Base-Catalyzed Addition of Thiols to α,β-Unsaturated Anhydrides

FERDINAND B. ZIENTY, BILLY D. VINEYARD, AND ALFRED A. SCHLEPPNIK

The Advanced Organic Chemicals Research Laboratory, Organic Chemicals Division, Monsanto Chemical Company, Saint Louis, Missouri

Received March 9, 1962

Reaction of a variety of thiols, including hydrogen sulfide, with α,β-unsaturated cyclic anhydrides in the presence of a basic catalyst under anhydrous conditions produced alkylthio and arylthio anhydrides rapidly and in high yields. The addition of thiols to maleic anhydride afforded a convenient direct method of making *dl*-alkylthio- and arylthiosuccinic anhydrides; the heretofore inaccessible *tert*-alkylthiosuccinic acids and anhydrides can be made easily by this reaction. The mechanism appears to involve dissociation of the thiol and addition of the RS^- anion to a polarized double bond. The effect of the character of the base on this reaction is discussed. The addition reaction is kinetically controlled. No ester formation was encountered under the preferred conditions.

Since anhydrides are convenient intermediates for preparation of resins and many other useful materials, it was of interest to seek a potentially facile preparation of alkylthio and arylthio cyclic anhydrides. A major portion of this work is directed to a study of the conversion of maleic anhydride to *dl*-alkylthio- and arylthiosuccinic anhydrides.

Many thiols previously have been added to aqueous maleic acid using alkali catalysis.[1] However, tertiary mercaptans do not react with disodium maleate using a general procedure suitable for addition of a wide variety of other mercaptans.[2–4] Thiols add to citraconic and itaconic acids,[5] itaconic esters, acrylates,[6] and methacrylates.[7] Hydrogen sulfide adds to dialkyl maleates,[8] fumarates,[9] and itaconates,[10,11] to form the alkyl esters of thiodisuccinic acids; to acrylic esters to form thiodipropionates[12]; and to acrylic acid[13] to form thiodipropionic acid. Using base catalysts hydrogen sulfide does not react with β,β-dimethylacrylic acid[14] or with methyl methacrylate.[12]

The reaction of thiols with α,β-unsaturated anhydrides to produce the corresponding substituted mercapto anhydrides appears to be largely uninvestigated. Thiolacetic acid (acetothiolic acid), CH_3COSH,[15] diethyl phosphorodithioate, $(EtO)_2$-

TABLE I

ADDITION REACTION OF *tert*-DODECYL MERCAPTAN WITH MALEIC ANHYDRIDE AT 25°

(0.2 mole of each reactant in 140 g. of dioxane and 0.0018 mole of triethylenediamine catalyst)

Time, sec.	% Mercaptan reacted
300	5.1
600	9.4
1800	14.5
7200	23.2
14400	32.8
[a]	
15300	45.6
17100	54.2
23400	65.5

[a] At this point 0.0027 mole additional triethylenediamine catalyst in 10 g. of dioxane is added.

TABLE II

ADDITION REACTION OF *tert*-DODECYL MERCAPTAN WITH MALEIC ANHYDRIDE. EFFECT OF SOLVENT AND STRUCTURE OF BASE AT 85° FOR 30 MINUTES

(0.1 mole of each reactant in 70 g. of solvent)

Base		Yield, %[a]	
Amine	Mole × 10^{-3}	Benzene	Dioxane
Pyridine	6.3	13	10
Triethylamine	4.9	29	54
N,N-Dimethylbenzylamine	3.7	31	48
Triethylenediamine	4.5	45	59
	2.25	43	52
	0.225	13	30

[a] Yield refers to *dl-tert*-dodecylthiosuccinic anhydride.

---

[1] J. G. Hendrickson and L. F. Hatch, *J. Org. Chem.*, **25**, 1747 (1960).

[2] Ref. 1, p. 1750.

[3] W. B. Chilcote, U.S. Patent 2,581,514 (January 8, 1952) [*Chem. Abstr.*, **47**, 4363g (1953)], reports a low yield in the addition of *tert*-butyl mercaptan to disodium maleate and no yield whatsoever with higher *tert*-alkyl mercaptans.

[4] Few additions of *tert*-alkyl mercaptans to double-bonded compounds are known. *tert*-Butyl mercaptan adds to (a) acrylonitrile and to methyl acrylate in high yield using base catalysis [see C. D. Hurd and L. L. Gershbein, *J. Am. Chem. Soc.*, **69**, 2328 (1947); (b) α-Substituted acrylonitriles in low yields [see R. M. Ross, H. L. Bushey and R. J. Rolih, *J. Am. Chem. Soc.*, **73**, 540 (1951)]; and (c) olefins under pressure in the presence of metal catalysts [see E. E. Reid, "Organic Chemistry of Bivalent Sulfur," Vol. II, Chemical Publishing Co., Inc., New York, 1960, p. 32.]

[5] B. Holmberg and E. Schjänberg, *Chem. Abstr.*, **35**, 2114 (1941).

[6] C. Knuth, A. Bavley, and W. A. Lazier, *J. Org. Chem.*, **19**, 845 (1954).

[7] C. D. Hurd and L. L. Gershbein, *J. Am. Chem. Soc.*, **69**, 2330 (1947).

[8] L. W. Newton, (a) U.S. Patent 2,603,616 (July 15, 1952) [*Chem. Abstr.*, **47**, 3337h (1953)], and (b) U.S. Patent 2,668,847 (February 9, 1954) [*Chem. Abstr.*, **48**, 3995f (1954)].

[9] A. Emr, Czech. Patent 85,677 (June 15, 1956) [*Chem. Abstr.*, **51**, 8782g (1957)]; A. Emr and F. Roubinek, *Chem. Abstr.*, **50**, 8460d (1956).

[10] L. W. Newton, Brit. Patent 663,201 (December 19, 1951) [*Chem. Abstr.*, **47**, 5431i (1953)].

[11] P. M. Kerschner, U.S. Patent 2,845,390 (July 29, 1958) [*Chem. Abstr.*, **52**, P 19115 f (1958)].

[12] L. L. Gershbein and C. D. Hurd, *J. Am. Chem. Soc.*, **69**, 241 (1947).

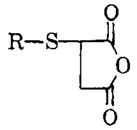
[13] R. Dahlbom, *Acta Chem. Scand.*, **5**, 690 (1951) [*Chem. Abstr.*, **46**, 430g (1952)].

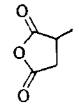
[14] Z. Földi and J. Kollonitsch, *J. Chem. Soc.*, 1683 (1948).

[15] R. Brown, W. E. Jones, and A. R. Pinder, *J. Chem. Soc.*, 2123 (1951), use peroxide catalysis. Ref. 5 uses no catalyst.

TABLE III

dl-ALKYLTHIO- AND ARYLTHIOSUCCINIC ANHYDRIDES



R	M.p.[a] or b.p. (mm.)	Yield, %	Formula	Sulfur, % Calcd.	Sulfur, % Found	Mol. wt.
CH_3	142 (2)	64	$C_5H_6O_3S$	21.9	21.4	146.17
n-C_4H_9	122–124 (0.3)	89	$C_8H_{12}O_3S$	17.0	17.3	188.25
tert-C_4H_9	83.5–84.5[b]	41	$C_8H_{12}O_3S$	17.0	16.7	188.25
n-C_8H_{17}	175–179 (0.6)	89	$C_{12}H_{20}O_3S$	13.1	13.1	244.36
n-$C_{12}H_{25}$	42–43[c]	94	$C_{16}H_{28}O_3S$	10.7	10.0	300.46
tert-$C_{12}H_{25}$—	160–170 (0.01)[d]	60	$C_{16}H_{28}O_3S$	10.7	10.5	300.46
—CH_2CH_2—	128–130[e]	42[f]	$C_{10}H_{10}O_6S_2$	22.1	22.0	290.32
$C_2H_5OOCCH_2$	140–145 (0.2)	76	$C_8H_{10}O_5S$	14.7	14.9	218.23
$HOOCCH_2$—	[g]	100[h]	$C_6H_6O_5S$	16.9	[i]	190.18
$C_6H_5CH_2$—	150–155 (0.03)[d]	88	$C_{11}H_{10}O_3S$	14.4	14.4	222.26
C_6H_5—[j]	176–178 (1.5)	88	$C_{10}H_8O_3S$	15.4	15.3	208.24
p-$CH_3C_6H_4$—[k]	155–160 (0.01)[d]	65	$C_{11}H_{10}O_3S$	14.4	14.5	222.26
p-ClC_6H_4—	96–98[l]	97	$C_{10}H_7ClO_3S$	13.2	13.4[m]	242.69
p-$CH_3OC_6H_4$—	[g]	45[h]	$C_{11}H_{10}O_4S$	13.5	[i]	238.26
p-$AcNHC_6H_4$—	186–188 (dec.)[n]	77	$C_{12}H_{11}NO_4S$	12.1	11.8[o]	265.29
p-$O_2NC_6H_4$—	114–115[p]	90	$C_{10}H_7NO_5S$	12.7	12.7[q]	253.24
o-$O_2NC^9H_4$—	124–125[p]	96	$C_{10}H_7NO_5S$	12.7	12.8[r]	253.24
C_6Cl_5—	166–168[s]	87	$C_{10}H_3Cl_5O_3S$	8.4	8.4[t]	380.46
	[g]	90	$C_8H_6O_6S$	13.9	12.6	230.20

[a] All melting points and boiling points are uncorrected. [b] Recrystallized from carbon tetrachloride. [c] From petroleum ether; ref. 17, p. 225, reported m.p. 45–46°. [d] Distilled in short path still; ranges are air bath temperatures. [e] Washed with chloroform. [f] Yield of crude product was 100%. [g] Decomposed on attempted distillation. [h] Yield of crude material. [i] Not analyzed. [j] Oil, very soluble in benzene. [k] Solid. Soluble in benzene. [l] From toluene; soluble in acetone. [m] Calcd.: Cl, 14.6. Found: Cl, 14.5. [n] From dioxane. [o] Calcd.: N, 5.3. Found: N, 5.0. [p] From glacial HOAc–Ac_2O. [q] Calcd.: N, 5.5. Found: N, 5.4. [r] Calcd.: N, 5.5. Found: N, 5.6. [s] From acetone. Also recrystallizes from benzene. [t] Calcd.: Cl, 46.6. Found: Cl, 46.5.

P(S)SH,[16] and benzyl mercaptan[17] have been added directly to maleic anhydride. The few other known S-substituted mercaptosuccinic anhydrides are made by indirect methods. Several n-alkylthiosuccinic anhydrides[18] and S-(2-methyl-1,4-naphthoquinonyl-3)thiosuccinic anhydride[19] are made by dehydration of the corresponding succinic acids.

In this work, direct addition of thiols to maleic anhydride is accomplished under anhydrous conditions using a catalytic quantity of a base. The addition reaction is rapid with normal aliphatic mercaptans and with most aromatic thiols, giving nearly quantitative yields of substituted succinic anhydrides within a few minutes. Reaction with *tert*-alkyl mercaptans is more sluggish but still produces respectable yields (60–65%) of the desired *tert*-alkylthiosuccinic anhydrides when preferred conditions are used. With anhydrides of higher molecular weight it is desirable to neutralize the base catalyst prior to distillation to avoid decomposition (β-elimination of RSH).

Substituted succinic anhydrides prepared in this study are shown in Table III. Infrared spectral analysis shows the typical anhydride bands in the regions of 1860 and 1784 cm.$^{-1}$ and the anhydrides show the usual reactivity with alcohols and amines to form monoesters and monoamides, and with water to form the dicarboxylic acids. The S-substituted mercaptosuccinic anhydrides, because of the negative group in the α-position, are appreciably more susceptible to hydrolysis than maleic, succinic, and alkenylsuccinic anhydrides. Therefore, they should be stored in well sealed containers. Some of the anhydrides are liquids. The corresponding acids are solids and are listed in Table IV.

Although thiols react with anhydrides to form thiol esters,[20] no ester formation is observed in this addition reaction. Although little appears to be recorded on base-catalyzed esterification of an-

---

(16) J. H. Fletcher and E. I. Hoegberg, U.S. Patent 2,630,451 (March 3, 1953) [*Chem. Abstr.*, **48**, 7047b (1945)], use no catalyst.

(17) J. L. Szabo and E. T. Stiller, *J. Am. Chem. Soc.*, **70**, 3667 (1948), use Triton B (35% aqueous solution of benzyltrimethylammonium hydroxide) as a catalyst and the benzylthiosuccinic anhydride is obtained by dehydration of the resulting mixture of succinic acid and anhydride.

(18) V. C. Barry, L. O'Rourke, and D. Twomey, *Proc. Roy. Irish Acad.*, **51B**, 223 (1947) [*Chem. Abstr.*, **42**, 4134 (1948)].

(19) L. F. Fieser and R. B. Turner, *J. Am. Chem. Soc.*, **69**, 2335 (1947).

(20) F. W. Wenzel, Jr., and E. E. Reid, *J. Am. Chem. Soc.*, **59**, 1089 (1937); E. Wertheim, *ibid.*, **51**, 3661 (1929).

TABLE IV

dl-ALKYLTHIO- AND ARYLTHIOSUCCINIC ACIDS[a]

$HO_2C{-}CH(SR)CH_2CO_2H$

R	M.p.	Formula	Sulfur, %		Mol. wt.
			Calcd.	Found	
CH_3	138[b]	$C_5H_8O_4S$	19.5	19.2	164.18
n-C_4H_9	104–105[c]	$C_8H_{14}O_4S$	15.5	15.6	206.26
tert-C_4H_9	169–170[d]	$C_8H_{14}O_4S$	15.5	15.5	206.26
n-C_8H_{17}	92–94[e]	$C_{12}H_{22}O_4S$	12.2	12.2	262.37
n-$C_{12}H_{25}$	96–97[f]	$C_{16}H_{30}O_4S$	10.1	9.6	318.48
tert-$C_{12}H_{25}$	Glassy	$C_{16}H_{30}O_4S$	10.1	9.5	318.48
$—CH_2CH_2—$	183–184	$C_{10}H_{14}O_8S$	19.6	18.8	326.35
$C_2H_5OOCCH_2$	104–105	$C_8H_{12}O_6S$	13.6	13.3	236.25
$HOOCCH_2—$	129–130	$C_6H_8O_6S$	15.4	15.1	208.19
$C_6H_5CH_2—$	185–185.5[g]	$C_{11}H_{12}O_4S$	13.3	13.1	240.28
$C_6H_5—$	110–111[h]	$C_{10}H_{10}O_4S \cdot H_2O$	13.1	13.4	244.26
p-$CH_3C_6H_5—$	169[i]	$C_{11}H_{12}O_4S$	13.3	13.0	240.28
p-$ClC_6H_4—$	165[j]	$C_{10}H_9ClO_4S$	12.3	12.4[k]	260.70
p-$CH_3OC_6H_4—$	130	$C_{11}H_{12}O_5S$	12.5	12.3	256.27
p-$AcNHC_6H_4—$	190–191	$C_{12}H_{13}NO_5S$	11.3	11.8	283.30
p-$NO_2C_6H_4—$	161–162	$C_{10}H_9NO_6S$	11.8	11.6[l]	271.25
o-$NO_2C_6H_4—$	172–174	$C_{10}H_9NO_6S$	11.8	11.1[m]	271.25
$C_6Cl_5—$	220–221	$C_{10}H_5Cl_5O_4S$	8.0	8.2[n]	398.47
$HO_2CCH_2\overset{\vert}{C}HCO_2H$	195–197[o]	$C_8H_{10}O_8S$	12.0	11.9	266.23

[a] All acids were obtained in quantitative yields by hydrolysis of the anhydrides. [b] Made by T. Kaneko and S. Mii, *J. Chem. Soc. Japan*, **59**, 1382 (1939) [*Chem. Abstr.*, **33**, 2106^2 (1939)], who reported no constants. Ref. 2 gives m.p. 133°. [c] Ref. 1, p. 1748, reports 103.7–104.0°. [d] Ref. 2 reports 164°. [e] Ref. 1, p. 1748, reports 96.1–96.6°. [f] Ref. 17, p. 225, reports 102–103°. [g] Ref. 16 gives 192°. [h] W. A. Proell and C. E. Adams, U.S. Patent 2,561,673 (July 24, 1951) [*Chem. Abstr.*, **46**, 3083a (1952)], and J. Schmutz, H. Lauener, R. Hirt, and M. Sanz, *Helv. Chim. Acta.*, **34**, 775 (1951), report this acid was obtained as a liquid. [i] French Patent 845,793 (September 1, 1939) [*Chem. Zentr.*, **I**, 1571 (1940)], reports 168–169°. [j] E. W. Bousquet, U.S. Patent 2,434,100 (January 6, 1948) [*Chem. Abstr.*, **42**, 2289c (1948)], gives 163–164°. [k] Calcd.: Cl, 13.6. Found: Cl, 13.8. [l] Calcd.: N, 5.2. Found: N, 5.2. [m] Calcd.: N, 5.2. Found: N, 5.6. [n] Calcd.: Cl, 44.5. Found: Cl, 44.8. [o] A. S. Schwab, *J. Am Chem. Soc.*, **76**, 623 (1954), gives 196–197°.

hydrides, it appears to be a relatively slow process.[21] Since the base-catalyzed addition of thiols to the double bond of the α,β-unsaturated anhydride appears to be fast, it is apparent addition occurs to the exclusion of esterification through kinetic control of these competitive reactions.

Dark-colored reaction mixtures are obtained in most cases in reactions with maleic anhydride and at times, particularly in nonpolar solvents, a dark-colored precipitate is obtained. This color formation and precipitate appear to be the result of a small amount of base-induced polymerization of maleic anhydride.[22] This color can be reduced substantially by conducting reactions at 0° or lower.

Lewis acids such as sulfuric acid and boron trifluoride do not catalyze this reaction, indicating that polarization of the maleic anhydride molecule which would be expected to be favored by acids, is not a rate-limiting step. Peroxide-catalyzed addition[23] of *n*-butyl mercaptan to maleic anhydride produces only a 29% yield of adduct and 9–10% of ester.

When 4-chlorobenzenethiol is heated with maleic anhydride in toluene solution at 100° with no catalyst, 31% of the 4-chlorophenylthiosuccinic anhydride is obtained in twenty-six hours. No ester is found. Reaction at 25° is very slow with no catalyst or with benzoyl peroxide as the catalyst.

Citraconic anhydride reacts readily with *p*-chlorobenzenethiol using triethylamine as the catalyst. No difficulty is observed with color formation as in the case of maleic anhydride. N.m.r. spectra indicate the product is a mixture of approximately three parts of *dl*-α-methyl-α-4-chlorophenylthiosuccinic anhydride and one part of α-methyl-β-4-chlorophenylthiosuccinic anhydride (two *dl*-pairs possible).[24]

Itaconic anhydride also adds *p*-chlorobenzenethiol readily with triethylamine catalyst. The addition undoubtedly is on the methylene carbon atom.

Discussion

Mechanism.—The addition reaction of thiols with α,β-unsaturated anhydrides may be represented as a Michael-type addition of the thiol anion to a polarized double bond. The apparent function of the base is to effect dissociation of the thiol to its anion. The degree of dissociation is influenced by structural or steric effects in the thiol, by the polarity of the environment in which the reaction is conducted and by the basicity of and steric effects in the base used.

Rough kinetic experiments indicate the forward

---

(21) B. W. Tronow and N. Ch. Ssibgatullin, *Chem. Ber.*, **62**, 2852 (1929).

(22) P. Pfeiffer and Th. Böttler, *Chem. Ber.*, **51**, 1819 (1918).

(23) F. R. Mayo and C. Walling, *Chem. Rev.*, **27**, 387 (1940) review the peroxide effect in the addition of thiols to unsaturated compounds.

(24) B. Holmberg and E. Schjänberg, ref. 5, report that under conditions used by them thiolacetic acid adds to the β-position of citraconic acid to give two diastereoisomers.

(addition) reaction proceeds at a reproducible rate with pseudo second-order kinetics. Taking as a model the addition of *tert*-dodecyl mercaptan to maleic anhydride and using a constant amount of base catalyst, a second-order rate constant of approximately 10^{-4} l. mole^{-1} sec.$^{-1}$ was calculated from the data in Table I. Further studies are needed to establish the order of this reaction.

In the reverse (β-elimination) reaction in the presence of the base catalyst a rate constant of approximately 10^{-7} sec.$^{-1}$ may be calculated if first-order kinetics are assumed. Thus, assuming an activation energy of 20 kcal. per mole, the forward reaction appears to be at least one thousand times as fast as the reverse reaction at the same temperature.

Aromatic Thiols.—Some difference in reactivity among aromatic thiols is observed. For example, 4-methoxybenzenethiol reacts much more slowly with maleic anhydride than does 4-chlorobenzenethiol. On the other hand, 4-nitrobenzenethiol reacts much more rapidly than 4-chlorobenzenethiol. This order of reactivity might be expected since the *p*-MeO, an electron-donating group, would retard heterolytic dissociation of the thiol, while the *p*-NO_2, an electron-withdrawing group, would favor dissociation.[25] The pK_a values for the 4-methoxy-(8.08),[26] 4-chloro-(6.96),[27] and 4-nitro-(5.11)[27] benzenethiols are also consistent with the observed order of reactivity.

***tert*-Alkyl Mercaptans.**—The sluggish reactivity of *tert*-alkyl mercaptans affords an opportunity to study this addition reaction in more detail. The results are summarized in Tables I and II. The increase in yield in a polar solvent as shown in Table II strongly supports the view that this addition is an ionic reaction and that *tert*-alkyl mercaptans are not highly dissociated by base in nonpolar solvents but are appreciably more highly dissociated in polar solvents.

Interpretation of the results is complicated somewhat by the fact that three competing reactions may occur at the same time: the addition of thiol to α,β-unsaturate, esterification of the thiol, and polymerization of maleic anhydride. When reactive thiols such as normal alkyl mercaptans or aromatic thiols are used, the addition reaction is so fast that neither of the other two is important. However, the relatively slow addition of *tert*-alkyl mercaptans requires that the other two reactions be considered for their possible influence on the course of the addition reaction.

Esterification may be dismissed as a complicating reaction since no ester function is detectable by infrared analysis in reactions involving *tert*-butyl mercaptan and *tert*-dodecyl mercaptan with maleic anhydride even after three to eight hours, although unchanged mercaptan still is present in substantial quantity.

The polymerization of maleic anhydride in the presence of base is a relatively slow reaction at 25°. However, in reactions requiring more than about fifteen minutes, this polymerization must be considered a complicating reaction. The reaction product ("polymer") of the self-polymerization of maleic anhydride appears to contain free carboxyl groups and the "polymer" and its salts are insoluble in nonpolar solvents. Consequently, this "polymer" removes base catalysts from solution and the reaction of thiol with maleic anhydride in a nonpolar solvent like benzene stops or plateaus as may be seen in Table I. Addition of more base catalyst results in further reaction until all of the maleic anhydride is consumed either as RS-succinic anhydride or as maleic anhydride "polymer" or until all of the base catalyst is precipitated out with the "polymer." Since the "polymer" and its salts are soluble in polar solvents such as dioxane, reaction in polar solvents proceeds for some time, although slowly, after a similar reaction in nonpolar solvent has stopped. As a result of this complicating polymerization reaction kinetic and other interpretations preferably are made on measurements taken early in the reaction—*viz.* the first ten minutes.

The possibility was considered that *tert*-alkyl mercaptans might be less nucleophilic than the corresponding *n*-alkyl mercaptans because of the inductive effect of the three α-alkyl groups. This seems to be only a minor effect and does not appear to account satisfactorily for the large difference in reactivity observed. In this series of mercaptans, it seems reasonable that the nucleophilic character might be approximately proportional to the basicity.[28] Since the pK_a's of *n*- and *tert*-butyl mercaptans are 12.4 and 12.6, respectively,[29] it is clear that no significant difference in nucleophilic character could be predicted on this basis.

A further possibility to account for the difference in reactivity between *n*- and *tert*-alkyl mercaptans is the steric factor. It would not seem likely that there would be any appreciable difference in ability of the highly hindered *tert*-butylthiol anion to approach maleic anhydride as compared to acrylonitrile. The high yield (95%) of adduct with acrylonitrile[4a] may be rationalized on the basis that acrylonitrile does not polymerize under the conditions used and the addition proceeds until substantially completed.

Examination of a variety of base catalysts showed some interesting results. Tertiary amines —including triethylamine, benzyldimethylamine,

---

[25] In similar fashion, the presence of electron-attracting groups qualitatively increases reactivity of RS· radicals toward olefins, presumably by favoring homolytic dissociation. Ref. J. I. Cunneen, *J. Chem. Soc.*, **150**, 134 (1947).

[26] F. G. Bordwell and P. J. Boutan, *J. Am. Chem. Soc.*, **78**, 854 (1956).

[27] F. G. Bordwell and H. M. Andersen, *ibid.*, **75**, 6019 (1953).

[28] J. O. Edwards and R. G. Pearson, *ibid.*, **84**, 20 (1962).

[29] J. Maurin and R. Paris, *Compt. rend.*, **232**, 2428 (1951). The values are those determined spectrophotometrically in aqueous ethanol.

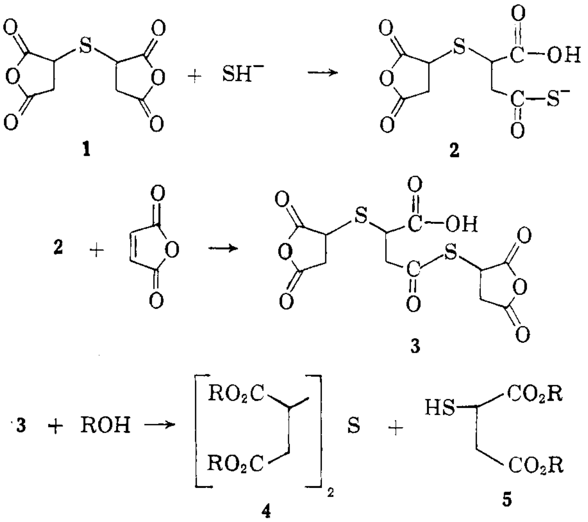
triethylenediamine[30] and pyridine, alkali alkoxides, alkali thiolates, and salts of carboxylic acids—all were effective in catalytic amounts (0.0001–0.02 mole %).

In the group triethylenediamine, dimethylbenzylamine, and triethylamine the effectiveness decreases as steric hindrance of the base catalyst increases.[31] This effect, as illustrated by the data in Table II, may be attributed to "Front strain"[32] and interpreted as showing that a sterically hindered mercaptan is approached with greater difficulty by a hindered base than by an unhindered base and the degree of dissociation of the mercaptan is increased as the steric hindrance of the base is decreased.

On the basis of the above evidence and argument one may conclude that the lower rate of reaction of *tert*-alkyl mercaptans as compared to the primary is due to steric hindrance in the *tert*-alkyl mercaptans. This steric factor apparently lowers the degree of dissociation of the *tert*-alkyl mercaptan.

Hydrogen Sulfide.—Maleic anhydride does not react with hydrogen sulfide in benzene solution in the absence of a basic catalyst; the solution remains colorless and the maleic anhydride is recovered unchanged. With base present in catalytic amounts, reaction with maleic anhydride occurs as rapidly as hydrogen sulfide is introduced to the reaction mixture. Under a variety of conditions and ratios of reactants the product obtained is in every case the adduct of two moles of maleic anhydride and one of hydrogen sulfide. There is no evidence that the reaction can be interrupted at the 1:1 addition stage. This finding indicates that the thiol in mercaptosuccinic anhydride is more nucleophilic than hydrogen sulfide,[33] and therefore reacts immediately with a second mole of maleic anhydride to form thiodisuccinic anhydride (**1**) in Chart I.

CHART I



When the addition of hydrogen sulfide is about 95% complete, ester bands begin to appear in the infrared spectrum. This indicates a small amount of reaction of thiodisuccinic anhydride **1** with hydrogen sulfide to form a thiolic acid **2**. Then **2**, a strong nucleophile, apparently reacts with maleic anhydride to form the ester **3**. When maleic anhydride is fed into a solution of hydrogen sulfide and the amine catalyst in dioxane, ester formation is favored and polymers with three or more repeating ester units are the predominant products. When **3** or the polymeric esters react with ethanol, two esters, presumably tetraethyl thiodisuccinate (**4**) and diethyl mercaptosuccinate (**5**) are obtained.

Experimental[34]

Materials.—Maleic anhydride, citraconic anhydride, mercaptans, thiophenols, solvents, and amine bases were commercial pure or research grade materials unless otherwise noted.

General Method of Preparation.—A solution of 0.10 mole of maleic anhydride in 100 ml. of dioxane was heated to 65°. Then 0.005 mole of triethylenediamine was added and finally 0.10 mole of the thiol. In most cases a temperature rise of a few degrees occurred within the first 5 min. The mixture was held at 65° for 30–60 min. 0.005 to 0.01 mole of concentrated sulfuric acid was added and the solvent distilled. The product was recrystallized or distilled under reduced pressure.

Kinetic Experiments. A. The Addition of *tert*-Dodecyl Mercaptan to Maleic Anhydride.—To a solution of 0.20 mole of maleic anhydride in 140 g. of dioxane 0.20 mole of *tert*-dodecyl mercaptan was added. The solution was stirred and the temperature adjusted to 25°. Then 0.0018 mole of triethylenediamine was added and stirring continued. Samples (1.0 g.) were taken at the desired intervals into bottles containing 1 ml. of 0.1 *N* sulfuric acid solution in dioxane and mixed to stop the reaction. The samples were analyzed for thiol content using a colorimetric procedure.[35] The data are given in Table I. The same results were obtained, within experimental error, whether the yield was calculated from the amount of thiol reacted or from the amount of substituted succinic anhydride isolated.

B. Dissociation of *tert*-Dodecylthiosuccinic Anhydride.—The anhydride, 0.20 mole, was dissolved in 145.5 g. of dioxane and 0.0045 mole of triethylenediamine was added. The solution was heated at 85° and samples taken at intervals of 3.5 and 12 hr. The free thiol indicated from these samples was 0.007 mole (3.5% of theory) and 0.0099 mole (4.95% of theory), respectively.

***dl*-4-Chlorophenylthiosuccinic Anhydride.**—A solution of 28.9 g. (0.2 mole) of 4-chlorobenzenethiol and 21.6 g. (0.22

---

(30) 1,4-Diazabicyclo[2.2.2]octane under the trademark "Dabco" is available from Houdry Process Corp. of Marcus Hook, Pa. Farkas, G. A. Mills, W. E. Erner, and J. B. Maerker, *Ind. Eng. Chem.*, **51**, 1299, ref. A (1959).

(31) A. Farkas and K. G. Flynn, *J. Am. Chem. Soc.*, **82**, 642 (1960); explain the several-fold better catalytic activity of triethylenediamine over triethylamine and other amines in the reaction of isocyanates with alcohols as being due to the lack of steric hindrance in triethylenediamine and the consequent availability of the nitrogen to form complexes.

(32) This subject is reviewed by E. L. Eliel, "Steric Effects in Organic Chemistry," M. S. Newman, ed., J. Wiley and Sons, Inc., New York, 1956, pp. 75 and 157–160.

(33) L. W. Newton, ref. 8b and 10 observes that the second stage in the reaction of hydrogen sulfide with dialkyl fumarates, etc., is much faster than the first.

(34) All melting points are uncorrected.

(35) R. E. Keller and G. W. Ashworth, submitted for publication.

mole) of maleic anhydride in 60 ml. of toluene was heated to 70° and 0.0002 mole (0.25 ml. of a 1:10 solution of triethylamine in toluene) was added. A small temperature rise was noted immediately and the addition of more catalyst had no effect on the temperature. Then the mixture was cooled with stirring, the solid product was filtered off, washed with 25 ml. of toluene, and dried. Yield, 92–98%; m.p. 96–98°. Recrystallization from toluene did not raise the melting point. The product was soluble in acetone.

***dl*-Pentachlorophenylthiosuccinic Anhydride.**—A mixture of 21.6 g. (0.22 mole) of maleic anhydride, 150 ml. of toluene, and 0.5 ml. (0.0035 mole) of triethylamine was heated to 80°. Then 56.4 g. (0.2 mole) of pentachlorobenzenethiol was fed in during about 10 min. The temperature rose about 6°. The mixture was heated at 85° for 20 min. longer and then cooled with stirring to 25°. The solid product was filtered off and washed with 10 ml. of toluene. Yield, 87%. After recrystallization from acetone, the m.p. was 166–168°. The anhydride also could be recrystallized from toluene or benzene. The infrared spectrum showed bands at 1860 and 1784 (anhydride) and at 1330 cm.$^{-1}$ (pentachlorophenyl).

***dl*-Pentachlorophenylthiosuccinic Acid.**—Pentachlorophenylthiosuccinic anhydride, 3.8 g. (0.01 mole), was dissolved in 15 ml. of acetone at reflux. One milliliter of water was added and the mixture refluxed for 10 min., evaporated to 5 ml., cooled, and the acid filtered, m.p. 218–220° with slow effervescence. A second crop of equivalent quality was obtained by adding water to the filtrate; total yield, 100%.

***dl*-*n*-Butylthiosuccinic Anhydride.**—A solution of 29.4 g. (0.3 mole) of maleic anhydride in 150 ml. of benzene was heated to 60° and 0.5 ml. (0.0035 mole) of triethylamine was added. Then 28.8 g. (0.3 mole) of *n*-butyl mercaptan was fed in during 5 min. The temperature rose to 70°. After heating at 65–70° for 30 min., 0.3 ml. of concentrated sulfuric acid was added and the reaction mixture was filtered to clarify and distilled. B.p. 122–124° (0.3 mm.); yield, 85–89%. The infrared spectrum had strong bands at 1860 and 1784 cm.$^{-1}$ (anhydride).

***dl*-*n*-Butylthiosuccinic Anhydride (Peroxide-Catalyzed Reaction).**—A solution of 16 g. (0.2 mole) of *n*-butyl mercaptan, 19.6 g. (0.2 mole) of maleic anhydride, 0.4 g. of benzoyl peroxide, and 60 ml. of benzene reacted under a nitrogen atmosphere at 80–85° for 24 hr. The benzene was distilled and the unchanged mercaptan and maleic anhydride distilled under reduced pressure. The infrared spectrum of the crude product showed the expected anhydride bands but also an ester band from which the amount of ester was estimated to be about 9–10 mole %. The *n*-butylthiosuccinic anhydride distilled at 155° (2 mm.) as a colorless liquid; yield 10.2 g. (29%).

***dl*-*n*-Dodecylthiosuccinic Anhydride.**—This anhydride was prepared by the base-catalyzed procedure described for *dl*-*n*-butylthiosuccinic anhydride. The crude product was obtained in 93% yield. After one recrystallization from petroleum ether, the melting point was 41–43°.

Thiodisuccinic Anhydride.—A solution of 29.4 g. (0.3 mole) of maleic anhydride in 100 g. of substantially anhydrous benzene was heated to 40° and 1 g. of triethylamine added. Hydrogen sulfide was introduced at a rate of 0.3–0.4 mole per hour for a period of 1.5 hr. The temperature rose to 55° within a few minutes, remained at that level for 15–20 min. and then gradually dropped. The solvent was removed by decantation since the product separates as a semisolid. The infrared spectrum showed bands at 1860 and 1784 cm.$^{-1}$ (anhydride). This dianhydride could not be distilled without decomposition.

Thiodisuccinic Acid.—The crude thiodisuccinic anhydride obtained above was heated at 80° with 100 ml. of water to effect hydrolysis. The resulting solution was treated with decolorizing carbon, filtered, and the water removed by azeotropic distillation with benzene. The thiodisuccinic acid was filtered from the benzene, m.p. 195–197°. The infrared spectrum shows a strong band at 1690 cm.$^{-1}$ (carboxylic acid) and no anhydride bands.

Reaction of Maleic Anhydride with Excess Hydrogen Sulfide.—A solution of 0.1 g. (0.001 mole) of triethylamine in 40 ml. of dioxane was saturated with hydrogen sulfide at 25°; a yellow solution formed. While hydrogen sulfide was bubbled through the stirred solution continuously, a solution of 19.6 g. (0.2 mole) of maleic anhydride in 40 ml. of dioxane was added dropwise at such a rate as to keep the temperature below 45°. No dark-colored products were formed. When all of the maleic anhydride had been added, an infrared spectrum showed a small amount of unchanged maleic anhydride and a new anhydride of the thiosuccinic type (strong band at 935 cm.$^{-1}$). A strong band at 1739 cm.$^{-1}$. indicated the presence of a new carbonyl compound (probably ester). After standing 30 min. at 25°, all the maleic anhydride had been consumed and most of the new thiosuccinic type anhydride also had been consumed and the carbonyl with a strong band at 1739 cm.$^{-1}$ was predominant. The yellow solution was evaporated leaving 30.2 g. of a yellow brittle resin. Calculated from a 2:1 mole ratio of maleic anhydride–H_2S, 23.0 g.; for 1:1 ratio, 25.4 g.; for 2:3 ratio, 28.8 g. The product was soluble in dioxane, acetone, and glacial acetic acid, and insoluble in carbon tetrachloride, chloroform, benzene, and toluene.

The resinous product was esterified by dissolving in a solution of 100 ml. of anhydrous ethanol, 100 ml. of benzene, and 1 ml. of concentrated sulfuric acid and refluxing for 24 hr. The usual work-up yielded two products: a) yellow liquid, b.p. 120–130° (0.5 mm.), yield 10.1 g.; and b) orange oil, b.p. 165–175° (0.08 mm.), yield 10.1 g. Both products had infrared spectra very similar to that of an authentic sample of diethyl mercaptosuccinate. They were not investigated further.

Reaction of 4-Chlorobenzenethiol with Citraconic Anhydride.—Citraconic anhydride, 11.2 g. (0.1 mole), was dissolved in 10 ml. of toluene. Then 14.4 g. (0.1 mole) of 4-chlorobenzenethiol was added and the mixture warmed to 32° to effect solution. Then 0.4 ml. of 10% solution of triethylamine in toluene was added. The pale yellow reaction mixture did not change color, but the temperature rose 3°. The mixture was heated at 70° for 10 min.; cooled, and 0.05 ml. of sulfuric acid added. The toluene was distilled to a still temperature of 90° (50–70 mm.). The yield of crude anhydride, a viscous, yellow liquid, was quantitative. Infrared spectra on this product showed good bands at 1870 and 1785 cm.$^{-1}$ (anhydride). Citraconic anhydride was at a low level and free thiol was at a low level or absent (no band at 2510 cm.$^{-1}$).

In n.m.r.[36] spectra a proton resonance signal for the ring $>CH_2$ with reference to phenylthiosuccinic anhydride and double signals for $>CH—$ were used for isomer assignments. The anhydride as obtained directly from the reaction contained 5–10% citraconic anhydride and an estimated four parts of the α-methyl-α-RS-configuration and one part of α-methyl-β-RS-configuration. These several isomers have not been separated.

Anal. Calcd. for $C_{11}H_9ClO_3S$ (256.72): Cl, 13.8. S, 12.1. Found: Cl, 12.6. S, 11.0.

***dl*-[Methyl-(4-chlorophenylthio)]succinic Acid.**—Reaction of the corresponding anhydride with water produced a dicarboxylic acid melting at 158–159°. The structure of this acid has not been elucidated as yet.

Anal. Calcd. for $C_{11}H_{11}ClO_4S$: mol. wt., 274.732. Cl, 12.91. Found: mol. wt. (neut. equiv.), 274.2. Cl, 13.1.

4-Chlorophenylthiomethylsuccinic Anhydride.[37]—A mix-

---

(36) A Varian HR-60 Mc./sec., high resolution n.m.r. spectrometer was used. The product was examined without dilution with reference to an internal standard, tetramethylsilane, using 5-mm. sample tubes with spinning.

(37) Benzylthiomethylsuccinic anhydride can be made by dehydration of the acid according to C. G. Overberger and H. Aschkenasy, *J. Am. Chem. Soc.*, **82**, 4359 (1960). The acid is made by free radical addition of benzyl mercaptan to itaconic acid using a 60-hr. reaction time.

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.

Acknowledgment.—The kinetic calculations were done by Dr. Basil Dmuchovsky, the n.m.r. spectra were performed and interpreted by Dr. Robert E. Keller, the thiol determinations by Mr. George W. Ashworth, and the infrared spectra by Mr. O. E. Kinast and Dr. B. Katlafsky.

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

ALAN C. DUCKWORTH

Ballistic Research Laboratories, Aberdeen Proving Ground, Maryland

Received March 1, 1962

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:

---

[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).