Transmission of Conjugation by the Cyclopropane Ring

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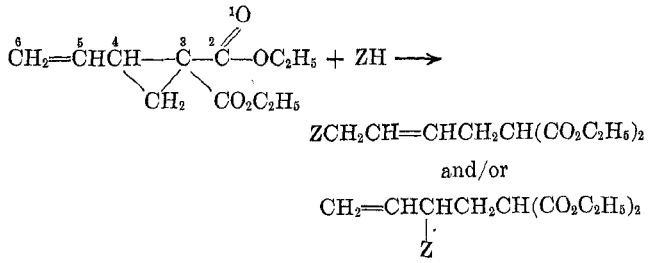
This study was made in an effort to elucidate further the question of whether a cyclopropane ring can participate in transmission of conjugation between one contiguous unsaturated group and another attached to a different carbon atom of the ring. Analyses of the product mixtures from reactions of typical nucleophiles with diethyl 2-vinylcyclopropane-1,1-dicarboxylate have shown that in some cases such transmission does occur, resulting in 1,6 addition to the system being studied. Uncatalyzed reactions of thiols gave exclusively 1,6-addition products, base-catalyzed reactions of thiols gave mixtures of 1,6-addition products and 1,4-addition products resulting from simple ring opening, and reactions of amines gave only 1,4-addition products.

One report from this laboratory[1] has described ring-opening addition reactions between nucleophilic reagents and cyclopropanes which were substituted on one carbon atom of the ring by two electron-withdrawing groups. A second report[2] describes a few cases of extension of a conjugated system by participation of the cyclopropane ring during base-catalyzed reactions with thiols by 1,6 addition.

The ability of a cyclopropane ring to participate in conjugation has been recognized for many years. On the basis of much earlier work it has appeared necessary, however, to draw a distinction between the ability of a cyclopropane ring to *extend* a conjugated system (see above for example), and its ability to *transmit* conjugative effects from one unsaturated group to another. As outlined in an excellent review of the subject by Trachtenberg and Odian,[3] although there is a good deal of evidence in support of the first, there are conflicting reports with regard to the second. For example, Mohrbacher and Cromwell[4] studied ultraviolet (uv) and infrared (ir) spectra of *cis*- and *trans*-1-(4-phenylbenzoyl)-2-phenylcyclopropanes, the corresponding carboxylic acids, and their esters. Bathochromic shifts were considered evidence for transmission of conjugative effects. Other typical spectral studies[5,6] offered supporting evidence for this point of view. Chemical evidence for transmission of conjugation has been offered in the report[7] that the diethyl malonate anion can add to diethyl 2-vinylcyclopropane-1,1-dicarboxylate in both a 1,4 and, to a lesser extent, a 1,6 manner, since the malonate anion does not ordinarily add to either an olefin or to vinylcyclopropane. On the other hand, a number of investigators have reported uv studies[8] which indicate that, although the cyclopropane ring is capable of extending a system of conjugation, it is incapable of transmitting conjugative effects. Trachtenberg and Odian[3] reported that the ρ values for a series of substituted *trans*-2-phenylcyclopropanecarboxylic acids were close to those of their saturated analogs and differed markedly from those of the α,β-unsaturated acid analogs. This study, however, was based on pK's measured in water and, when this study was repeated by Fuchs, *et al.*,[9] using pK values measured in 50% ethanol, they found that the cyclopropane ring transmitted electronic effects moderately better than a $-CH_2CH_2-$ group. They attributed this to the ability of the cyclopropane ring to transmit resonance effects *via* a π-bond system, provided that sufficient demand is made at the reaction site. In one chemical attempt to test the transmission of conjugation by cyclopropane rings, Cannon, *et al.*,[10] were unable to alkylate or acylate the methyl group in diethyl 2-methylcyclopropane-1,1-dicarboxylate and concluded that transmission of conjugative effects in the transition state for carbanion formation are small compared with analogous α,β-unsaturated compounds. Trachtenberg and Odian[3] concluded from their review of the various conflicting reports that a cyclopropane ring is incapable of transmitting conjugation in the ground state but may be able to do so in some excited states. It is likely that, during chemical reactions, such transmission occurs only in a transition state, *i.e.*, after bond breaking of the ring has commenced.

In this investigation, the reaction products of nucleophilic reagents with diethyl 2-vinylcyclopropane-1,1-dicarboxylate (1) were analyzed to determine whether any 1,6 addition had occurred, indicating transmission of conjugation, or whether only 1,4 addition had occurred, involving only extension of conjugation. The

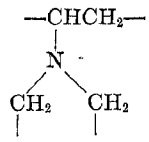


dimethyl ester (**1a**) was also employed in some of this work.

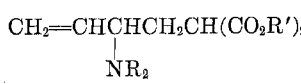
The reactions of both primary and secondary amines with **1** and **1a** apparently proceeded entirely by the 1,4-addition mechanism through simple ring opening, and thus no transmission of the conjugation occurred in these reactions. With individual products, arbitrary distillation cuts showed uniformity in refractive indices, and thin layer chromatograms indicated only one component. The nmr spectra all showed a typical complex vinyl group multiplet between the limits of

(1) J. M. Stewart and H. H. Westberg, *J. Org. Chem.*, **30**, 1951 (1965).
(2) J. M. Stewart and D. R. Olsen, *ibid.*, **33**, 4534 (1968).
(3) E. N. Trachtenberg and G. Odian, *J. Amer. Chem. Soc.*, **80**, 4018 (1958), and references therein.
(4) R. J. Mohrbacher and N. H. Cromwell, *ibid.*, **79**, 401 (1957).
(5) G. W. Cannon, A. A. Santelli, and P. Shenian, *ibid.*, **81**, 1660 (1959).
(6) R. P. Mariella, L. F. A. Peterson, and R. C. Ferris, *ibid.*, **70**, 1494 (1948).
(7) R. W. Kierstead, R. P. Linstead, and B. C. L. Weedon, *J. Chem. Soc.*, 3616 (1952).
(8) For example, (a) L. I. Smith and E. R. Rogier, *J. Amer. Chem. Soc.*, **73**, 3840 (1951); (b) R. H. Eastman, *ibid.*, **76**, 4115 (1954); **77**, 6642 (1955).
(9) R. Fuchs, C. A. Kaplan, J. J. Bloomfield, and L. F. Hatch, *J. Org. Chem.*, **27**, 733 (1962).
(10) G. W. Cannon, A. A. Santelli, and P. Shenian, *J. Amer. Chem. Soc.*, **81**, 4264 (1959).

4.9–6.1 ppm and with a relative intensity of 3. They also showed complete absence of peaks attributable to cyclopropane ring protons. Other pertinent signals in the spectrum (using the piperidine adduct) were a triplet at 3.56 ppm, intensity 1, for the proton between the two ester groups, a complex multiplet between the limits of 1.78 and 3.08 ppm, intensity 7, including all of the protons in the grouping



and a broad singlet at 1.44 ppm, intensity 6, assigned to the other six protons in the piperidine moiety. The ir spectra of all of these products showed a strong absorption peak in the 915–925-cm^{-1} region and a smaller peak at 990–995 cm^{-1} characteristic of the C–H bending vibrations of a terminal vinyl group and identical with those in the starting compounds **1** and **1a**. There was no observable absorption in the vicinity of 965 cm^{-1} which would have been attributable to the C–H bending vibrations of an internal ethylenic group in the *trans* configuration. The assigned structures were also confirmed by near-ir spectra. In these there was a peak of weak to medium intensity at 1.62–1.64 μ, and a peak two to three times as strong at 2.245–2.255 μ. These peaks were present in the spectra of all model compounds examined which had a terminal vinyl group and were not present in model compounds having an internal ethylenic group. There was also an absorption peak of weak to medium intensity at 2.11–2.12 μ in all of these products and the starting material, which does not appear in the products of 1,6 addition described later nor in model compounds with internal double bonds. The addition products of secondary amines and **1** or **1a** then have the structure



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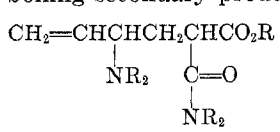
A much higher boiling secondary product



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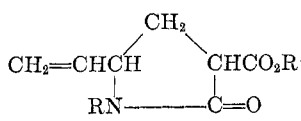
resulting from reaction of one of the ester groups with the amine was also isolated from a number of these reactions, and the structure was confirmed as indicated for the initial addition products by means of ir, near-ir, and nmr spectra.

The reactions of primary amines apparently proceeded in the same manner as those of secondary amines. However, no simple addition products corresponding to structure **2** were ever isolated. The initial addition compound underwent a further internal reaction between the secondary amine group and one of the ester groups to form a lactam



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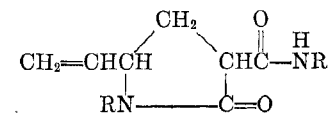
A second product resulting from amide formation through the second ester group was also isolated from some of these reactions and shown to have the structure



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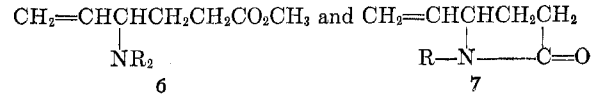
In addition to the structural proofs indicated previously the ir spectra of the compounds of type **4** showed no N–H absorption band in the 3300-cm^{-1} region. A strong absorption peak at 1690–1700 cm^{-1} was attributed to the lactam "amide I" band. Another strong absorption at 1730–1740 cm^{-1} showed that one of the ester groups was still present. The spectra of the compounds of type **5** showed an N–H stretching band at 3300 cm^{-1} and a strong absorption peak at 1540 cm^{-1} corresponding to the "amide II" band absorption of a secondary amide. The strongest absorption peak at 1670 cm^{-1} was assigned to the combined absorptions of the lactam group and the "amide I" band of the secondary amide.

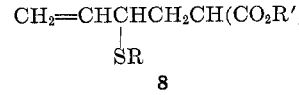
In reactions of some secondary or primary amines with the dimethyl ester analog **1a**, other by-products were isolated which were never obtained in reactions of the diethyl ester **1**. These were apparently formed by loss of one entire ester group and had the type structures



6 **7**

A study was made of the effects of varying the ratio of reactants, the temperature, the solvent on the reaction rates, and the yields of the two types of products obtained from either primary or secondary amines. Best results were obtained with equimolar amounts of reactants and a polar solvent such as ethanol or N,N-dimethylformamide at a temperature of 78–105° for 20 hr. Use of the polar solvent compared with benzene or with no solvent greatly increased the rate of the reactions and also greatly reduced the amount of secondary-type products **3** or **5**. The increased rates of reactions in polar solvents support the supposition that the ring-opening reaction proceeds through a transition state requiring charge separation.

The reactions of either **1** or **1a** with benzenethiol and with 1-butanethiol which were carried out in the presence of a sodium alkoxide catalyst gave mixtures of the addition products resulting from 1,4 addition



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(**8**) and from 1,6 addition, $RSCH_2CH{=}CHCH_2CH(CO_2R')_2$ (**9**). Thin layer chromatograms of arbitrary distillation fractions revealed the presence of two components. Infrared spectra of these mixtures had absorption peaks at 915–919 and 987–991 cm^{-1}, characteristic of a terminal vinyl group. They also showed a peak of medium intensity at 966 cm^{-1} attributable to the C–H bending vibrations of an internal olefinic group in the *trans* configuration. Near-infrared spec-

tra confirmed the presence of a terminal vinyl group in one of the components with absorption peaks at 1.62–1.635 and at 2.25 μ. The nmr spectra of several of these product mixtures showed a broad complex alkene pattern between the limits of 4.8 and 6.0 ppm. Using different arbitrary distillation fractions within the limited boiling range of the mixtures, integration of the nmr spectra gave relative intensity values from 2.2 to 2.8 for the alkene protons, indicating that the amount of 1,6-addition product in the mixture varied from 80 to 20%, respectively. Attempted gas chromatographic analysis appeared to result in decomposition.

Uncatalyzed reactions of the same thiols with **1** or **1a** apparently resulted in exclusive 1,6 addition to form the type compound **9**. The olefinic proton pattern in the nmr spectra of several samples was much simpler than in those products previously described which contained isomers having terminal vinyl groups. These peaks were all between the limits of 5.4 and 5.7 ppm, and integration gave a relative intensity value of 2. Other signals in the nmr spectrum assigned to the structure

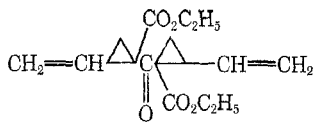
$$C_6\overset{a}{H}_5S\overset{b}{C}H_2CH{=}CH\overset{c}{C}H_2\overset{d}{C}H(CO_2\overset{e}{C}H_2)_2$$

are (a) a multiplet at 7.27 ppm, intensity 5; (b and d) a multiplet at 3.40 ppm, intensity 3; (c) a multiplet at 2.58 ppm, intensity 2; (e) a singlet at 3.69 ppm, intensity 6. Near-infrared spectra showed no absorption at 1.62–1.64 μ, and ir spectra showed no absorption at either the 915- or the 990-cm^{-1} regions, indicating again the absence of a terminal vinyl group. In all of the ir spectra there was an absorption band of medium intensity at 967–969 cm^{-1} for the internal —CH=CH— group in the *trans* configuration.

The possibility was considered that the uncatalyzed thiol additions might be initiated by electrophilic attack of a proton at the vinyl group, followed by addition of the thiol anion to a rearranged carbonium ion species. However, all of the possible structures resulting from such a mechanism would have the grouping $CH_3CH{=}CH{-}C{-}$, in which the terminal methyl group should appear as a double doublet at 1.9–2.0 ppm in the nmr spectrum. There were no peaks in this region of the spectrum, and in the case of the benzenethiol product there was no signal at less than 2.4 ppm.[11]

It was also considered possible that the uncatalyzed thiol reactions might have followed a free-radical mechanistic pathway. However, additions of relatively large amounts of hydroquinone to these reaction mixtures did not significantly inhibit the reactions and resulted in only the same single isomer. Further work has been planned to elucidate the differences in base-catalyzed and uncatalyzed additions to these systems.

Several attempts were made to effect an addition of ethanol to **1** in the presence of varying amounts of sodium ethoxide. In no case was any addition product isolated, but, in addition to much unreacted **1**, small yields of a product resulting from condensation of two molecules of **1** with loss of a molecule of diethyl carbonate were obtained, for which the probable structure



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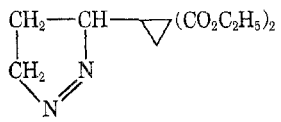
is proposed. An ir spectrum showed the presence of both ketone and ester groups, as well as cyclopropane rings and terminal vinyl groups. A similar condensation with loss of diethyl carbonate was noted by Kierstead, *et al.*,[7] during reactions of **1** with ethyl sodiomalonate. An nmr spectrum showed only the vinyl group multiplet and the usual complex cyclopropane protons pattern in addition to the protons in the ethoxy groups, with a correct integration ratio.

One reaction between diazomethane and **1** was carried out to determine how diazomethane might react with such a system. However, the only product isolated was the product of simple 1,3 dipolar addition of the diazomethane to the terminal vinyl group to form diethyl 2-(3′-Δ^1-pyrazolinyl)cyclopropane-1,1-dicarboxylate



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Although the nmr spectrum was rather complex owing to superimposed signals for various types of protons, integration of the areas assigned to expected proton signals[12,13] gave supporting evidence for the substituted 1-pyrazoline structure.

Experimental Section

Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Nuclear magnetic resonance spectra were recorded by Professor Graeme Baker of Montana State University, Bozeman, Mont., and Dr. I. J. Wilk, Stanford, Calif., using Varian Associates A-60 spectrometers. Near-infrared spectra were obtained with a Hitachi-Perkin-Elmer Model EPS-3T, and the infrared spectra were obtained with a Beckman Model IR-5. Boiling points are uncorrected.

Diethyl 2-Vinylcyclopropane-1,1-dicarboxylate (1).—The general method of preparation described by Murdock and Angier[14] was followed, with the exception that *trans*-1,4-dichloro-2-butene was used rather than the *cis* isomer. Yields as high as 56% were obtained: bp 83° (1 mm); n^{25}D 1.4501 [lit.[7] bp 69–72° (1.5 mm); n^{25}D 1.4502].

Dimethyl 2-Vinylcyclopropane-1,1-dicarboxylate (1a).—The same procedure was used as for the diethyl ester, but addition of the hot methanol slurry of the sodiodimethyl malonate salt to the 1,4-dichloro-2-butene was made through a heated dropping funnel adapted for introduction of solids. Yields as high as 48% of pure product were obtained: [bp 71–73° (1 mm) and 114–116° (20 mm); n^{25}D 1.4602.

Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.56. Found: C, 58.83; H, 6.71.

General Procedure for the Reactions of 1 or 1a with Amines or Thiols.—The reactants (with or without added solvent) were either heated at reflux temperatures or (in the case of lower

(11) One referee has suggested that the exclusive 1,6 additions of thiols to **1** and **1a** in uncatalyzed reactions might be explained by assuming a cyclic transition state in which the sulfur atom could act as a nucleophilic center and the attached proton as electrophilic center, either at a carbonyl oxygen (eight-membered ring) or at a cyclopropane carbon adjacent to the carbonyl (six-membered ring). He also, however, pointed out that, if such a reaction were concerted, it would appear that the internal olefin product should have a *cis* geometry, which is not substantiated by the ir spectra.

(12) D. E. McGreer, N. W. K. Chiu, M. G. Vinje, and K. C. K. Wong, *Can. J. Chem.*, **43**, 1407 (1965), and references therein.

(13) R. J. Crawford, A. Mishra, and R. J. Dummel, *J. Amer. Chem. Soc.*, **88**, 3959 (1966).

(14) K. C. Murdock and B. Angier, *J. Org. Chem.*, **27**, 2395 (1962).

TABLE I

DIETHYL 2-VINYLCYCLOPROPANE-1,1-DICARBOXYLATE PRODUCTS (TYPES 2, 3, 4, 5, AND 9)

Reactant	Product	Registry no.	Yield, %	Bp, °C (mm)	$n^{25}D$	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
Piperidine	Diethyl 2-piperidino-3-butenyl malonate (2)	17447-82-4	71.5	108–109 (0.1)	1.4642	64.64	9.08	4.71	64.82	9.09	4.72
	2-Carbethoxy-4-piperidino-5-hexenopiperidide (3)	17447-50-6		167 (0.3)	1.4949	67.92	9.53		67.64	9.37	
Diethylamine	Diethyl 2-diethylamino-3-butenyl malonate (2)	17447-63-1	46	113 (0.3)	1.4536	63.16	9.48		63.49	9.40	
	2-Carbethoxy-4-diethylamino-5-hexeno-N,N-diethylamide (3)	17447-64-2	12	146 (0.3)	1.4641	65.38	10.25		65.52	10.21	
n-Butylamine	1-*n*-Butyl-3-carbethoxy-5-vinyl-2-pyrrolidone (4)	17447-65-3	39	118–119 (0.4)	1.4705	65.27	8.80	5.85	65.43	9.01	6.00
	1-*n*-Butyl-5-vinyl-2-pyrrolidone-3-N-*n*-butylcarboxamide (5)	17447-66-4	18[a]	145–146 (0.4)	1.4872	67.67	9.76	10.52	67.50	9.90	10.58
Cyclohexylamine	1-Cyclohexyl-3-carbethoxy-5-vinyl-2-pyrrolidone (4)	17447-67-5	35	138–140 (0.4)	1.4938	67.92	8.68	5.27	68.23	8.93	5.43
1-Butanethiol	Diethyl 4-*n*-butylthio-2-butenylmalonate (9)	17447-68-6	36	127–129 (0.4)	1.4685	59.63	8.61		59.85	8.73	

[a] Yield increased to 57.5% by using 3:1 molar ratio of amine to ester.

TABLE II

DIMETHYL 2-VINYLCYCLOPROPANE-1,1-DICARBOXYLATE PRODUCTS (TYPES 2, 5, 6, 7, AND 9)

Reactant	Product	Registry no.	Yield, %	Bp, °C (mm)	$n^{25}D$	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
Piperidine	Dimethyl 2-piperidino-3-butenyl malonate (2)	17447-69-7	26	100–101 (0.2)	1.4722	62.42	8.60		62.82	8.79	
	Methyl 4-piperidino-5-hexenoate (6)	17447-70-0	30	66–67 (0.2)	1.4700	68.21	10.02		68.12	10.17	
Benzylamine	1-Benzyl-5-vinyl-2-pyrrolidone (7)[a]	17447-71-1	30	106–107 (0.2)	1.5398	77.60	7.45	6.96	76.62	7.62	6.80
	1-Benzyl-5-vinyl-2-pyrrolidone-3-N-benzylcarboxamide (5)	17447-83-5		103–104 (mp)		75.42	6.63	8.38	75.01	6.55	8.45
1-Butanethiol	Dimethyl 4-*n*-butylthio-2-butenylmalonate (9)	17447-72-2	36.4	125–126 (0.4)	1.4795	56.90	8.09		57.09	8.21	
Benzenethiol	Dimethyl 4-phenylthio-2-butenylmalonate (9)	17447-73-3	62–72	149–150 (0.2)	1.5391	61.20	6.16		61.21	6.30	

[a] Impure if carbon analysis is correct.

boiling amines and the thiols) sealed in glass tubes and heated in pressure bombs at 100–150°. In some cases the reactant solutions were heated in pressure bottles in an oven. The best yields of primary addition products were obtained with a ratio of 0.03 mol of the ester to 10 ml of ethanol and a slight molar excess of amine or thiol at about 100° for 20 hr. The products of amine reactions were isolated by direct vacuum distillation, or by the following procedure. The alcohol was stripped, and the product mixture was dissolved in ether. The ether solution was washed several times with water, and the amine products were then extracted by several washings with 3 *N* hydrochloric acid. The combined acid extracts were made basic by addition of 3 *N* sodium hydroxide; the amine products were extracted with ether; and the ether solutions were dried over anhydrous potassium carbonate. The products were then distilled.

The products of thiol reactions were isolated usually by direct vacuum distillation.

Yields, physical constants, and elemental analysis data for the various products of these reactions are listed in Tables I and II. The pertinent nmr, ir, and near-ir spectral data have been given in the discussion.

Base-Catalyzed Reactions of 1 or 1a with Thiols.—The same general procedure was used as described above with the addition of 0.1 mol equiv of sodium, compared with moles of ester used, dissolved in the appropriate alcohol (ethyl or methyl). The crude product solutions were stripped of alcohol, and the residue was dissolved in ether, washed with 2 *N* hydrochloric acid, and dried over anhydrous magnesium sulfate before final distillation. Inasmuch as the distilled products were mixtures of 1,4- and 1,6-addition-type isomers **8** and **9**, the physical constants differ slightly from those listed for the 1,6-addition products in Tables I and II and are given below. Elemental analyses data were obtained for these isomer mixtures to show the absence of other types of compounds and were within acceptable limits. The pertinent nmr, ir, and near-ir spectral data have been given in the discussion.

Product isomers from 1-butanethiol and 1 (diethyl 4-*n*-butylthio-2-butenylmalonate and diethyl 2-*n*-butylthio-3-butenylmalonate) were obtained: 56%; bp 125–130° (0.4 mm). The refractive index varied from $n^{25}D$ 1.4696 to 1.4711 in successive arbitrary distillation fractions.

Product isomers from 1-butanethiol and 1a (dimethyl 4-*n*-butylthio-2-butenylmalonate and dimethyl 2-*n*-butylthio-3-butenylmalonate) were obtained: 50.5%; bp 113–115° (0.3 mm); $n^{25}D$ 1.4760.

Product isomers from benzenethiol and 1a (dimethyl 4-phenylthio-2-butenylmalonate and dimethyl 2-phenylthio-3-butenylmalonate) were obtained: 61%; bp 160–166° (0.4 mm); $n^{25}D$ 1.5378.

Attempted Addition of Ethanol to 1.—A solution of 0.80 g (0.035 g-atom) of sodium in 20 ml of absolute ethanol and 7.4 g (0.035 mol) of diethyl 2-vinylcyclopropane-1,1-dicarboxylate was heated at reflux for 7 hr. The mixture was then cooled and poured into a solution of 10 ml of 6 *N* hydrochloric acid in 100 ml of water. The product was extracted with ether, and the ether solution was washed four times with water and dried over calcium chloride. Stripping of the ether left 5.6 g of thick oil. During distillation a liquid which had a boiling point range corresponding to that of diethyl carbonate was obtained but was not further identified. A much higher boiling product was obtained, which on redistillation gave a colorless viscous oil believed to be compound **10**: bp 136–138° (0.2 mm); ir $\lambda_{max}^{CCl_4}$ 1745 (s, O=C—OR), 1715 (s, R_2C=O), 990 (m, CH_2=CH—), and 921 (s, CH_2=CH—) cm^{-1}.

Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.21; H, 7.85. Found: C, 65.89; H, 8.07.

Reaction of Diazomethane and 1 [Diethyl 2-(3′-Δ^1-pyrazolinyl)-cyclopropane-1,1-dicarboxylate (11)].—Into a solution of 9.3 g (0.044 mol) of 1 in 35 ml of ether, chilled by an ice bath, was distilled an ether solution of diazomethane prepared from 10.7 g (0.05 mol) of N-methyl-N-nitroso-*p*-toluenesulfonamide in the usual manner.[15] The resulting solution was kept in a tightly stoppered flask in the refrigerator for 4 days and at room temperature for 36 hr. Distillation gave 5 g of unreacted starting ester and 3.5 g (32%) of a viscous, colorless liquid: bp 146–148° (1 mm); $n^{25}D$ 1.4700. Redistillation provided an analytical sample: bp 123–124° (0.3 mm); $n^{25}D$ 1.4718; ir, λ_{max}^{neat} 1718 (s, O=C—OR), 1546 (w, —N=N—), and 1026 (m, cyclopropyl); nmr ($CDCl_3$) δ 1.23 (double triplet superimposed on multiplet), 8 [(—OCH_2CH_3)$_2$ and —CH_2CH_2CH—], 1.67 (m, 3, cyclopropyl hydrogens), 4.15 [m, 7, (—OCH_2CH_3)$_2$ plus —CH_2—N= and —CH—N=].

Anal. Calcd for $C_{12}H_{18}N_2O_4$: C, 56.68; H, 7.13. Found: C, 56.82; H, 7.05.

Registry No.—**1a**, 17447-60-8; **10**, 17447-61-9; **11**, 17447-62-0; diethyl 2-*n*-butylthio-3-butenylmalonate,

(15) Th. J. deBoer and H. J. Becker, "Organic Syntheses," Coll. Vol. IV John Wiley & Sons, Inc., New York, N. Y., 1963, p 250.

17447-74-4; dimethyl 2-*n*-butylthio-3-butenylmalonate 17447-75-5.

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The Tscherniac–Einhorn Reaction. I. Equilibria in Solutions of N-Hydroxymethylphthalimide in Strong Sulfuric Acid

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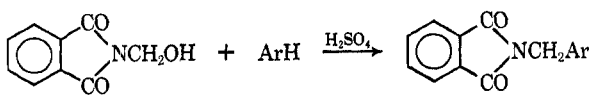
Nmr, uv, and cryoscopic measurements have been combined with chemical methods to study the behavior of solutions of N-hydroxymethylphthalimide (I) in strong sulfuric acid. In 75% sulfuric acid the protonated substrate II begins to equilibrate rapidly with detectable amounts of the corresponding protonated sulfate ester III. Conversion into III is virtually complete in 94% acid, but over the range 75–100% acid, III also is in rapid equilibrium with the protonated bis(phthalimidomethyl) ether (IV). The ratio of III to IV (~2.3–2.5) appears to be relatively independent of acid concentration.

In 1901, Tscherniac reported the condensation of N-hydroxymethylphthalimide (I) with a series of aromatic compounds in strong sulfuric acid.[1] Later



I

Einhorn extended the reaction to a series of readily available N-hydroxymethylamides.[2] This aromatic substitution process thus has come to be known as the Tscherniac–Einhorn reaction.[3] Of exceptional interest, however, is the powerful electrophilic reactivity of Tscherniac's original reagent, I, in strong sulfuric acid. More recent work has shown, for example, that benzoic acid undergoes *meta* substitution in 60% yield in 95% sulfuric acid at 10–15°.[4] In 20% oleum at 50–60° even nitrobenzene is attacked at both *meta* positions,[5] and 2,4-dinitrophenol is quantitatively substituted by I in 5% oleum at 100°.[6] It was the purpose of the present work to study the behavior of I in strong sulfuric acid and to identify potentially reactive species or their precursors. A companion paper[7] describes a kinetic study of the reaction of I with 2,4-dinitrophenol and the most likely mechanism.

Experimental Section

Nuclear magnetic resonance spectra were obtained with a Varian Model A-60 spectrometer. A Cary Model 14 spectrometer was used for the ultraviolet absorption spectra.

Materials.—Benzamide, mp 130°, was purified by recrystallization of the commercial material. N-Methylphthalimide, mp 133–134°, was prepared by alkylation of potassium phthalimide with dimethyl sulfate using the general method of Sheehan and Bolhofer.[8] N-Hydroxymethylbenzamide, mp 103–105°,[3a] and N-hydroxymethylphthalimide (I),[9] mp 144–146° (from isopropyl alcohol), were prepared by reported methods.

Protonation of Amides and Imides in Sulfuric Acid.—Four compounds, benzamide, N-hydroxymethylbenzamide, N-methylphthalimide, and N-hydroxymethylphthalimide (I), were studied by the method of Davis and Geissman[10] in which differences ($\Delta\epsilon$) in ultraviolet extinction at two selected wavelengths, in water and in 20 different concentrations (1–98.5%) of aqueous sulfuric acid, were measured. Plotting $\Delta\epsilon$ *vs.* acid concentration gave, for the first two compounds, a typical sigmoid titration curve from which the acid concentrations at half-protonation of the substrates could be estimated. By using 225 and 240 mμ as the analytical wavelengths for benzamide, it was found that this compound is half-protonated in 36% sulfuric acid.[11] Similarly, using 227 and 245 mμ as the analytical wavelengths, N-hydroxymethylbenzamide was found to be half-protonated in 50% sulfuric acid. Unfortunately, the ultraviolet spectra of the two phthalimides did not change with acid concentration as much as did the spectra of the two benzamides. Consequently, sharp-breaking curves were not obtainable, and only approximations of half-neutralization points could be made. Using 320 and 325 mμ as the wavelengths for N-methylphthalimide and 220 and 228 mμ for N-hydroxymethylphthalimide it could be estimated, roughly, that these imides are half-protonated somewhere in the range 60–70% sulfuric acid.

Quenching of Solutions of N-Hydroxymethylphthalimide (I) in Sulfuric Acid. Bis(phthalimidomethyl) Ether (V).—A solution of I (0.444 g) in 97.35% sulfuric acid (5 ml) was kept at 35° for 1 hr and then poured into vigorously stirred ice–water (50 ml). The precipitate (0.038 g, 9%, mp 203–205°) was collected at the filter, washed with cold water (10 ml), and dried. Recrystallization from glacial acetic acid gave a sample, mp 207–209°, identical (ir, nmr, and mixture melting point) with an authentic sample[12] of V. In nine runs, yields of 5–17% of V were obtained in 70–100% sulfuric acid at temperatures of 20–50°. Between 60 and 70% acid, the solution rate of I was so low that much longer times (8–16 hr) were required to give comparable yields. At concentrations below 60% acid, the low solubility of I precluded the occurrence of appreciable reaction.

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