion of the relationship between coupling constants and configuration in rings of the type involved in the present work.

(5) The acid dissociation constants for all the acids prepared in the present work and for most of those prepared in earlier studies (ref. 2) have been determined. The complete results will be reported in another paper.

(6) G. Kortum, W. Vogel, and K. Andrussow, "Dissociation Constants of Organic Acids in Aqueous Solution," Butterworths, London, 1961, pp. 274, 290.

suitable cases. For the 1-chloro-3-methyl derivatives only two isomers, one *cis* and one *trans*, of the four possible were isolated. The *cis* isomer is

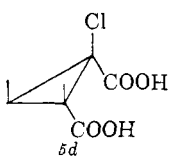


(R_1 = CH_3, R_2 = R_3 = H, R_4 = Cl, Chart I)

assigned structure *5c* on the basis of its acid dissociation constants, pK_1 2.66, pK_2 5.41, and ΔpK 2.75. Support for this assignment is given by the mode of crystallization of the *cis* isomer. Of all the diacids observed in this and previous[2a,b] work, only two compounds, *5a* and the chloro *cis* compound presently being considered, have been observed to crystallize in more than one form. The two crystal forms for both compounds are very similar in appearance; at times, both forms of either compound have been observed to crystallize together. This similar and almost unique crystallization characteristic suggests that *5a* and the chloro *cis* isomer are very closely related structurally, and consequently, that the chloro *cis* compound is *5c*.

We have no reliable evidence upon which to make a definite structural assignment for the chloro *trans* isomer. The *trans* isomer is only observed in the polar reaction medium, conditions which probably lead to isomer mixtures based approximately on the relative stabilities of the isomers.[2b] Here, only one of the two possible *trans* isomers is formed, and it might be expected that *7c* would be more stable than *6c*. Tentatively, then, we have assigned the chloro *trans* isomer structure *7c*.

The remaining compound observed in this work is one of the *cis* isomers of the 1-chloro-2,3-dimethyl derivatives. Its acid dissociation constants, pK_1 2.91, pK_2 5.41, ΔpK 2.50, suggest that it has structure *5d*.



(R_1 = R_3 = CH_3, R_4 = Cl, R_2 = H, Chart I)

Gas Chromatographic Analysis.—The distilled cyclopropane product mixtures were analyzed by gas phase chromatography to determine the isomer ratios. Unfortunately, not all of the possible isomers of each structure were available for comparison, and in one case a coincidence of retention time was observed for two isomers. Consequently, there is some ambiguity possible in the interpretation of the data from these analyses. Thus, for the product analyses of the 1,3-dimethyl compounds, *5a–8a*, four peaks were observed in all of the chromatograms; the first corresponded to *7a*, the second to *6a and 8a*, the third to *5a*, and the fourth was unidentified.[7] The 1,2,3-trimethyl derivatives, *5b–8b*, pose a different problem. Only two of the isomers were obtained as methyl esters for comparison, but three peaks are observed in the chromatogram, and three isomers are known to be present (see Experimental). There is no way to decide whether the third peak corresponds to the third isomer, or whether as in the case of the 1,2-dimethyl derivatives the third peak is some extraneous product and the third isomer is "buried" under one of the two identified isomer peaks. Subsequent discussion will be based on the isomer ratio determined for the two identified isomers; isomer ratios based on the assumption that the third peak corresponds to the third isomer lead to the same conclusions. Only peaks corresponding to the isolated isomers were observed for the chloro derivatives. A coincidence of retention time for the unknown chloro isomers with the known isomers is possible, but if this does occur, the missing isomers are unlikely to be present in appreciable amount since saponification of the chloro ester mixtures gave no indication for the presence of any isomers other than those actually isolated. The results of these analyses are presented in Table I.

Stereochemistry of the Reactions.—β-Substituted acrylic ester starting materials allow the possibility of *cis* and *trans* isomers. On the basis of previous studies[2a,b] it is reasonable to conclude that the intermediate anions 3 and 4 will have sufficiently long lifetimes to permit "equilibration" of the α-carbon. This would preclude any stereospecific relation between the starting olefinic component and the cyclopropane product. However, the steric factors influencing the Michael addition are not identical in a pair of *cis–trans* isomers. Therefore, each of the geometric isomers could lead to a different ratio of the intermediate anions *3* and *4*, and subsequently to different ratios of the cyclopropane isomers. Methyl *cis*-crotonate and methyl *trans*-crotonate were allowed to react with methyl α-chloropropionate in a hydrocarbon solvent in the cold. In each case 96% of the cyclopropane products were present as the same two isomers, one isomer arising from each intermediate

(7) This fourth peak varied from less than 5% (benzene solvent, cold) to about 30% (benzene solvent, excess *cis*-crotonate) of the total product; also, for the same ratio of reactants, the peak was greater for reactions run in polar solvents. It is possible that this product arises from the anion of the crotonic ester, and might be $CH_3OOCCH{=}CHCH_2C(CH_3)HCOOCH_3$, an acyclic isomer of the cyclopropanes.

TABLE I

THE YIELDS AND ISOMER RATIOS OF POLYSUBSTITUTED CYCLOPROPANES

Reactants[a] and conditions[b]	Yield of ester	% of isomer[a,b]			
		5a	*6a*	*7a*	*8a*
1a + *2a*, C_7H_8, 23°	75	44	5[c]	52	[c]
1a + *2a*, C_7H_8, reflux	56	26	18[c]	55	[c]
1a + *2a*, C_6H_6 + $[(CH_3)_2N]_3PO$	33	29	33[c]	38	[c]
1b + *2a*, C_6H_6, 25°	83[d]	52	5[c]	44	[c]
1b + *2a*, C_6H_6 + $[(CH_3)_2N]_3PO$	55	22	20[c]	58	[c]
		5b	*6b*	*7b*	*8b*
1c + *2a*, C_6H_6, 80°	29	49		51	
1c + *2a*, C_6H_6 + $[(CH_3)_2N]_3PO$	10	32		68	
		5c	*6c*	*7c*	*8c*
1a + *2b*, C_6H_6, 25°	40	100			
1a + *2b*, C_6H_6 + $[(CH_3)_2N]_3PO$	33	61		39	
		5d	*6d*	*7d*	*8d*
1c + *2b*, C_7H_8	51	100			
1c + *2b*, C_6H_6 + $[(CH_3)_2N]_3PO$	26	100			

[a] See Chart I. [b] See Experimental. [c] Because of coincidence of retention times these isomers could not be differentiated. [d] This yield is misleading due to the considerable amount of material represented by the fourth unidentified chromatographic peak; correction for this indicates a yield of about 50% of the cyclopropane compounds are obtained.

3 and *4*. The difference in isomer ratios is not large, and there is considerable doubt as to its significance. In the reaction with methyl *cis*-crotonate, excess ester was used and the excess was analyzed for isomerization after the reaction. The methyl *cis*-crotonate was about *80% isomerized* to the *trans* isomer.[8] In view of the isomerization and the small difference in isomer ratio, it is unlikely that the use of the less accessible *cis* olefinic isomers will offer any advantage.[8]

As shown in Chart I, the intermediate anion may exist in two diastereomeric forms. No attempt is made here to "predict" the ratio of these two anions, but it was expected that since there is no very large difference in size of the groups, at least a moderate amount of each anion would be formed. The isomer ratios for the 1,3-dimethyl derivatives[9] and for the 1,2,3-trimethyl derivatives indicate no strong preference for either *3* or *4*. In other cases, where the substituents show considerably greater attractive or repulsive interactions, it may be possible to predict which anion will predominate.

In the ring closure step, the effect of solvent is similar to that observed previously.[10] However, the solvent effects observed in the several systems are overshadowed to various extents by other factors, presumably steric in origin. These steric factors can be summarized by the statement: During the formation of the cyclopropane derivative the substituents will arrange themselves where possible so as to give approximately the same amount of bulk on each side of the three-membered ring. This rule and the previous one concerning the solvent effect[2b] sometimes work together and other times oppose each other. In coöperative cases, formation of *5a* in nonpolar solvent for example, the results are clean cut and afford a high degree of stereoselectivity. In opposing cases, the results also are clean cut, provided the distribution of substituents presents a large difference in the two possible arrangements, in which case the "steric rule" dominates, or the distribution presents very little difference in the two possible arrangements, in which case the "solvent rule" is dominant.[2b] In order for the "steric rule" to dominate, the substitution pattern probably must be either 1,2,3-trisubstitution[11] or 1,1,2,3-tetrasubstitution. In both cases the accumulation of three substituents on one side of the cyclopropane ring is clearly highly unfavorable.[11,12] In all other patterns of substitution the "solvent rule" will be the exclusive or dominant factor.

For compounds substituted on all three ring carbons, Table I shows that generally their formation in polar solvents gives more complex isomer mixtures than their formation in nonpolar solvents. Consequently, from the preparative standpoint, the use of polar solvents in the formation of these compounds generally would appear to offer no advantage over nonpolar solvents, and in some cases their use might be detrimental. A possible exception is in the formation of the 1-chloro derivatives. With these compounds nonpolar solvents often lead exclusively to the *cis* isomer, while polar solvents usually allow the formation of some of the *trans* isomer.

The present work in conjunction with previous work[2a,b] strongly suggests that the formation of

(8) It is not clear whether the isomerization was due to Michael addition, isomerization, reverse Michael addition, or due to methyl crotonate anion formation, or possibly some third cause. If the isomerization, were due to methyl crotonate anion, $\overline{C}H_2CH{=}CHCOOCH_3$, it is possible that compounds like *cis*-cinnamic esters might not be isomerized under the reaction conditions. This might lead to a considerably greater difference in the ratio of *3* to *4* from the *cis* and *trans* isomers, and consequently a much greater observed difference in ratios of cyclopropane isomers; racemization of the α-carbon of the anions *3* and *4*, however, would still be possible.

(9) This is based primarily on the ratios observed in nonpolar solvents where essentially only two isomers are observed, one arising from each of the anions. The ratio of the sums of isomers from each anion would be more appropriate, but, as pointed out, two of the isomers of the 1,3-dimethyl derivatives, those present in smallest amount, could not be differentiated by our method of analysis.

(10) A second effect (probably small) of the solvent might influence the formation (the ratio) of the two anions 3 and 4. The results of the present work are not sufficiently refined to support any conclusions about this effect, but the data for the 1,3-dimethyl derivatives shown in Table I do suggest that such an effect is probably present.

(11) R. Fraisse and M. Guitard, *Bull. soc. chim. France*, 200 (1961).

(12) In the case of *5a–8a*, the *trans* arrangement of the carboxyl groups might actually favor by some small amount *6a* as opposed to *5a*. In the actual formation of the ring, however, because of the small difference in stability the solvent effect would be expected to be dominant. For nonpolar solvents this is clearly true. For polar solvents this is also true, as indicated by the data of Table I, if it is assumed that changes in "*6a*" reflect exclusively changes in *6a* and not in *8a* also. This is reasonable since *7a* is *trans* and has a balanced substituent distribution making it markedly more stable than *8a*.

any substituted 1-chloro-1,2-diester will be highly stereoselective in nonpolar solvents, leading exclusively or very predominantly to the *cis* isomer.

The formation of 1,2,3-trisubstituted 1,2-diesters probably will usually show rather small solvent effects and cannot be considered as stereoselective. The formation of 1,3-disubstituted 1,2-diesters, however, may be considered as stereoselective. By use of a nonpolar solvent and low temperature, essentially only two of the possible four isomers are formed, and each of these comes from a different anionic intermediate. In principle the two isomers may be separated readily by converting the *cis* isomer to an anhydride. Since each of these isomers may be isomerized by suitable means to an isomeric partner, all four of the possible isomers may be made available. An example of this is afforded in the present work by the formation of the four possible isomers of 1,3-dimethyl-1,2-cyclopropanedicarboxylic acid.

Apparently 3,3-disubstituted 1,2-diesters[3] and 1,3,3-trisubstituted 1,2-diesters cannot be made by the present method. However, it is possible that such compounds can be made from appropriately substituted glutaric esters and that the "solvent rule" will dominate.[2b] 3-Substituted 1,2-diesters have not been examined in the present study, but the work of Fraisse and Guitard[11] suggests that *trans* isomers will predominate, *i.e.*, the "steric rule" is dominant.

Experimental[13]

The general procedures previously described for the formation of polysubstituted cyclopropanes were used.[2,14] A Craig polyethylene glycol succinate substrate was used in the gas phase chromatographic analyses. Unlike previous systems, in which only two readily resolved isomeric products were present,[2a,b] the present work included product mixtures which in some cases consisted of four isomeric products. Retention times of the pure isomers[15] were quite close in several cases, but, with the exception of compounds *6a* and *8a*, it was easily possible to observe directly from the chromatographic recording the number of components and in a qualitative way the changes in amounts of components in the product mixtures prepared under various conditions. However, not all of the component peaks were completely resolved, and there was some tailing off of the peaks. By an approximation method allowing for overlap but not accounting for tailing off of the peaks, estimates were made of the relative amounts of the various isomers; the results are shown in Table I. The maximum error in these analyses is estimated at ±5%, but in most cases is probably much less.[16]

Isomers of 1,3-Dimethyl-1,2-cyclopropanedicarboxylic Acid.—Methyl crotonate (60.0 g., 0.6 mole), methyl α-chloropropionate (73.8 g., 0.6 mole), and sodium hydride (14.4 g., 0.6 mole) in toluene (60 ml.) gave a mixture of isomeric dimethyl 1,3-dimethyl-1,2-cyclopropanedicarboxylates, b.p. 108–115°/18 mm., 84 g. (75%). The product mixture (80 g.) was saponified with sodium hydroxide (52 g.) in water (293 ml.) and the resultant solution was evaporated almost to dryness on the steam bath. Dissolution of the residue in water (total volume of solution was about 300 ml.) and acidification with 125 ml. of concentrated hydrochloric acid gave on cooling a crystalline white precipitate. Suction filtration of the mixture gave 45 g. of a white solid which was repeatedly extracted with boiling acetonitrile until no additional solid dissolved. On cooling the acetonitrile extracts, crystals of a *trans* isomer, *7a*, were deposited; a small additional quantity was obtained by concentration of the acetonitrile mother liquors. Complete removal of acetonitrile from the second crop filtrate left 5.6 g. of a viscous oil which very slowly crystallized. This residue was combined with the acids obtained from the aqueous phase by extraction (see below). The total yield of *7a* (first and second crops) was 31.8 g., m.p. 198–200°. A small sample recrystallized from acetonitrile had m.p. 199–200° (reported[14] m.p. 203°).

The aqueous filtrate after removal of *7a* was extracted continuously with ether for about 48 hr. The extract was dried over magnesium sulfate and the ether was removed under reduced pressure (aspirator). After several hours the residue, 32 g., crystallized. To the crystalline residues (37 g., see above) was added 20 ml. of acetyl chloride. When hydrogen chloride ceased to be evolved, the mixture was filtered (negligible solid) and distilled. The distillate, b.p. 120–136°/10–12 mm., weighed 22.1 g.; the small amount of red tarry residue deposited 0.6 g. of very impure *7a* on trituration with chloroform. The distillate did not crystallize. Subsequently it was shown by infrared spectra that the distillate was the slightly impure anhydride of *5a*.

The crude anhydride (22 g.) was esterified[17] giving 23.0 g. (83%) of the crude dimethyl ester of *5a*, b.p. 106–112°/15 mm. The crude diester (22 g.) was refluxed with 1 g. of sodium methoxide in methanol (45 ml.) for about 18 hr. Then sodium hydroxide (14.2 g.) in water (81 ml.) was added slowly with continued reflux. Some solid separated, resulting in mild bumping. The mixture was evaporated to dryness on a steam bath and the residual solid was redissolved in water. Filtration of the solution removed a small amount of gummy material, and acidification of the filtrate followed by cooling in an ice bath resulted in the deposition of a crystalline solid. Filtration of the mixture gave 5.1 g. of solid which after several recrystallizations from acetonitrile gave 3.0 g. of *6a*, m.p. 204–205°. The infrared spectra of *6a* and *7a* are similar but easily distinguished, and the mixed m.p. is 175–190°. The residues from the acetonitrile mother liquors were shown by their infrared spectra to be approximately 50:50 mixtures of the two *trans* isomers *6a* and *7a*. An analytical sample of *6a* was recrystallized from acetonitrile and then sublimed, m.p. 205–206°.

Anal. Calcd. for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 53.51; H, 6.46.

The aqueous filtrate from removal of crude *6a* was extracted continuously with ether for about 42 hr. Work-up of the extract gave 14 g. of crude acid which was treated with acetyl chloride (10 ml.). After cessation of hydrogen chloride evolution, the resultant solution was distilled, giving the anhydride of *5a*, b.p. 135°/15 mm., 7.3 g., which slowly crystallized. Recrystallization of a small sample from cyclohexane and then sublimation gave the anhydride of *5a*, m.p. 45–46°.

(13) Melting points and boiling points are uncorrected. Analyses are by Micro-Tech Laboratories, Skokie, Ill.

(14) L. L. McCoy, *J. Am. Chem. Soc.*, **80**, 6568 (1958).

(15) Small samples of each of the pure acids isolated in the present work were esterified by diazomethane (from N-nitroso-N-methylurea) in ether. The esters so obtained were not distilled, but were shown to be chromatographically pure except for traces of ether.

(16) For the purpose of the present work this accuracy was considered to be adequate; some variations in the analytical conditions were examined and it is felt that considerably better analyses could be obtained, but only at excessive cost in time and effort.

(17) R. O. Clinton and S. C. Laskowski, *J. Am. Chem. Soc.*, **70**, 3135 (1948). Ethylene chloride was the solvent used in the present work.

Anal. Calcd. for $C_7H_8O_3$: C, 59.99; H, 5.75. Found: C, 59.50; H, 5.62.

Hydration of the anhydride gave the *cis* acid, *5a*, m.p. 123–125°. Recrystallization of an analytical sample from nitromethane gave *5a*, m.p. 129.8–130.4°.

Anal. Calcd. for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 52.93; H, 6.36.

This *cis* acid crystallizes in two radically different modifications, small compact chunks and extremely fine interlocking bunches of needles. Both forms melted at the same temperature and no phase change was observed prior to melting. The infrared spectra of the two forms taken as mineral oil mulls, however, are markedly different. Conditions for obtaining the two pure forms were not determined; in some cases both forms crystallized from the same solution. A similar phenomena appeared in one of the *cis*-chloro compounds described below.

trans Acid *7a* (15.8 g.) was refluxed with acetyl chloride (80 ml.) for about 4 hr. The solution was then distilled slowly at atmospheric pressure to remove most of the excess acetyl chloride and acetic anhydride. Distillation of the residue at 19 mm. gave 12.5 g. of distillate, b.p. 117–123°/19 mm. Hydration of the distillate in 24 ml. of water and chilling of the solution produced 6.4 g. of crystalline *8a*, m.p. 154–156°. Continuous ether extraction of the aqueous phase gave 3 g. of a sticky gum smelling strongly of acetic acid; this material was not examined further. An analytical sample of *8a* recrystallized from nitromethane had m.p. 157–158°; the melting point may vary by a degree or two depending on the rate of heating.

Anal. Calcd. for $C_7H_{10}O_4$: C, 53.16; H, 6.37. Found: C, 53.25; H, 6.44.

The anhydride of this *cis* acid was not obtained in a crystalline form.

Dimethyl 1,3-Dimethyl-1,2-cyclopropanedicarboxylate.—A. Methyl crotonate (10.0 g., 0.1 mole), methyl α-chloropropionate (12.3 g., 0.1 mole), and sodium hydride (2.4 g., 0.1 mole) in refluxing toluene (10 ml.) gave 10.5 g. (56%) of dimethyl 1,3-dimethyl-1,2-cyclopropanedicarboxylate, b.p. 93–98°/10 mm.

B. The same reactants (same quantities) in a mixed solvent, benzene (50 ml.), and hexamethylphosphoramide (50 ml.), gave 6.1 g. (33%) of the dimethyl ester, b.p. 95–101°/10 mm.

C. Methyl *cis*-crotonate[18] (4.0 g., 0.04 mole), methyl α-chloropropionate (2.5 g., 0.02 mole) and sodium hydride (0.5 g., 0.02+ mole) in benzene (2 ml.) gave 3.1 g. of the dimethyl ester, b.p. 67–68°/0.5 mm. The unchanged methyl crotonate in benzene was shown by gas chromatography to be 80% *trans*, 20% *cis*.

D. Methyl *cis*-crotonate (2.0 g., 0.02 mole), methyl α-chloropropionate (2.5 g., 0.02 mole), and sodium hydride (0.5 g., 0.02+ mole) in benzene (10 ml.) and hexamethylphosphoramide (10 ml.) gave 2.0 g. of the dimethyl ester, b.p. 83–86°/1.8 mm.

Isomers of 1,2,3-Trimethyl-1,2-cyclopropanedicarboxylic Acid.—Methyl tiglate (28.5 g., 0.25 mole), methyl α-chloropropionate (30.7 g., 0.25 mole), and sodium hydride (6.0 g., 0.25 mole) were mixed in benzene (25 ml.); reaction was negligible at about 25°, but a reasonable rate of gas evolution occurred when the mixture was warmed to 65–80°. The product, dimethyl 1,2,3-trimethyl-1,2-cyclopropanedicarboxylate, 4.4 g. (29%),[19] had b.p. 103–110°/16 mm. Saponification of this ester (14.0 g.) with sodium hydroxide (8.4 g.) in water (50 ml.) produced some insoluble salt which dissolved with additional water. The solution was filtered to remove a small amount of gummy material, concentrated on the steam bath to remove methanol, cooled, and acidified with concentrated hydrochloric acid. Some solid which separated was removed by filtration, and the filtrate was extracted continuously with ether. The solid and extracted material were combined (12 g.) and treated with acetyl chloride (11 ml.). After several hours at about 20° the mixture was filtered and the solid washed thoroughly with chloroform. Recrystallization of the solid from acetonitrile eliminated some insoluble material (sodium chloride?) and gave the *trans* isomer, *6b*, 2.1 g., m.p. 202–205°. An analytical sample recrystallized from acetonitrile and then sublimed had m.p. 205–206°.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 55.93; H, 7.05.

The acetyl chloride filtrate and chloroform washes (see above) were combined and distilled to give a mixture of the anhydrides of *5b* and *8b*, 4 g.,[20] b.p. 125–133°/14 mm. This mixture which slowly crystallized was recrystallized several times by dissolution in the minimum amount of chloroform, addition of three to five times as much (vol.) hexane, and chilling in the refrigerator. In this way one of the anhydrides, 1.0 g., m.p. 94.5–95.5°, was isolated. An analytical sample was sublimed, m.p. 95.8–96.8°.

Anal. Calcd. for $C_8H_{10}O_3$: C, 62.32; H, 6.54. Found: C, 62.15; H, 6.39.

Hydration of the anhydride gave the corresponding *cis* acid, *5b*. An analytical sample was recrystallized from water, m.p. 143.0–143.8°.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.80; H, 7.03. Found: C, 55.95; H, 7.25.

Evaporation of the chloroform–hexane mother liquors left 2.7 g. of mixed anhydrides. Warming this mixture with water (4 ml.) left an oil which showed no tendency to hydrolyze (dissolve) on continued warming. Separation of the oil (0.5 g.) and cooling produced a crystalline mass. The aqueous phase deposited fine needles (0.2 g.) on cooling. By their infrared spectra, the needles and crystallized oil appeared to be essentially the same mixture, *5b* and an anhydride probably from *8b*. Later, the aqueous phase rather suddenly deposited more crystals (0.4 g.) of *6b*. Combination of the oil and needles and fractional sublimation of the mixture gave the second anhydride, 0.15 g. Recrystallization of an analytical sample from chloroform–hexane gave the anhydride of *8b*, m.p. 84–85°.

Anal. Calcd. for $C_8H_{10}O_3$: C, 62.32; H, 6.54. Found: C, 62.46; H, 6.44.

The two anhydrides have very similar infrared spectra, but some mutually exclusive bands clearly show them to be different. Infrared spectral examination of the materials recovered from the various aqueous mother liquors show them to be mixtures of carboxylic acid and anhydride. Although *8b* was not obtained and consequently direct comparison could not be made, apparently there was no band in the infrared spectra of the mixtures which could not be accounted for by either *5b* or the anhydride of *8b*. The anhydride of *8b* appears to be very resistant to hydrolysis.

Dimethyl 1,2,3-Trimethyl-1,2-cyclopropanedicarboxylate.—Methyl tiglate (5.7 g., 0.05 mole), methyl α-chloropropionate (6.1 g., 0.05 mole), and sodium hydride (1.2 g., 0.05 mole) in benzene (25 ml.) and hexamethylphosphoramide (25 ml.) gave 1.0 g. (10%)[19] of the dimethyl ester, b.p. 108–112°/20 mm.

Isomers of 1-Chloro-3-methyl-1,2-cyclopropanedicarbox-

(18) Tetrolic acid [L. A. Carpino, *J. Am. Chem. Soc.*, **80**, 599 (1958)] was esterified[17] and catalytically reduced (Lindlar catalyst) [F. Dalton, P. S. Ellington, and G. D. Meakins, *J. Chem. Soc.*, 3681 (1960)] to methyl *cis*-crotonate. By gas chromatography there was only a trace (<2%) of the *trans* isomer present. To attain this selectivity required a high substrate to catalyst ratio; using the ratio reported by Dalton, *et al.*, gave a considerable amount of the *trans* isomer and some completely reduced material. A similar analysis of the commercial methyl *trans*-crotonate used in other reactions showed only a trace (<2%) of the *cis* isomer.

(19) In all reactions involving methyl tiglate as the olefinic component, considerable unreacted methyl tiglate, usually about 50–60% of the initial amount, was recovered.

(20) The low recovery of the anhydride mixture is probably due to their volatility which, unfortunately, was not at first appreciated. The structures of the anhydrides are quite compact and bear some resemblance to certain bicyclic systems which are known to be quite volatile.

ylic Acid.—Methyl crotonate (25 g., 0.25 mole), methyl dichloroacetate (35.8 g., 25.9 ml., 0.25 mole), and sodium hydride (6.0 g., 0.25 mole) in benzene (125 ml.) and hexamethylphosphoramide (125 ml.) gave 17 g. (33%) of dimethyl 1-chloro-3-methyl-1,2-cyclopropanedicarboxylate, b.p. 121–125°/18 mm. The diester (16.0 g.) was saponified at about 25° by swirling with sodium hydroxide (9.3 g.) in water (50 ml.) until complete solution was attained. Evacuation (aspirator) of the solution removed much of the methanol. The solution was then acidified with concentrated hydrochloric acid and extracted continuously with ether for about 48 hr. Concentration of the ethereal solution left a viscous oil which slowly crystallized. This crystalline material was allowed to stand with acetyl chloride (9 ml.) for about 18 hr. at 25°. The mixture was filtered and the solid (1.8 g.) was washed thoroughly with chloroform. The filtrate and washings were combined and distilled to give a distillate, 8 g., b.p. 130–137°/16–18 mm. and a residue which deposited some crystals (1.8 g.) on trituration with chloroform. By their infrared spectra the two solids were the same. Consequently, they were combined and recrystallized from nitromethane giving a *trans* isomer, *7c*, 2.0 g., m.p. 180–182°. An analytical sample was recrystallized from nitromethane and then sublimed, m.p. 180–181°.

Anal. Calcd. for $C_6H_7O_4Cl$: C, 40.35; H, 3.95; Cl, 19.85. Found: C, 40.37; H, 3.97; Cl, 19.62.

The distillate slowly crystallized. It was recrystallized from hexane (oils out readily) and then sublimed to give the anhydride of *5c*, m.p. 56–57°.

Anal. Calcd. for $C_6H_5O_3Cl$: C, 44.88; H, 3.14; Cl, 22.08. Found: C, 45.08; H, 3.30; Cl, 22.07.

Hydration of the anhydride gave the *cis* acid, *5c*. An analytical sample was recrystallized from nitromethane, m.p. 149–150°.

Anal. Calcd. for $C_6H_7O_4Cl$: C, 40.35; H, 3.95; Cl, 19.85. Found: C, 40.36; H, 4.01; Cl, 19.82.

This *cis* acid, *5c*, was similar to the related 1,3-dimethyl derivative, *5a*, in that it crystallized in two distinct modifications, very fine needles and small compact chunks, both forms showing the same melting point but radically different infrared spectra in the solid state (mineral oil mulls). It was shown that a mixture of the two forms suspended in the mother liquor from which they crystallized at room temperature slowly changed over a period of several days completely to the compact chunky form.

Dimethyl 1-Chloro-3-methyl-1,2-cyclopropanedicarboxylate.—Methyl crotonate (20 g., 0.2 mole), methyl dichloroacetate (28.6 g., 20.7 ml., 0.2 mole), and sodium hydride (4.8 g., 0.2 mole) in benzene (60 ml.) gave the diester product, 16.5 g. (40%), b.p. 120–125°/15 mm.

Dimethyl 1-Chloro-2,3-dimethyl-1,2-cyclopropanedicarboxylate.—A. Methyl tiglate (5.9 g., 0.05 mole), methyl dichloroacetate (5.7 g., 0.04 mole), and sodium hydride (0.96 g., 0.04 mole) in toluene (45 ml.) gave 4.5 g. (51%) of the diester, b.p. 61–64°/0.5 mm. Saponification of the ester (3.3 g.) with sodium hydroxide (1.8 g.) in water (15 ml.) gave a suspension of the sodium salt in the aqueous solution. Additional water gave a clear solution which was then concentrated to remove methanol. Acidification with concentrated hydrochloric acid gave a thick paste which was diluted with water to give a clear solution. Continuous extraction with ether for about 48 hr. gave *5d*, 2.5 g., m.p. 168–170°. The acid is relatively insoluble in nitromethane—1.4 g. of acid required about 100 ml. of nitromethane at steam bath temperature for complete solution, but 1.3 g. of the acid crystallized on cooling—but this is still the best solvent for recrystallization. The acid crystallizes in extremely fine interlocking needles, and in the example mentioned above the recrystallization mixture "gelled" completely. Filtration occurs readily, but the crystals occlude solvent rather tenaciously. An analytical sample recrystallized from nitromethane had m.p. 183°.

Anal. Calcd. for $C_7H_9O_4Cl$: C, 43.65; H, 4.71; Cl, 18.41. Found: C, 43.75; H, 4.74; Cl, 18.30.

The acid readily forms crystalline anhydride on treatment with acetyl chloride. Recrystallization from chloroform–cyclohexane followed by sublimation gave the anhydride, m.p. 71–72°.

Anal. Calcd. for $C_7H_7O_3Cl$: C, 48.16; H, 4.04; Cl, 20.31. Found: C, 48.17; H, 4.11; Cl, 20.28.

B. Repetition of the previous experiment but using a solvent mixture of benzene (25 ml.) and hexamethylphosphoramide (25 ml.) gave 2.3 g. (26%)[19] of the diester, b.p. 63–66°/0.5 mm. Saponification of this ester gave the same acid as obtained in A and no indication of other isomers.

Dimethyl 1,3,3-Trimethyl-1,2-cyclopropanedicarboxylate.—A. Methyl β,β-dimethylacrylate (17.1 g., 0.15 mole), methyl α-chloropropionate (18.4 g., 0.15 mole), and sodium hydride (3.6 g., 0.15 mole) in benzene (35 ml.) gave 1.1 g. (3.7%) of the "diester."

B. Repetition of the experiment in refluxing benzene gave 1.0 g. of the "diester."

C. Repetition using a solvent mixture of benzene (50 ml.) and hexamethylphosphoramide (50 ml.) gave 7 g. (23%) of the "diester," b.p. 47–55°/2 mm.

In the three experiments considerable amounts of the unsaturated starting material were recovered. Gas chromatographic analyses of the "diesters" showed that they consisted of at least five components, none of them starting materials and all present in moderate amounts. Because of the poor yields and the complex nature of the products, they were not investigated further.

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