concentration of equatorial isomer and of the energy difference between the two conformations.

Infrared analysis, on the other hand, may be taken as a direct measure of the equilibrium in the ground state, providing, however, that our assumption of equal absorptivities in fixed and flexible molecules is valid. There may also be solvent effects which need to be considered. In connection with this latter question, a check was made by running an analysis of cyclohexanol in cyclohexane. When a cyclohexane solution was compared with a carbon disulfide solution on a mole fraction basis, no appreciable change in the intensity of the C–OH absorption was apparent.

Experimental

Materials.—Following the procedure of Winstein and Holness,[3] the pure *cis*- and *trans*-4-*t*-butylcyclohexanols were isolated by chromatography of crude 4-*t*-butylcyclohexanol (supplied by the Dow Chemical Co.; now commercially available from Matheson, Coleman and Bell) using neutral alumina as absorbent and either pentane–ether or petroleum ether (low boiling)–ether to elute. The purity of the eluted fractions was followed by infrared analysis. The pure epimers thus obtained were identical in infrared spectra and melting points to authentic samples (furnished by E. L. Eliel). The cyclohexanol (Matheson, Coleman and Bell) was distilled twice through a small Vigreux column, b.p. 161°.

Analysis.—The infrared analyses were made on a Perkin-Elmer model 21 spectrophotometer, using sodium chloride optics. Analytical conditions for the runs using 0.1-mm. fixed thickness cells: slits at 225 μ, gain 3.5, suppression 0, response 1:1, scattered light filter in. Direct absorbance measurement was used, the base lines being reasonably identical. A large number of solutions were made up and interpolations made to the desired concentrations. To eliminate all possible variables and reduce sources of error, final analyses were made at concentrations precisely duplicating the intensities of the analytical bands. By using great care in reproducible technique the experimental precision in measuring concentrations of equal absorption was brought to $\pm 0.5\%$ in the final determinations. Care also was taken to minimize the time of exposure to the radiant beam energy, several tests being made to ascertain that the intensity did not change within experimental limits. Integrated absorbance was not used since the instrument was linear in wave length and any additional precision likely to result from a calculated integrated intensity was offset by the uncertainty in the purity of the *trans* compound and in the basic assumption, as discussed. The three spectra in the 9–11 μ region are illustrated in Fig. 1.

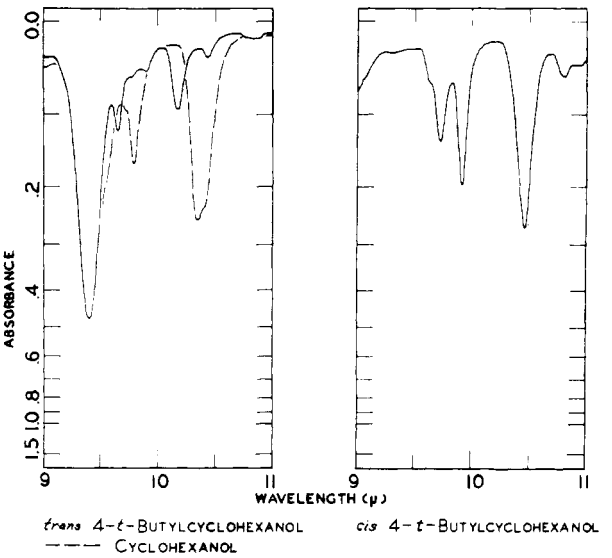

Fig. 1.—Infrared spectra in carbon disulfide solution: left, *trans*-4-*t*-butylcyclohexanol (31.04 mg./g.), ———, and cyclohexanol (30.05 mg./g.), ---------; right, *cis*-4-*t*-butylcyclohexanol (29.25 mg./g.). The cyclohexanol curve has been shifted 0.05 μ to superimpose the major C–OH absorption.

Acknowledgment.—Acknowledgment is gratefully made to the National Science Foundation for financial support, to E. L. Eliel for specimen samples and helpful suggestions and to E. C. Britton and the Dow Chemical Co. for a generous quantity of starting material.

PHILADELPHIA 4, PENNA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF BRANDEIS UNIVERSITY]

Preparation and Reactions of Acylals[1] of Disubstituted Malonic Acids

BY PAUL J. SCHEUER[2a] AND SAUL G. COHEN[2b]

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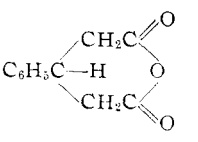
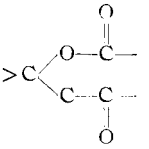
Cyclic acylals (4,6-dioxo-1,3-dioxanes) have been prepared from acetone and phenylmalonic acid (V), acetone and ethylphenylmalonic acid (VI), acetone and methylphenylmalonic (VII), and cyclopentanone and methylphenylmalonic acid. Acylals VI and VII react rapidly and practically quantitatively with sodium methoxide to form the methyl half-esters. Reactions of VI and VII with alkali metal salts of 2-propanol and other secondary alcohols did not proceed well, leading largely to the disubstituted malonic acids. Acylal VII reacted with benzylamine, forming the N-benzyl half-amide, but reaction of VI and VII with α-phenylethylamine failed to form the half-amides. Methyl ethylphenylmalonanilide and methyl N-benzylmethylphenylmalonamide are also described. The infrared absorption spectra are discussed.

In our study of asymmetry in the reactions of molecules of type C, a,b,d,d, with optically active reagents at the two sites d we have reported[3] results of the reaction of β-phenylglutaric an-



(1) The term *acylal* was proposed by C. D. Hurd and S. M. Cantor, THIS JOURNAL, **60**, 2678 (1938), for compounds containing the grouping

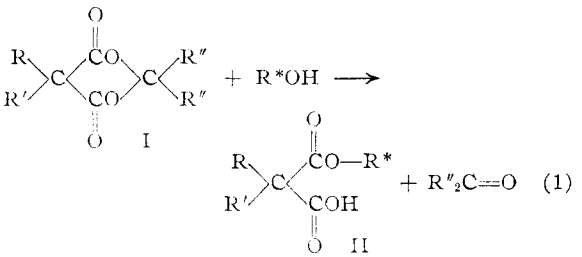


(2) (a) On sabbatical leave from University of Hawaii. (b) To whom inquiries should be addressed.

(3) R. Altshul, P. Bernstein and S. G. Cohen, THIS JOURNAL, **78**, 5091 (1956).

hydride with *l*-menthol. Asymmetry also has been reported[4] in the reaction of β-phenylglutaric anhydride with *l*-α-phenylethylamine. It seemed desirable to us to study the reaction of an optically active reagent with a derivative of an α-substituted malonic acid. The absence of the two methylene groups as compared with the derivative of glutaric acid would bring the site of reaction closer to the center of asymmetry which would be in process of formation in the diastereomeric transition states and the more restrictive steric situation might lead to greater specificity in the reactions at the two carbonyl groups. Because of the rapid possible enolization of the α-hydrogen of derivatives of malonic acid, which would lead to racemization, we undertook to work with derivatives of α,α-disubstituted malonic acids.

A derivative is desired in which reaction of one carbonyl with an alcohol or amine, with formation of an ester or amide, converts the second carbonyl to a functional group of considerably lesser reactivity than in the original compound. Thus a diester is not desirable, while a cyclic anhydride is not available from the malonic acids. It seemed that a cyclic acylal I would be a satisfactory derivative, reacting irreversibly with an alcohol or amine to form a half-ester II or half-amide of the malonic acid and a ketone or aldehyde. This reaction



might be preferable to that of the anhydride[3] in which reversibility rendered interpretation difficult.

Although acylals of acetic acid, methylene diacetate, ethylidene diacetate and benzylidene diacetate are well known, few such derivatives of acids other than acetic have been reported. Reaction of malonic acid with paraldehyde in acetic anhydride has led[5] to crotonic acid and to ethylidene diacetate, and treatment of malonic acid with acetone and glacial acetic acid led[5] neither to the acylal nor to α-isopropylidenemalonic acid, the latter being accessible through base-catalyzed condensation. However, treatment of malonic acid and acetone in acetic acid with concentrated sulfuric acid led[6] to the cyclic acylal of type I, but the incorrect β-lactone structure III $(CH_3)_2C(-O-C(=O))-CHCO_2H$ was assigned to it. Subsequently acylals of malonic acid and methylmalonic acid with acetaldehyde, acetone, heptanone-4, cyclopentanone and cyclohexanone were prepared,[7] but to all of these products the β-lactone structure of type III was assigned. Davidson and Bernhard[8] reinvestigated Meldrum's work, preparing isopropylidenemalonate in 50% yield and dimethylisopropylidenemalonate in 9% yield, and they demonstrated the acylal structure I of these compounds.

Despite the low yields of acylals reported from the disubstituted[3] malonic acid and from methylmalonic acid,[7d] with only minor variations in the procedure of reference 8, we were able to prepare isopropylidene phenylmalonate (V), m.p. 133–134°, 56% yield; isopropylidene ethylphenylmalonate (VI), m.p. 93–94°, 83% yield; and isopropylidene methylphenylmalonate (VII), m.p. 146–148°, 88% yield. Isopropylidene malonate (IV) also was prepared for comparison, 50% yield, m.p. 96.5–97.5°, reported[8] m.p. 94–95°. In each case the acylal was prepared by treatment of a solution or a suspension of the malonic acid in acetic anhydride, first with a small amount of sulfuric acid and then with acetone.

Attempts were made to substitute aldehydes for acetone in the preparation of acylals of methylphenylmalonic acid. Treatment of this acid, in acetic anhydride, with sulfuric acid and trioxane apparently led to methylene diacetate, b.p. 55° (5 mm.), carbonyl band at 5.63–5.70 μ. Similar use of benzaldehyde in this procedure appeared to lead in part to benzylidene diacetate. To minimize formation of diacetate, a modified procedure[7d] was used in which the malonic acid and acetic anhydride and sulfuric acid were allowed to stand for 24 hours and the remaining acetic anhydride and acetic acid were removed in vacuum before addition of the aldehyde. This procedure, carried out with trioxane, acetaldehyde and benzaldehyde did not lead to pure acylals. It was successful in leading to the acylal from cyclopentanone, cyclopentylidene methylphenylmalonate, m.p. 88–89°.

The reaction of isopropylidene ethylphenylmalonate (VI) with cyclohexanol was examined first as a model for the desired reaction with optically reactive menthol, and difficulties were found. Treatment with an equivalent quantity of potassium cyclohexylate in ether led to acetone and ethylphenylmalonic acid in low yield, and not to the desired ester. Treatment with potassium or sodium cyclohexylate in benzene at room temperature and at the boiling point also led to the malonic acid, while treatment with sodium cyclohexylate in cyclohexanol led to the acid in 41% yield. Treatment of the acylal with magnesium cyclohexylate in ether, with cyclohexanol in benzene in the presence of pyridine and with cyclohexanol in ether saturated with dry hydrogen chloride led to the recovery of unreacted acylal.

The formation of ethylphenylmalonic acid from treatment with the alkali cyclohexylates may be due to traces of water in the system, despite attempts to maintain anhydrous conditions. However, the yield of the acid in the presence of excess cyclohexanol may indicate that in this case reaction with the alcohol may be proceeding by alkyl–oxygen cleavage, although this seems un-

(4) P. Schwartz and H. E. Carter, *Proc. Natl. Acad. Sci.*, **40**, 499 (1954).

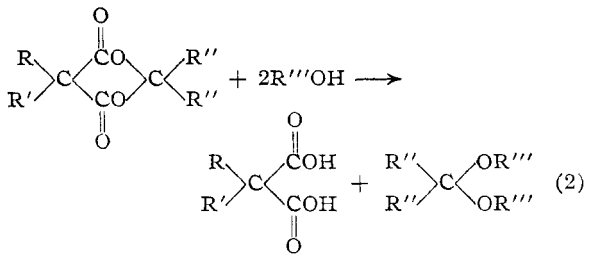
(5) T. Komnenos, *Ann.*, **218**, 147 (1883).

(6) A. N. Meldrum, *J. Chem. Soc.*, **93**, 598 (1908).

(7) (a) E. Ott, *Ann.*, **401**, 159 (1913); (b) A. Khandiah, *J. Chem. Soc.*, 1215 (1932); (c) A. Michael and J. Ross, THIS JOURNAL, **55**, 3684 (1933); (d) A. Michael and N. Weiner, *ibid.*, **58**, 680, 969 (1936).

(8) D. Davidson and S. A. Bernhard, *ibid.*, **70**, 3426 (1948).

likely in base. It then seemed desirable to examine the reaction of the acylal VI with methanol.



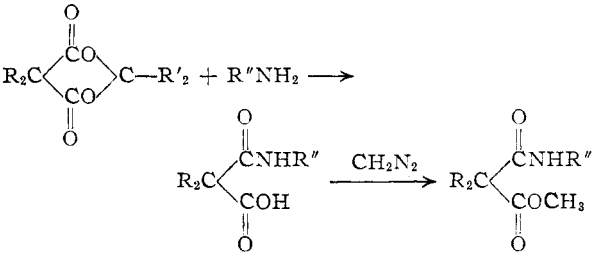
(2)

It is not clear *a priori* whether an acylal should be more sensitive to acid-catalyzed solvolysis, by alkyl–oxygen cleavage, at the acetal linkage or to base-catalyzed attack at the ester carbonyl groups. Kinetic hydrolysis data[9] on methylene and ethylidene diacetates, and the work of Davidson and Bernhard,[8] indicate that these materials are much more reactive to alkali than to acid, indicating that alkyl–oxygen acetal cleavage is not occurring. Similarly, that methylene diacetate is more rapidly hydrolyzed both in acid and in base than the ethylidine diacetate may confirm this and may also indicate that attack at the carbonyl groups is strongly affected by steric factors. We found that treatment of the acylal VI with methanolic hydrogen chloride under reflux for one hour led to 60% recovery of VI, while treatment with 0.2 *N* sodium methoxide in methanol led in 15 minutes to essentially complete conversion to the methyl half-ester (equation 1), m.p. 87.5–89°. Indeed the sequence malonic acid → isopropylidene derivative → monomethyl malonate may provide a useful synthesis of monomethyl esters of malonic acids. Before we appreciated the rapidity of the reaction of the acylal VI with methoxide ion, a reaction was run at room temperature for 24 hours, decarboxylation occurring to a considerable extent.

However, when the reaction of the acylal VI with sodium isopropylate in anhydrous isopropyl alcohol was examined under the same conditions, a very rapid reaction was observed which did not stop after consumption of one equivalent of alkoxide; 1.63 equivalents of base was consumed within 5 minutes, the major product, as in the reaction with cyclohexanol, was ethylphenylmalonic acid, 53% yield, and only a small quantity of the mono-isopropyl ester, m.p. 67–69°, was isolated pure. The secondary alcohol in each case failed to react with the acylal as the primary alcohol had. This may be due to steric hindrance in this rather "tight" system, but the reason is not clear nor is the mode of formation of the malonic acid. The possibility of effecting reaction of this acylal VI with *dl*-α-phenylethylamine was then examined. In two reactions the acylal was recovered unreacted while in a third, in which a solution of the acylal in the amine was allowed to stand for four weeks, a reaction occurred, but the product apparently lost carbon dioxide, which reacted with the amine and led to a carbamate.[10]

The reactions of isopropylidene methylphenylmalonate (VII), which might be somewhat less hindered sterically than the ethyl derivative VI, were then examined. Treatment with sodium methoxide in methanol led to consumption of 1.00 equivalent of alkoxide within five minutes and only 1.06 equivalents after ten minutes, and to formation of the methyl half-ester, m.p. 77–79°, in 88% yield, in accordance with equation 1. However, reactions with secondary alcohols did not proceed simply. Reaction with sodium isopropylate in 2-propanol appeared to consume only one equivalent of alkoxide, but starting material VII was recovered in 38% yield, along with diacid, 24%, and an oil. Reaction with the sodium salt of 1-phenylethanol led to a low yield of the diacid and an oil, while reaction with menthol also led to an oil. On the assumption that these oils were the desired half-esters, they were treated with either aniline and N,N′-dicyclohexylcarbodiimide or with thionyl chloride and aniline, but solid mono-ester mono-anilides were not obtained. During this work an analogous half-ester, from acylal VI, methyl ethylphenylmalonate, was treated with thionyl chloride and aniline leading to this mono-ester mono-anilide in 39% yield, m.p. 78–79°. An attempt to prepare this by treatment of the half-ester and aniline with dicyclohexylcarbodiimide failed.

As an alternate route toward preparing mono-ester mono-amide derivatives of substituted malonic acids that might be suited to our purposes, the sequence acylal → mono-amide → ester-amide was examined



Treatment of acylal VII with benzylamine at room temperature for one hour led to the mono-N-benzylamide in 47% yield, m.p. 111–113° dec. The material is easily decarboxylated and lost carbon dioxide in one experiment in which an attempt was made to purify it by chromatography on Florisil. Reaction of the purified amide with diazomethane led to the ester-amide quantitatively, m.p. 81–82°. However, reaction of VII with 1-α-phenylethylamine was unsuccessful, leading under comparable conditions to unreacted acylal, 71%, and to methylphenylmalonic acid, 17%, and, when the treatment was prolonged, to a higher yield of the di-acid.

Infrared Absorption Spectra.—The cyclic acylals showed split bands in the carbonyl stretching region, isopropylidene phenylmalonate at 5.58 and 5.70 μ, isopropylidene ethylphenylmalonate at 5.62 and 5.75 μ, isopropylidene methylphenylmalonate at 5.61 and 5.73 μ, cyclopentylidene methylphenylmalonate at 5.60 and 5.73 μ. Isopropylidene malonate alone showed no splitting, but broad absorption at 5.55–570 μ. The acyclic acylal, methylene diacetate $CH_2(OCOCH_3)_2$, shows a single strong absorption band at 5.63–5.69 μ, while the acyclic malonate ester, diethyl ethylphenylmalonate shows

(9) A. Skrabal and A. Schiffrer, *Z. physik. Chem.*, **99**, 290 (1921).
(10) J. Tafel, *Ber.*, **19**, 1924 (1886).

a single strong absorption band at 5.76–5.81 μ with slight shoulders at 5.72 and 5.90 μ. The splitting appears to require the cyclic acylal structure. Somewhat similar double absorption bands are found in acid anhydrides, β-phenylglutaric anhydride showing bands at 5.49 and 5.64 μ; these bands do not require cyclic structure in anhydrides.

Of the half-esters, methyl hydrogen ethylphenylmalonate and isopropyl hydrogen ethylphenylmalonate showed three maxima in the carbonyl–carboxyl region, the former at 5.68, 5.76 and 5.92 μ, the latter at 5.69, 5.81 and 5.96 μ, while methyl hydrogen methylphenylmalonate showed a single strong absorption at 5.76–5.79 with small shoulders at 5.66 and 5.92 μ. A glutarate half-ester, *l*-menthyl β-phenylglutarate, showed a single fairly sharp absorption at 5.91 μ. Data of the spectra of N-benzyl hydrogen methylphenylmalonamide, methyl N-benzyl methylphenyl-malonamide and methyl ethylphenylmalonamide are given.

Experimental

Melting points are uncorrected; microanalyses are by Dr. S. M. Nagy, Massachusetts Institute of Technology.

Isopropylidene Malonate (IV) (2,2-Dimethyl-4,6-dioxo-1,3-dioxane).—A suspension of malonic acid (Matheson, 52 g., 0.5 mole, m.p. 126–134°) in 60 ml. of acetic anhydride was treated with 1.5 ml. of concentrated sulfuric acid and, over a period of 10 minutes, with 40 ml. of acetone with slight external cooling. The solution was filtered and refrigerated overnight. The crystalline precipitate was collected and was dried, 37 g., 51% yield, m.p. 86–90° dec., m.p. 96.5–97.5° dec. after crystallization from acetone–water, reported[8] 94–95° dec.

Isopropylidene Ethylphenylmalonate (VI) (2,2-Dimethyl-5-ethyl-5-phenyl-4,6-dioxo-1,3-dioxane).—Diethyl ethylphenylmalonate (Matheson, practical) was redistilled, 158–160° (7 mm.). The hydrolysis of the ester according to Tassilly, *et al.*,[11] proved unsatisfactory and the following procedure was developed. Diethyl ethylphenylmalonate (66 g., 0.25 mole) was stirred under gentle reflux with 40 g. (1 mole) of sodium hydroxide and 500 ml. of water for 18 hours. The resulting solution was acidified with 6 *N* sulfuric acid and extracted with ether. The ether solution was dried over sodium sulfate and distilled. The residual oil solidified in the refrigerator. The waxy solid was treated with 150 ml. of boiling benzene. The benzene-insoluble material was ethylphenylmalonic acid, m.p. 149–151° dec., 33.4 g. (64% yield). An additional benzene treatment brought the melting point to 156–157° dec., reported[11] 182.5° (apparently incorrect), and in the patent literature,[12] 155°.

Ethylphenylmalonic acid (20.8 g., 0.1 mole), was stirred with 30 ml. of acetic anhydride, and 1.5 ml. of concentrated sulfuric acid was added dropwise. Acetone (25 ml.) was added over 10 minutes with cooling, and the slightly yellow solution was stirred for 75 minutes at room temperature and cooled overnight. The crystalline product was collected, washed well with ice-water and dried, m.p. 78–85°, 20.6 g. (83%). Recrystallization from acetone–water at room temperature and from petroleum ether (30–60°) brought the melting point to 93–94°. *Anal.* Calcd. for $C_{14}H_{16}O_4$: C, 67.72; H, 6.50; mol. wt., 248. Found: C, 67.50; H, 6.39; mol. wt., 243.

Isopropylidene Phenylmalonate (V) (2,2-Dimethyl-5-phenyl-4,6-dioxo-1,3-dioxane.—Diethyl phenylmalonate (Matheson) was redistilled and hydrolyzed.[13] Fifty-nine grams (0.25 mole) of ester was stirred without heating with 500 ml. of 1 *N* (0.5 mole) sodium hydroxide for 3 hours. The mixture was allowed to stand overnight and the unreacted ester was extracted with ether. The basic solution was acidified with 6 *N* sulfuric acid and extracted with ether. The extract was dried over sodium sulfate and concentrated and the residual oil crystallized on cooling. The acid was collected and dried, m.p. 142–148° dec., 29.7 g. (66%), m.p. 149–150° dec. after recrystallization from ether–petroleum ether, reported[13] m.p. 153°. The isopropylidene ester was prepared from a suspension of 9 g. (0.05 mole) of phenylmalonic acid in 24 g. of acetic anhydride. Addition of 1 ml. of concentrated sulfuric acid caused complete solution. The product began to precipitate within one minute after the addition of 6 ml. of acetone. The reaction mixture was stirred for 10 minutes, cooled and filtered. The precipitate was washed thoroughly with ice-water and dried, 6.2 g. (56%), m.p. 118–125° dec., m.p. 133–134° dec., after two crystallizations from acetate–ligroin. *Anal.* Calcd. for $C_{12}H_{12}O_4$: C, 65.44; H, 5.49. Found: C, 65.33; H, 5.47.

Isopropylidene Methylphenylmalonate (VII) (2,2-Dimethyl-5-methyl-5-phenyl-4,6-dioxo-1,3-dioxane).—Diethyl phenylmalonate (236 g., 1 mole, b.p. 157–160° (6 mm.)) was converted to diethyl methylphenylmalonate (216 g., 0.86 mole, b.p. 156–158° (10 mm.), reported[14] 165–166° (16 mm.)). The procedure was fashioned after that for the preparation of diethyl ethylbutylmalonate.[15] The ester was hydrolyzed with a small excess of 2 *N* sodium hydroxide under reflux leading to methylphenylmalonic acid, 58% yield, m.p. 156–157° dec., reported[16] 157° dec. The isopropylidene compound was prepared from a suspension of 16.3 g. (0.084 mole) of methylphenylmalonic acid in 30 ml. of acetic anhydride. Dropwise addition of 1.5 ml. of concentrated sulfuric acid afforded a colorless solution to which was added 10 ml. of acetone over 15 min. The product began to precipitate when *ca.* half of the acetone had been added. After further stirring for 30 minutes the white crystalline solid was collected, washed with ice-water and dried, 17.4 g. (88.5%), m.p. 131–145°; after two recrystallizations from acetone–water, m.p. 145–148°. An analytical sample was recrystallized from acetone–petroleum ether, m.p. 146–148°. *Anal.* Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02; mol. wt., 234. Found: C, 65.75, 66.41; H, 5.98, 6.05; mol. wt., 254.

Cyclopentylidene Methylphenylmalonate.—A solution of 5.82 g. (0.03 mole) of methylphenylmalonic acid and 0.1 ml. of sulfuric acid in 15 ml. of acetic anhydride was allowed to stand for 24 hours at room temperature and was then concentrated in vacuum, below 40°. Cyclopentanone (2.86 g., 0.034 mole) was added to the residue, the solution becoming dark brown and failing to crystallize. This was dissolved in acetone and passed through a column of alumina, treated with charcoal and concentrated. The brown residue was crystallized from cyclohexane, from ethyl acetate–petroleum ether and from cyclohexane, m.p. 88–89°. *Anal.* Calcd. for $C_{15}H_{16}O_4$: C, 69.21; H, 6.20. Found: C, 69.13; H, 6.25.

Treatment of Isopropylidene Ethylphenylmalonate (VI) with Cyclohexanol.—(1) A solution of 1.2 g. (0.012 mole) of freshly distilled cyclohexanol in 40 ml. of dry ether was treated with 0.4 g. (0.01 mole) of potassium, leading to a gelatinous precipitate. A solution of 2.48 g. (0.01 mole) of VI in 50 ml. of dry ether was added to this and the mixture was allowed to stand overnight. The suspension was acidified, the ether solution was dried and concentrated and the distillate was treated with 2,4-dinitrophenylhydrazine, leading to acetone 2,4-dinitrophenylhydrazone, 0.55 g., 23% yield, m.p. and mixed m.p. 124–126°. The residue was taken up in ether, extracted with sodium bicarbonate, precipitated with acid and washed with hot benzene, leading to a powdery solid, 0.270 g., m.p. 161–162° dec., ethylphenylmalonic acid, 13% yield.

(2) A solution of 0.246 g. (0.011 mole) of sodium in 50 ml. of cyclohexanol was treated with 1.24 g. (0.005 mole) of the acylal VI at 70° for 5 minutes, washed with acid and water and extracted with bicarbonate. This was acidified and extracted with ether, leading to ethylphenylmalonic acid, m.p. and mixed m.p. 153–155°, 0.423 g., 41% yield.

Treatment of Isopropylidene Ethylphenylmalonate (VI) with Methanol.—(1) A solution of 1.24 g. (0.005 mole) of

(11) E. Tassilly, A. Belot and M. Descombes, *Compt. rend.*, **186**, 149 (1928).

(12) German patents 247,952 and 249,722; *cf.* "Beilstein," Erstes Ergaenzungswerk, Vol. 9, p. 384.

(13) S. Basterfield and L. A. Hamilton, *Trans. Royal Soc. Canada*, **III27**, 156 (1933).

(14) I. M. Heilbron and H. M. Bunbury, eds., "Dictionary of Organic Compounds," revised edition, Oxford University Press, New York, N. Y., 1953, Vol. 3, p. 480.

(15) A. I. Vogel, "Practical Organic Chemistry," third edition, Longmans, Green & Co., London, 1956, p. 485.

(16) W. Wislicenus and K. Goldstein, *Ber.*, **28**, 815 (1895).

VI in 50 ml. of absolute methanol was treated with dry hydrogen chloride, heated under reflux for one hour, and concentrated in vacuum. The residue was washed with bicarbonate and water and dried, 0.750 g., 60% recovery of VI, m.p. 87–89°, mixed m.p. 90–93°.

(2) A solution of 0.23 g. (0.01 mole) of sodium in 50 ml. of absolute methanol was prepared and an aliquot, 5 ml., was titrated, consuming 8.52 ml. of 0.124 *N* HCl, 1.05 meq. per aliquot. Acylal VI (1.24 g., 0.005 mole) was added, and aliquots were titrated after 5, 15 and 30 minutes, consuming 5.08, 4.76 and 4.62 ml. of acid, respectively, corresponding to 76, 83 and 87% conversion to the half-ester, respectively.

(3) Methyl Hydrogen Ethylphenylmalonate.—To 50 ml. of absolute methanol was added 0.110 g. (0.005 mole) of sodium. After solution was complete, 1.24 g. (0.005 mole) of isopropylidene ethylphenylmalonate was added with stirring. A 5-ml. aliquot was titrated after 15 minutes, showing complete reaction. The reaction mixture was distilled in vacuum. The distillate was treated with 2,4-dinitrophenylhydrazine reagent[17] yielding 907 mg. (85.5%) of acetone 2,4-dinitrophenylhydrazone, m.p. 124–126°, identified by comparison with an authentic sample. The gummy white distillation residue was dissolved in water and acidified with concentrated hydrochloric acid. The resulting oil soon crystallized, 907 mg. (85%, allowing for removal of aliquot), m.p. 90–91°. The analytical sample was recrystallized from carbon tetrachloride. *Anal.* Calcd. for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.75; H, 6.17.

Isopropyl Hydrogen Ethylphenylmalonate.—To 50 ml. of absolute isopropyl alcohol (distilled from magnesium) was added 0.23 g. (0.010 mole) of sodium and the flask was heated until solution was complete. The yellowish solution was cooled to room temperature and 1.24 g. (0.005 mole) of isopropylidene ethylphenylmalonate was added. The suspension was stirred for 5 minutes and a 5-ml. aliquot was titrated showing that 1.63 equivalents of base had been consumed. The reaction was quenched with hydrochloric acid and ether was added to allow separation of inorganic material. The isopropyl alcohol–ether solution was dried over sodium sulfate and the solvent was removed in vacuum leaving a white solid residue. This residue was treated with boiling benzene yielding 549 mg. of benzene-insoluble material, m.p. 153–155° dec., which was identified as ethylphenylmalonic acid (53%). Evaporation of the wash solvent led to an oil which crystallized on cooling. The solid was recrystallized from benzene–petroleum ether, m.p. 73–75°. Recrystallization from cyclohexane yielded a sample m.p. 67–69°, which was analyzed. *Anal.* Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.52; H, 6.89.

Reaction of Isopropylidene Ethylphenylmalonate (VI) with α-Phenylethylamine.—(1) A solution of 0.496 g. of VI in 9.68 g. of the amine (which had been dried over potassium hydroxide and distilled, b.p. 77–79° (14 mm.), was allowed to stand at room temperature for 3 days, leading to recovered VI, 0.368 g., 74% yield, m.p. 84–86°.

(2) A solution of 0.496 g. of VI and 0.968 g. of the amine in 5 ml. of benzene was allowed to stand for 3 weeks and was then boiled under reflux for two hours, leading to recovered VI, m.p. and mixed m.p. 88–92°, 0.417 g., 84% yield.

(3) A solution of 0.496 g. (0.002 mole) of VI in 4.14 g. (0.034 mole) of the amine was allowed to stand for 4 weeks at room temperature leading to a precipitate, 0.242 g., m.p. 85–88° dec., which was soluble in water and did not liberate carbon dioxide from bicarbonate, and did lead to gas evolution when acidified. From the filtrate of the original reaction mixture was obtained an acidic component, 0.206 g., m.p. 90–120°, which we were unable to purify.

Methyl Hydrogen Methylphenylmalonate.—To 50 ml. of absolute methanol was added 0.228 g. (0.010 mole) of sodium. When the metal was dissolved, 1.17 g. (0.005 mole) of isopropylidene methylphenylmalonate was added with stirring. A 5-ml. aliquot was titrated after 5 minutes, showing consumption of one equivalent of base. After five more minutes, the reaction was quenched by the addition of 10 ml. of 1 *N* hydrochloric acid. The solvent was removed in vacuum, leaving a semi-solid white residue. This residue was taken up in 5% sodium bicarbonate solution, acidified with concentrated hydrochloric acid and extracted with ether. The solution was washed with water and dried over sodium sulfate. Removal of the solvent led to a colorless oil which crystallized on cooling, 712 mg. (88% allowing for the removal of aliquots), m.p. 69–73°. Two recrystallizations from cyclohexane raised the melting point to 77–79°. *Anal.* Calcd. for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.31; H, 5.56.

Reaction of Isopropylidene Methylphenylmalonate (VII) with Secondary Alcohols.—(1) A solution of 0.219 g. (0.0095 mole) of sodium in 50 ml. of anhydrous propanol-2 was prepared and analyzed; acylal VII (1.17 g., 0.005 mole) was added and aliquots were titrated after 5 and 10 minutes, indicating consumption of 0.90 and 1.07 equivalents of alkoxide, respectively. Ten ml. of 1 *N* hydrochloric acid was added, the solvents were removed in vacuum and the residue was extracted with sodium bicarbonate. The bicarbonate insoluble residue was starting material VII, 0.348 g., 38% yield, m.p. 138–140°; m.p. and mixed m.p., afte crystallization from acetone–water, 146–149°. The bicarbonate solution was acidified, extracted with ether, dried, concentrated, crystallized from ethyl acetate–petroleum ether to give 0.178 g., 24% yield, of methylphenylmalonic acid, m.p. and mixed m.p. 149–151°. The residue from the mother liquors was an oil.

(2) A solution of 11.7 g. (0.10 mole) of 1-phenylethanol (b.p. 96–97° (12 mm.)) in 50 ml. of anhydrous ether was treated with 0.283 g. (0.0123 mole) of sodium for 4 hours with stirring under reflux, cooled and analyzed. Acylal VII was added (1.17 g., 0.005 mole) and aliquots were titrated after 5 and 10 minutes, both indicating that 1.24 equivalents of alkoxide had been consumed. The mixture was treated with acid, washed with water and extracted with bicarbonate. The latter was acidified and extracted with ether, which was dried and concentrated, leading to an oil which, on treatment with carbon tetrachloride led to the diacid, m.p. and mixed m.p. 150–153° dec., 0.128 g., 17% yield, and to an oil residue, which, on treatment with 0.5 g. of aniline and 1 g. of N,N′-dicyclohexylcarbodiimide in 15 ml. of tetrahydrofuran led to N,N′-dicyclohexylurea and an oil.

Methyl Ethylphenylmalonanilide.—Methyl hydrogen ethylphenylmalonic acid (563 mg.) was refluxed on the water-bath with 5 ml. of freshly distilled thionyl chloride for 30 min. The excess thionyl chloride was removed in vacuum. The residual oil was dissolved in benzene and 2 g. of aniline in 15 ml. of benzene was added. The resulting mixture was extracted with dilute hydrochloric acid, washed with water, dried over sodium sulfate and concentrated. The residual yellow oil was taken up in petroleum ether and chromatogrammed on an acid-washed alumina. Fractions 9–12 yielded crystalline material, m.p. 68–73°. Recrystallization from dilute methanol led to 0.307 g. of anilide, 39% yield, m.p. 78–79°. *Anal.* Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44. Found: C, 71.98; H, 6.53.

N-Benzyl Hydrogen Methylphenylmalonamide.—Isopropylidene methylphenylmalonate (1.17 g., 0.005 mole) was dissolved in 10.7 g. (0.1 mole) of benzylamine and allowed to stand for 1 hour at room temperature. The solution was then acidified with 3 *N* hydrochloric acid and extracted with ether. The ethereal solution was washed with water, dried over sodium sulfate and distilled. The residual nearly colorless oil crystallized after standing in the refrigerator for one week, m.p. 116–119° dec. It was recrystallized from benzene–cyclohexane, 673 mg. (47.5%), m.p. 121–123° dec. One further recrystallization lowered the m.p. to 111–113° dec. *Anal.* Calcd. for $C_{17}H_{17}NO_3$: C, 72.06; H, 6.05. Found: C, 72.93; H, 6.25.

N-Benzyl Methyl Methylphenylmalonamide.—To 20 ml. of ether and 5 ml. of methanol was added 283 mg. (1 mmole) of N-benzyl hydrogen methylphenylmalonamide. Diazomethane was generated from N-methyl-N-nitroso-*p*-toluenesulfonamide (Aldrich) and distilled into the cooled solution of the half-acid. The resulting yellow solution was refluxed for 20 minutes. After removal of the solvent the residual oil crystallized on cooling, 0.292 g., m.p. 84–92°, m.p. 81–82° after three crystallizations from acetone–water. *Anal.* Calcd. for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44. Found: C, 72.86; H, 6.63.

Reaction of Isopropylidene Methylphenylmalonate (VII) with *l*-α-Phenylethylamine.—(1) A solution of the acylal VII (1.17 g., 0.005 mole) in 12.1 g. of *l*-α-phenylethylamine (resolved by the procedure of (W. Theilacker and H. G. Winkler, *Ber.*, **87**, 690 (1954)), $[\alpha]^{24}_{4360}$ −55.2°) was allowed to stand for one hour and was treated with dilute acid and ether, leading to recovered VII, 0.828 g., 71%, m.p. and mixed m.p. 145–147°, and to acid material, m.p.

(17) G. D. Johnson, THIS JOURNAL, **73**, 5888 (1951).

148–151°, neutralization equivalent 102, 0.168 g., 17% yield of methylphenylmalonic acid.

(2) A suspension of 1.17 g. of VII in 2.42 g. of the amine was allowed to stand for 5 days and was then treated with acid and ether. The ether solution led to an oil, 1.014 g., apparently acidic to bicarbonate from which was obtained the di-acid, 0.296 g., 30%, m.p. 146–149° dec.

Infrared Absorption Spectra.—Spectra were determined in 1% solution in chloroform on a Perkin–Elmer model 21 double beam spectrophotometer. One spectrum, #14, below, was obtained in potassium bromide pellet; all units are micron.

(1) Isopropylidene malonate: 2.83(w), 3.42(w), 5.40-(shoulder), 5.55–5.70(s), 5.75(shoulder), 5.94(shoulder), 6.38(w), 6.85(w), 7.20(s), 7.40(s), 7.58–7.77(s), 9.28(s), 9.89(s), 10.28(s) 10.52(m), 11.17(w), 11.94(s).

(2) Isopropylidene phenylmalonate: 2.84(w), 5.58(s), 5.70(s), 6.67(w), 6.87(w), 7.16(m), 7.22(m), 7.44(m), 7.63–7.72(s), 9.10(w), 9.28–9.31(m), 9.88–9.91(m), 10.90-(w), 11.30(m), 11.55(w).

(3) Isopropylidene ethylphenylmalonate: 2.88(w), 3.42(w), 5.62(s), 5.75(s), 6.43(w), 6.70(w), 6.85(shoulder), 6.90(m), 7.19(m), 7.24(m), 7.50(s), 7.78–7.85(s), 9.07(w), 9.28(m), 9.37(ms), 10.05(ms), 10.53(w), 10.97(m), 11.25(w).

(4) Isopropylidene methylphenylmalonate: 2.87(w), 3.41(w), 5.61(s), 5.73(s), 6.24(w), 6.68(m), 6.90(m), 7.18(m), 7.25(s), 7.71(s), 9.07(m), 9.40–9.50(s), 10.07(m), 10.23(s), 11.48(w).

(5) Cyclopentylidene methylphenylmalonate: 3.38(w), 5.60(s), 5.73(s), 6.23(w), 6.72(w), 6.89(m), 7.24(ms), 7.44(s), 7.72(s), 8.93(s), 9.27(w), 9.42(w), 9.98(s), 10.41(w), 11.46(w).

(6) β-Phenylglutaric anhydride: 2.82(w), 3.25–3.37(w), 3.45(w), 5.49(s), 5.64(s), 6.23(w), 6.67(w), 6.87(w), 7.08(w), 7.28(w), 7.52(w), 7.85(w), 8.58(m), 9.05(m), 9.32–9.39(s), 10.52(s).

(7) Diethyl ethylphenylmalonate: 3.38(m), 4.18(w), 5.72(shoulder), 5.76–5.81(s), 5.90(shoulder), 6.23(w), 6.30(w), 6.67(m), 6.82(m), 6.91(m), 7.20(m), 7.30(m), 7.50(w), 7.67(s), 8.05–8.48(s), 8.89(s), 9.13(s), 9.77(s), 10.40(w), 10.70(w), 10.83(w), 11.67(m), 12.23(w).

(8) Methylene diacetate: 2.83(w), 3.35(w), 4.87(w), 5.63–5.69(s), 6.87(m), 7.07(m), 7.28(s), 8.00–8.45(m), 9.85–9.90(s), 10.15(s).

(9) Methyl hydrogen ethylphenylmalonate: 2.88(w), 3.39(m), 5.68(s), 5.76(s), 5.92(s), 6.25(w), 6.68(w), 6.95–7.00(m), 7.10–7.77(m), 7.52(m), 7.61(m), 8.25–8.42(s), 8.80(m), 9.95–10.02(w), 10.85–10.90(w).

(10) Isopropyl hydrogen ethylphenylmalonate: 2.87(w), 3.42(m), 5.69(s), 5.81(s), 5.96(s). 6.26(w), 7.11–7.16(m), 7.22(m), 7.28(m), 7.39(m), 7.62(m), 8.00–8.43(m), 8.77(m), 9.12(s).

(11) Methyl hydrogen methylphenylmalonate: 2.88(w), 3.41(w), 5.66(shoulder), 5.75–5.79(s), 5.89, 5.92(shoulder), 6.25(w), 6.70(w), 6.87(w), 6.92–7.00(m), 7.17(w), 7.30(w), 7.90–8.45(s), 8.95(s), 9.34(w), 9.74(w), 10.26(w).

(12) *l*-Menthyl β-phenylglutarate,[3] m.p. 107–109°: 2.88-(w), 3.44(m), 5.81(s), 6.23(w), 6.70(w), 6.87(m), 7.29(m), 7.89(m), 8.73(m), 9.24(w), 9.30(w), 9.65(w), 9.95(w), 10.17(m), 10.40(w), 11.00(w).

(13) N-Benzyl hydrogen methylphenylmalonamide: 2.92(w), 3.44(w), 3.78(w), 5.11(w), 5.71(s), 5.98(m), 6.14(s), 6.60(m), 6.90–6.98(s), 7.25(w), 7.35(w), 7.95–8.45(w), 8.75–8.95(w), 9.25(w), 9.32(w), 9.73(w).

(14) Methyl N-benzyl methylphenylmalonamide: 3.01-(s), 3.27(m), 3.33(m), 3.39(m), 5.10(w), 5.27(w), 5.75(s), 6.07(s), 6.23(m), 6.29(m), 6.49(s), 6.66(s), 6.86(m), 6.91-(m), 6.97(m), 7.03(m), 7.21(m), 7.33(m), 7.86(s), 8.06(s), 8.36(m), 8.80(m), 8.92(s), 9.02(m), 9.28(m), 9.36(m), 9.70(m), 10.00(m), 10.26(m), 10.92(w), 11.41(m), 11.80(w), 12.15(w), 12.45(w), 13.27(m), 13.57(m), 13.72(m), 14.30(s).

(15) N-Benzyl hydrogen methylphenylmalonamide: 2.93(w), 3.44(w), 3.75(w), 5.11(w), 5.30(w), 5.71(s), 5.93(m), 6.14(s), 6.61(m), 6.93(s), 7.35(w), 8.00–8.45(w), 8.75–8.95(w), 9.25(w), 9.33(w), 9.73(w).

(16) Methyl ethylphenylmalonanilide: 3.03(m), 3.40(w), 5.14(w), 5.35(w), 5.81(s), 5.91(m), 6.23(s), 6.50(s), 6.66-(m), 6.93(s), 7.23(w), 7.60(m), 8.02–8.40(m), 8.81(s), 9.26(w), 9.96(w), 10.13(w), 11.11(w), 11.51(w).

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[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY, UNIVERSITY OF PENNSYLVANIA AND DREXEL INSTITUTE OF TECHNOLOGY]

The Effect of *m*-Dichloro and *m*-Dibromo Groups on the Dissociation and Ultraviolet Spectra of *p*-Dimethylsulfoniophenols

BY SHIGERU OAE AND CHARLES C. PRICE

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The incorporation of two chlorine or bromine atoms *ortho* to the dimethylsulfonio group in *p*-dimethylsulfoniophenol seems to cause only additive effects on pK_a and ultraviolet spectra. This indicates that the interaction between the sulfonio group and the phenol function is not sensitive to steric factors at the former.

There have been many reports of the conjugative ability of sulfone,[1] sulfonic acid,[2] sulfoxide[3] thiosulfonate[4] and sulfonio groups[5] and it has become a well-established fact that a sulfur atom may stabilize unshared electrons on an adjacent carbon atom, perhaps in part through conjugation using its *d*-orbital.

(1) (a) E. P. Kohler and H. Potter, THIS JOURNAL, **57**, 1316 (1935); (b) F. G. Bordwell and W. H. McKellin, *ibid.*, **72**, 1985 (1950); (c) R. H. Eastman and R. M. Wagner, *ibid.*, **71**, 4089 (1949); (d) H. Heymann, *ibid.*, **71**, 260 (1949); (e) A. Kotch, L. H. Krol, P. E. Verkade and B. M. Wepster, *Rec. trav. chim.*, **71**, 108 (1952); (f) F. G. Bordwell and G. D. Cooper, THIS JOURNAL, **74**, 1058 (1952); (g) H. Kloosterziel and H. J. Backer, *Rec. trav. chim.*, **71**, 295 (1952); (h) H. H. Szmant and G. Suld, THIS JOURNAL, **78**, 3400 (1956); (i) C. C. Price and J. J. Hydock, *ibid.*, **74**, 1043 (1952); (j) F. G. Bordwell and H. M. Anderson, *ibid.*, **75**, 6019 (1953); (k) E. A. Fehnel and M. Carmack, *ibid.*, **71**, 231 (1949); **72**, 1292 (1950); (l) H. P. Koch, *J. Chem. Soc.*, 2892 (1950); (m) W. v. E. Doering and L. K. Levy, THIS JOURNAL, **77**, 509 (1955); (n) S. Oae, *Bull. Chem. Soc., Japan*, **28**, 41 (1955); (o) H. Kloosterziel and H. J. Backer, *Rec. trav. chim.*, **72**, 185 (1953); (p) J. Toussaint, *Bull. Soc. Chim. Belg.*, **54**, 319 (1945) (*C. A.*, **41**, 2297 (1947)).

(2) (a) H. Zollinger and W. Buchler, *Helv. Chim. Acta*, **36**, 1711 (1953); (b) E. E. Sagar, M. R. Schooley, H. S. Carr and S. F. Acree, *J. Research Natl. Bur. Standards*, **35**, 521 (1945); (c) K. B. Whetsel, G. E. Hawkins and F. E. Johnson, THIS JOURNAL, **78**, 3360 (1956).

(3) (a) F. G. Bordwell and P. J. Boutan, *ibid.*, **79**, 717 (1957); (b) G. Leandri, A. Mangini and R. Passerini, *J. Chem. Soc.*, 1386 (1957); (c) E. D. Amstutz, J. M. Hunsberger and J. J. Chessick, THIS JOURNAL, **73**, 1220 (1951).

(4) G. Leandri, A. Mangini and A. Tundo, *J. Chem. Soc.*, 52 (1957).

(5) (a) F. G. Bordwell and P. J. Boutan, THIS JOURNAL, **78**, 87 (1956); (b) S. Oae and C. C. Price, *ibid.*, **80**, 3425 (1958); (c) W. v. E. Doering and K. C. Schreiber, *ibid.*, **77**, 514 (1955); (d) W. v. E. Doering and K. Hoffman, *ibid.*, **77**, 521 (1955).