ture of 9.2 g. (0.082 mole) of itaconic anhydride and 11.85 g. (0.082 mole) of 4-chlorobenzenethiol in 50 ml. of benzene was heated with stirring to 34° to effect solution. Then 2.0 ml. of a 10% solution of triethylamine in benzene (0.002 mole) was added during 1.5 min. The color of the solution changed from yellow to bright red and the temperature rose to 55°. The reaction mixture was heated at 60° for 10 min., 0.2 ml. of sulfuric acid added, and the benzene removed to a final still temperature of 80° (60–70 mm.). The crude anhydride was obtained as a thick material which solidified on standing; yield, quantitative. After one recrystallization from toluene the m.p. was 142–144°. Infrared analysis showed good bands at 1850 and 1780 cm.$^{-1}$ (anhydride).

Anal. Calcd. for $C_{11}H_9ClO_3$: S, 12.4. Found: S, 11.8.

4-Chlorophenylthiomethylsuccinic Acid.—Seven grams of the above anhydride, 50 ml. of toluene, and 5 ml. of water were heated at 80° for 3.5 hr. The mixture was cooled to 25° and the acid filtered off; yield, 7 g.; m.p. 166–167°.

Anal. Calcd. for $C_{11}H_{11}ClO_4S$: S, 11.7. Found: S, 11.5.

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Substituted Malonic and Trifluoroacetic-Malonic Anhydrides and Their Pyrolysis to Ketenes

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Dialkylmalonic acids react readily with one or two moles of trifluoroacetic anhydride to give the mono-(I) or bis(II)-trifluoroacetic mixed anhydrides. Addition of pyridine to I results in near-quantitative formation of the substituted malonic anhydrides (III). Ketenes may be prepared in good yield by pyrolysis of III, or, less satisfactorily, by direct pyrolysis of II. With ethylphenylmalonic acid, however, pyrolysis of II is the only practical route to the ketene. With amyl and phenylmalonic acids, neither I, II, nor III could be obtained unequivocally. Pyrolysis of the impure products gave only traces of the aldoketenes.

Recent efforts in this laboratory to prepare new ketenes by the pyrolysis of substituted malonic anhydrides[1] or of mixed anhydrides[1] derived from diphenylacetic acid and substituted malonic acids led to a desire to improve these classical synthetic methods. The substituted malonic anhydrides had formerly been obtained from the malonic acids by treatment with acetic anhydride,[2] or from the malonyl chlorides by various methods,[3] but found little use because they were difficult to purify and generally were polymeric, necessitating a very slow pyrolysis.

Malonic-diphenylacetic anhydrides[4] may be obtained by reaction of the malonic acids with diphenylketene, but preparation of the latter is itself a not inconsiderable task. The mixed anhydride may also be difficult to purify if derived from a malonic acid of complex structure. A more serious objection to this method is the possibility of ketene interchange[1]

$$2R_2C{=}C{=}O + [(C_6H_5)_2CHCO]_2O \rightleftharpoons 2(C_6H_5)_2C{=}C{=}O + [R_2CHCO]_2O$$

when the desired ketene ($R_2C{=}C{=}O$) is high-boiling. To avoid this, Staudinger, *et al.*, attempted to prepare mixed anhydrides of substituted malonic acids with other acids[5] such that ketene interchange would be unlikely or impossible. In many instances, however, the chief product was not the mixed anhydride, and in no case could the latter be obtained in a pure state.

It seemed likely that such difficulties could be avoided by the use of mixed anhydrides of substituted malonic acids with trifluoroacetic acid. The monoanhydrides $R_2C(COOH)(COOCOCF_3)$ offered the possibility of easy cyclization to malonic anhydrides $R_2C(CO)_2O$, while the bisanhydrides $R_2C(COOCOCF_3)_2$ might be pyrolyzed directly to ketenes. Monocarboxylic acids are known to form anologous anhydrides $RCOOCOCF_3$ merely by addition of trifluoroacetic anhydride,[6] and the low boiling point of the trifluoro acid and its anhydride makes for easy separation of these from the product. Ketene interchange would not be possible upon pyrolysis of $R_2C(COOCOCF_3)_2$ because of the absence of alpha hydrogens.

We have found the reaction of trifluoroacetic anhydride with dialkylmalonic acids to be rapid and complete. With equimolar amounts of the two in ether solution a product I is obtained after evaporation of the ether and trifluoroacetic acid:

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[1] W. E. Hanford and J. C. Sauer, "Organic Reactions," Vol. 3, John Wiley and Sons, Inc., New York, 1946, p. 116.

[2] H. Staudinger, *Helv. Chim. Acta*, **8**, 306 (1925).

[3] H. Staudinger and E. Ott, *Ber.*, **41**, 2211, 3829 (1908); H. Staudinger and S. Bereza, *ibid.*, **41**, 4463 (1908); A. Einhorn and H. von Diesbach, *Ann.*, **359**, 159 (1908); *Ber.*, **39**, 1222 (1906).

[4] H. Staudinger, E. Anthes, and H. Schneider, *ibid.*, **46**, 3539 (1913).

[5] H. Staudinger, *et al.*, *Helv. Chim. Acta*, **6**, 289 (1923).

[6] W. D. Emmons, K. S. McCallum, and A. F. Ferris, *J. Am. Chem. Soc.*, **75**, 6047 (1953); E. J. Bourne, M. Stacey, J. C. Tatlow, and R. Worrall, *J. Chem. Soc.*, 2006 (1954); J. M. Tedder, *Chem. Rev.*, **55**, 810 (1955).

$$R_2C(COOH)_2 + (CF_3CO)_2O \longrightarrow \underset{\text{I}}{R_2C(COOH)(COOCOCF_3)} + CF_3COOH$$

I had infrared carbonyl bands at 1860 and 1780 cm.$^{-1}$ characteristic of carboxylic-trifluoroacetic anhydrides,[6] and a band at 1700 to 1750 cm.$^{-1}$ due to the —COOH carbonyl. The elementary analysis and behavior of I were also in accord with the mixed anhydride structure.

The addition of an equimolar amount of pyridine to I in ether results in precipitation of pyridinium trifluoroacetate, and the malonic anhydride III (carbonyl bands at 1824 and 1760 cm.$^{-1}$) is obtained in almost quantitative yield by filtration and evaporation:

$$R_2C(COOH)(COOCOCF_3) + C_5H_5N \longrightarrow \underset{\text{III}}{R_2C(CO)_2O} + C_5H_5NH^+CF_3COO^-$$

I may also be cyclized by heating *in vacuo* at 75°

$$R_2C(COOH)(COOCOCF_3) \xrightarrow[\Delta]{} R_2C(CO)_2O + CF_3COOH$$

but yields and purity of the malonic anhydrides so obtained are less satisfactory than with the pyridine method.[7]

With a 2:1 molar ratio of trifluoroacetic anhydride to disubstituted malonic acid, the mixed anhydride II is obtained (carbonyl bands at 1860 and 1780 cm.$^{-1}$):

$$R_2C(COOH)_2 + 2(CF_3CO)_2O \longrightarrow \underset{\text{II}}{R_2C(COOCOCF_3)_2} + 2CF_3COOH$$

The best method for preparation of dialkyl ketenes *via* these reactions is the pyrolysis of malonic anhydrides obtained from mixed anhydrides of type I by reaction with pyridine.[8] This gave dibutylketene in 85% yield and diethylketene in 56% yield, both in a high state of purity.

Pyrolysis of type II anhydrides gave good yields of both dialkyl (dibutylketene) and alkyl aryl (ethylphenylketene) ketenes, but the product always contained a substantial amount (20%) of two characteristic by-products (see Experimental). Consequently, this method should be used only when the cyclic anhydride cannot be readily prepared, as with ethylphenylmalonic acid.

The reaction of monosubstituted malonic acids and of alkyl aryl malonic acids with trifluoroacetic anhydride is more complex and needs further investigation.[9] With ethylphenylmalonic acid type I anhydride apparently formed but addition of pyridine gave only a low yield of impure cyclic anhydride; type II anhydride, however, formed normally. With monosubstituted malonic acids neither anhydrides I or II nor the cyclic anhydrides could be obtained in any degree of purity. The products usually had a broad, general carbonyl absorption rather than the expected sharp bands. Pyrolysis gave only traces of the aldoketenes, which have seldom been isolated in monomeric form by any means.

Experimental

Materials.—Dibutyl-,[10] diethyl-,[10] ethylphenyl-,[11] amyl-,[12] and phenymalonic[11] acids were obtained by saponification of their commercially available ethyl esters. The procedure of Speck[10] used for the dialkyl compounds was modified in that the ethanol was removed before acidification.

Solvents used in preparing the anhydrides were anhydrous reagent grade ether and petroleum ether (b.p. 38–55°). Eastman trifluoroacetic anhydride was used as received, and reagent grade pyridine was dried over molecular sieves.

Experimental Conditions.—All operations were performed in a room with low humidity. Reactions were carried out in an ordinary stoppered round-bottom flask which was flushed with nitrogen before use and equipped with a magnetic stirrer. Evaporate always means vacuum evaporation on a rotary evaporator protected from moisture. Once the solvents had been evaporated, the various anhydrides were kept under nitrogen at all times.[13]

Pyrolyses were conducted in a semimicro distillation apparatus consisting of pot, 10-cm. Vigreux distilling head, condensor, fraction cutter, and Dry Ice-cooled receiver. The resulting ketenes were always kept under nitrogen and refrigerated if necessary. A large pot should be used if the ketenes are redistilled since they foam vigorously during the first few minutes of the distillation.

Dibutylmalonic Anhydride.—To a stirred solution of 6.7 g. (0.031 mole) of dibutylmalonic acid in 35 ml. ether was added dropwise 4.35 ml. (6.5 g., 0.031 mole) of trifluoroacetic anhydride. The mixture was allowed to stand for 10 min., then was diluted up to 160 ml. with petroleum ether and 5.3 ml. (5.2 g., 0.0657 mole) of pyridine added with stirring. Neither addition need take more than a minute or so since there is only moderate evolution of heat. After addition of the pyridine the mixture was left standing for 1 hr. (a slight yellow color may sometimes develop). Since the resulting pyridinium trifluoroacetate is fairly soluble in ether, the latter was removed from the reaction mixture before filtering by repeatedly evaporating to a small volume, then adding more petroleum ether. The hygroscopic pyridinium salt was then filtered off quickly onto a Büchner funnel and washed with three small portions of petroleum ether. Evaporation of the filtrate gave 6.0 g. (98%) dibutylmalonic anhydride, a viscous liquid which slowly crystallized upon standing. The infrared carbonyl bands are at 1824 and 1760 cm.$^{-1}$.

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.65; H, 9.15; mol. wt., 198. Found: C, 66.38; H, 9.10; mol. wt., 199.

Diethylmalonic Anhydride.—Reaction times and procedure were essentially the same as for dibutylmalonic anhydride. To 10 g. (0.0625 mole) of diethylmalonic acid in 70 ml. ether was added 8.75 ml. (0.0625 mole) of trifluoroacetic anhydride; after standing and dilution to 275 ml. with petroleum ether the mixture was treated with 10.19 ml. (0.126 mole) of pyridine.

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(7) However, malonic anhydrides unobtainable by the pyridine method may sometimes be prepared in this way (ethylphenylmalonic anhydride).

(8) Pyrolysis of malonic anhydrides obtained from I by heating always gave ketenes containing considerable inpurity, with infrared absorption indicative of carboxylic-trifluoroacetic anhydrides.

(9) The infrared absorption at 2140 cm.$^{-1}$ noted in these mixtures (see Experimental) could be due to the presence of the ketene except in the case of ethylphenylmalonic acid–trifluoroacetic anhydride mixtures, which are colorless, whereas ethylphenylketene is orange.

(10) S. B. Speck, *J. Am. Chem. Soc.*, **74**, 2876 (1952).

(11) P. J. Scheuer and S. G. Cohen, *ibid.*, **80**, 4936 (1958).

(12) W. J. Gensler and E. Berman, *ibid.*, **80**, 4953 (1958).

(13) A. F. Ferris and W. D. Emmons, *ibid.*, **75**, 232 (1953), state that trifluoroacetic-carboxylic anhydrides "are hydrolyzed completely by standing in contact with moist air for even a few seconds."

Following the 1-hr. reaction period the pyridine salt was filtered off directly and washed with petroleum ether. The ethyl ether was not removed from the reaction mixture because of the relatively low solubility of diethylmalonic anhydride in pure petroleum ether. As a result, the product (7.6 g., 85%) obtained by evaporation of the filtrate contained a trace of pyridine salt, but this did not seem to affect pyrolysis of the anhydride seriously.

However, cyclic anhydrides containing substantial amounts of pyridine salt (as when pure ethyl ether was used as solvent) gave only traces of the ketenes upon pyrolysis. The ability of tertiary amine salts to catalyze dimerization of ketenes has been noted before.[14]

Anal. Calcd. for $C_7H_{10}O_3$: C, 59.12; H, 7.09; mol. wt., 142. Found: C, 58.52; H, 7.15; mol. wt., 144.

Dibutylketene.—Six grams of dibutylmalonic anhydride in a 50-ml. flask was pyrolyzed by heating at < 0.2 mm. pressure in the previously described semimicro distillation apparatus. Decomposition began at a pot temperature of about 140°; this was gradually increased to 180°, causing the ketene to distil. The entire pyrolysis took about 20 min., and gave 4.0 g. of dibutylketene (85% based on cyclic anhydride) with $n^{20}D$ 1.4312.

The product is of near analytical purity but sometimes contains a trace of fluorine compounds (infrared absorption at 1230, 1176, and 1103 cm.$^{-1}$) which may be removed by redistillation if desired. Pure dibutylketene is a yellow liquid with b.p. 68–69° (10.5 mm.), 75–76° (15 mm.), $n^{20}D$ 1.4308, d^{20} 0.831.

Anal. Calcd. for $C_{10}H_{18}O$: C, 77.89; H, 11.76. Found: C, 77.72; H, 11.90.

Comparable yields were obtained with smaller (1.7 g.) and larger (9 g.) amounts of cyclic anhydride.

Diethylketene.—Because of its volatility, diethylmalonic anhydride was pyrolyzed at atmospheric pressure in a slow stream of nitrogen. A 7.6-g. quantity was brought to 120° in 10 min., then gradually heated to 170° over the next 20 min. Although monomeric, this anhydride seemed to pyrolyze more slowly than the dibutyl anhydride. The diethylketene produced weighed 2.9 g. (56%); its infrared curve showed no carbonyl bands and only traces of fluorine compounds. Its $n^{20}D$ was 1.4126 (lit.[15] value 1.4112).

Ethylphenylketene was best prepared by the pyrolysis of ethylphenylmalonyl trifluoroacetate: To 10 g. (0.0480 mole) of ethylphenylmalonic acid in 65 ml. of ether was added 14.15 ml. (0.1 mole) of trifluoroacetic anhydride. After standing for 5 min. the mixture was evaporated at 2 mm. pressure for 1.5 hr. at room temperature, giving 18.2 g. (94%) of ethylphenylmalonyl trifluoroacetate with infrared carbonyl absorption at 1850 and 1780 cm.$^{-1}$.

Pyrolysis of the mixed anhydride was conducted at 15 to 20 mm. pressure and 140–160° temperature over a 20-min. period. The receiver was cooled with ordinary ice in order to trap only the ketene and not the trifluoroacetic anhydride presumably formed. The crude product (6.6 g.) had weak carbonyl bands at 1850, 1808, and 1780 cm.$^{-1}$ due to impurities which could only partially be separated from the ketene by fractionation through a 10-cm. Vigreux column.

The product was assayed for the ketene by treating with dry methanol, evaporating the excess methanol, and subjecting the residue to vapor phase chromatography. The area of the methyl 2-phenylbutyrate peak was then compared with a calibration curve prepared from an authentic sample of this ester and showed the crude product to contain 80% ethylphenylketene (the actual yield of the ketene was thus 0.8 × 6.6 g., or 5.3 g. (75%).

The chromatograms showed only two major impurities to be present, and neither formed methyl 2-phenylbutyrate upon reaction with methanol.

Infrared Spectra of Anhydride Mixtures.—Almost immediately after addition of trifluoroacetic anhydride (in a 1:1 molar ratio) to an ethereal solution of phenyl-, amyl-, or ethylphenylmalonic acid, an infrared band appeared in the ketene region of the spectrum (2200–2100 cm.$^{-1}$), then gradually diminished. The band was at 2140 cm.$^{-1}$ for the monosubstituted acids and 2130 cm.$^{-1}$ for ethylphenylmalonic acid. With a 2:1 molar ratio of anhydride to acid the band was much more intense for the monosubstituted acids but did not appear for ethylphenylmalonic acid.

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[14] H. Staudinger and H. W. Klever, *Ber.*, **41**, 594 (1908); J. C. Sauer, U. S. Patent 2,238,826 (1941); *Chem. Abstr.*, **35**, 4970 (1941).

[15] I. Heilbron, "Dictionary of Organic Compounds," Vol. II, Oxford University Press, New York, 1953, p. 186.

An Investigation of the Hofmann Reaction of Perhaloacetamides

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Reactions of trichloroacetamide with aqueous sodium hypobromite (Hofmann conditions) gave variable yields of cyanate (73–80%), bromotrichloromethane (34–53%), ammonia (4.5–6.8%), and chloroform (<0.5%); whereas the decomposition of N-bromotrichloroacetamide with sodium hydroxide solution gave reproducible yields of cyanate (88%), bromotrichloromethane (56%), ammonia (4.4%), and chloroform (<0.5%). The reaction of N-bromotribromoacetamide with aqueous sodium hydroxide gave cyanate (74%), carbon tetrabromide (39%), ammonia (24%), and bromoform (3.4%). The results are compared with those reported for the Hofmann reaction of trifluoroacetamide and are interpreted in terms of three simultaneous reaction paths: hydrolysis of the amide, a normal Hofmann reaction to give the trihalomethylamine, and an abnormal Hofmann reaction to give bromotrihalomethane.

In a reinvestigation of the Hofmann reaction of trifluoroacetamide, Barr and Haszeldine[2] found that bromotrifluoromethane and ammonia were the only volatile products; hexafluoroethane, previously reported[3] to be the product, was not found.

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[1] Abstracted from the Ph.D. dissertation of Donald D. Wilson, University of Kentucky, December, 1960.

[2] D. A. Barr and R. N. Haszeldine, *J. Chem. Soc.*, 30 (1957).

[3] E. Gryszkiewicz-Trochimowski, A. Sporzynski, and J. Wnuk, *Rec. trav. chim.*, **66**, 426 (1947).