2-(4″-Methoxy-α-hydroxybenzyl)-4′-methoxydiphenylcarbinol (XIV).—To 3.5 g. of 2-(4″-methoxybenzoyl)-4′-methoxybenzophenone, dissolved in 150 cc. of absolute alcohol, there was added 100 g. of 5% sodium amalgam. After several hours the reaction mixture was heated on a steam-bath for two hours, filtered while hot and the filtrate concentrated to one-half its original volume. Water was added gradually until the solution became turbid, the solution cooled and the crystalline precipitate recrystallized from alcohol; m. p. 139–140°; yield 2.8 g.

Anal. Calcd. for $C_{22}H_{22}O_4$: C, 75.39; H, 6.33. Found: C, 75.08; H, 6.39.

One and seven-tenths grams of the carbinol, dissolved in 20 cc. of acetic acid, was oxidized to 2-(4″-methoxybenzoyl)-4′-methoxybenzophenone with 2 g. of sodium dichromate, dissolved in 10 cc. of acetic acid; mixed m. p. 157–159°; yield 1.3 g.

2-Methoxy-9-(*p*-anisyl)-anthracene (XI).—To 1.5 g. of anhydrous zinc chloride, dissolved in a mixture of 7.5 cc. of acetic anhydride and 7.5 cc. of acetic acid, there was added 5.0 g. of 2.5-di-(*p*-anisyl)-2,5-dihydro-3,4-benzofuran. The furan dissolved with evolution of heat and the crystalline anthracene soon began to precipitate. After one hour the mixture was diluted with 50 cc. of water and the anthracene recrystallized from acetic acid; yield 3.9 g.; m. p. 177–179°.[5] Solutions of this compound exhibit a blue fluorescence.

Five grams of 2-(4″-methoxy-α-hydroxybenzyl)-4′-methoxydiphenylcarbinol was treated with zinc chloride in the manner described above. After one hour the crystalline anthracene was separated and recrystallized from acetic acid; yield 3.8 g.; m. p. 177–179°.

2-Methoxy-9-hydroxy-9-(*p*-anisyl)-anthrone-10 (XII).—Five grams of 2-methoxy-9-(*p*-anisyl)-anthracene, suspended in 25 cc. of acetic acid, was heated for two hours on a steam-bath with 4 g. of sodium dichromate, dissolved in 4 cc. of hot water. The mixture was diluted with an equal volume of water and the precipitated, crystalline anthrone recrystallized from acetic acid; yield 4.5 g.; m. p. 202–203°.[6]

2-Methoxy-9,9-di-(*p*-anisyl)-anthrone-10 (XV).—Two grams of 9-hydroxy-9-(*p*-anisyl)-anthrone-10, 6.0 g. of anisole and two drops of concd. sulfuric acid were heated for two hours on a steam-bath, the mixture treated with hot alcohol and the crystalline product recrystallized from acetic acid; yield 1.5 g.; m. p. 182–184°.[7]

Summary

It has been shown that a hydroxy- and a methoxyphenylanthrone can be obtained from a phthalin, from a benzofuran and from a benzoylbenzophenone.

A free radical of the anthraquinone type has been described.

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[5] Blicke and Weinkauff [THIS JOURNAL, **54**, 1463 (1932)] found 175–176°.

[6] Blicke and Weinkauff [*ibid.*, **54**, 1463 (1932)] reported 199–201°.

[7] Blicke and Patelski, [*ibid.*, **60**, 2640 (1938)] found 183–184°.

ANN ARBOR, MICHIGAN RECEIVED AUGUST 22, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Introduction of Substituted Vinyl Groups. I. Isopropenyl Alkyl Malonic Esters

BY ARTHUR C. COPE AND EVELYN M. HANCOCK

The wide application of the malonic ester synthesis to organic preparations has resulted in the description of a large number of mono- and dialkyl malonic esters, containing both saturated and unsaturated groups. While β,γ-unsaturated (allyl) groups and groups with the double bond further removed from the point of attachment are readily introduced into malonic ester by the ordinary method, α,β-unsaturated (vinyl) groups cannot be introduced directly, because of the inactivity of the vinyl and alkyl substituted vinyl halides. Indirect methods for the introduction of vinyl groups are difficult and give poor yields,[1] and as a result very few vinyl substituted derivatives of malonic ester have been prepared. In this paper a practical method is described for preparing disubstituted malonic esters in which one of the substituent groups is the isopropenyl or 1-methylvinvyl ($CH_2{=}C(CH_3)—$) group.

Kon and his associates,[2] in the course of their investigation of three-carbon tautomerism, methylated isopropylidene malonic ester, which forms a sodium derivative through migration of a hydrogen from the γ-carbon atom.

$$\mathrm{(CH_3)_2C{=}C(COOEt)_2 + NaOEt \longrightarrow}$$

$$\mathrm{EtOH} + \underset{\mathrm{(I)}}{\mathrm{[CH_2{=}C(CH_3)C(COOEt)_2]^-\ Na^+}} \xrightarrow{\mathrm{CH_3I}}$$

$$\mathrm{CH_2{=}C(CH_3)C(CH_3)(COOEt)_2 + NaI}$$

This reaction was employed to prove that the sodium enolate was derived from the isomeric β,γ-unsaturated ester $CH_2{=}C(CH_3)CH(COOEt)_2$, and was not extended as a possible synthetic method. The application of the reaction ap-

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[1] *Cf.* Cope and McElvain, THIS JOURNAL, **54**, 4311 (1932).

[2] Kon and Speight, *J. Chem. Soc.*, 2727 (1926).

peared to be limited, since the methylated ester undergoes alcoholysis readily in the presence of sodium ethoxide with the loss of a carbethoxy group as ethyl carbonate. The conditions of synthesis described by Kon and Speight,[2] therefore, induce alcoholysis, particularly since two treatments with alcoholic sodium ethoxide and methyl iodide were required to complete the methylation. The slow alkylations, to be expected with less active alkylating agents, would allow time for extensive cleavage during the synthesis.

We have found that the sodium enolate (I) can be prepared easily and almost quantitatively by reaction of isopropylidene malonic ester with sodamide, either in liquid ammonia solution or in an inert solvent. The resulting sodium derivative, preferably suspended in an inert solvent, can then be alkylated readily by the ordinary alkylating agents, such as the dialkyl sulfates or alkyl halides. Since the reaction mixtures are free from alcohol, the alkylations are successful even with the less reactive higher alkyl halides, some of which require long refluxing for appreciable reaction. The yields of pure isopropenyl alkyl malonic esters obtained by this method are as high as 90% when the more active alkylating agents are employed. Various primary alkyl groups have been introduced in good yield; the introduction of secondary groups is difficult. In cases in which the alkylation is not complete, the isopropenyl alkyl malonic esters may be purified conveniently by shaking with concentrated aqueous ammonia at room temperature. Like other dialkyl malonic esters, the isopropenyl alkyl derivatives are not affected by this treatment, while isopropylidene malonic ester is converted into acetone and malonamide.[3] The properties of nine isopropenyl alkyl malonic esters, prepared and purified in this manner, are described in the Experimental Part.

The sodium enolate (I) may also be prepared by the reaction of isopropylidene malonic ester with powdered sodium in an inert anhydrous solvent, such as ether or benzene. Unfortunately, a considerable amount of the isopropylidene malonic ester is reduced during the formation of the sodium enolate. Subsequent alkylation, therefore, produces a mixture of isopropenyl and isopropyl alkyl malonic esters which is difficult to separate.

Experimental Part

Ethyl Isopropylidene Malonate.—Improved yields of this ester were obtained by using an excess of acetone in a procedure otherwise similar to that described by Scheiber and Meisel.[4] A mixture of 1 kg. (6.25 moles) of ethyl malonate, 540 g. (9.3 moles) of acetone, 800 g. (7.8 moles) of acetic anhydride and 120 g. of freshly fused zinc chloride was heated under reflux in an oil-bath at 110° for twenty-four hours. The mixture was then cooled, and 800 cc. of benzene added. The nearly black solution was washed with four 500-cc. portions of water. The water washings were extracted with two 100-cc. portions of benzene, which were combined, washed with water and added to the main portion of the benzene solution. The wet benzene was removed by distillation under diminished pressure, and the remainder of the mixture was distilled in vacuum through a Vigreux column. A fore-run of acetic acid and acetic anhydride was collected, followed by 1200 g. of crude ester, b. p. 60–125° (18 mm.). The tarry residue amounted to 50 g. The crude ester was redistilled through an adiabatic, total reflux, variable take-off Fenske type column with a 70 × 1.2 cm. section packed with glass helices. The recovery of ethyl malonate, b. p. 81–83° (9 mm.), plus a small intermediate fraction was 411 g. (41%). A yield of 654 g. (52%) of ethyl isopropylidene malonate, b. p. 111–113° (9 mm.), was obtained, n^{25}_{D} 1.4478, d^{25}_{25} 1.0254, M_D calcd. 51.23, obsd. 52.42, exaltation + 1.19.

Alkylations of Ethyl Isopropylidene Malonate

A. Sodamide Procedure.—The ethylation will be described as a typical procedure. All apparatus was dried in an oven at 100 to 150° before use. A 1-liter, three-necked flask was equipped with an inlet tube, mercury-sealed stirrer and a reflux condenser attached to a soda lime tower. The tower was connected to a 3-liter bottle containing 1 liter of water (stirred with another mercury-sealed stirrer), and to the bottle was attached a water trap leading to the sink. Hydrated ferric nitrate (0.3 g.) was placed in the flask, which was then cooled in a dry ice–acetone bath while 300 cc. of anhydrous liquid ammonia was introduced through the inlet tube from an inverted ammonia cylinder. The cooling bath was then removed and 12.65 g. (0.55 mole) of sodium added in small pieces. One piece was added and the solution stirred until the blue color changed to gray, and the remainder added rapidly. Stirring was continued until the solution was gray (ten to thirty minutes), and fifteen minutes longer. All of the sodium should have reacted to form sodamide before the ester is added, since any sodium present will tend to reduce the ester. The solution was again cooled in the dry ice–acetone bath and the ethyl isopropylidene malonate (100 g. or 0.5 mole) added during ten minutes from a separatory funnel (introduced in the neck which originally held the inlet tube). The solution was stirred for ten to thirty minutes and 300 cc. of dry, sulfur-free toluene and 25 cc. of dry ether added. The solution was stirred until most of the ammonia had evaporated (one to two hours). The flask was then placed in an oil-bath which was gradually heated to 110°. During the heating the sodium derivative (I) precipitated as a gray solid and the last traces of the ammonia were distilled out through the reflux condenser

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[3] Kötz, *J. prakt. Chem.*, [2] **75**, 497 (1907).

[4] Scheiber and Meisel, *Ber.*, **48**, 247 (1915).

TABLE I

ETHYL ISOPROPENYL ALKYL MALONATES

Alkyl group	Alkylating agent	Hours refluxed[a]	Yield, %	Boiling point °C.	Boiling point Mm.	n^{25}_D	d^{25}_{25}	Mol. refraction Calcd.	Mol. refraction Found	Formula	Carbon, % Calcd.	Carbon, % Found[b]	Hydrogen, % Calcd.	Hydrogen, % Found
Methyl	Dimethyl sulfate	0	88	110–111	12	1.4370	1.0095	55.85	55.74	$C_{11}H_{18}O_4$	61.64	61.40	8.47	8.47
Ethyl	Diethyl sulfate	1	81	117–119	13	1.4402	1.0008	60.47	60.28	$C_{12}H_{20}O_4$	63.11	62.85	8.84	8.85
Allyl	Allyl bromide	3	82	122–123	10	1.4500	1.0036	64.62	64.50	$C_{13}H_{20}O_4$	64.96	64.96	8.39	8.45
Propyl	Propyl bromide	19	50	132–133	17	1.4418	0.9847	65.09	65.10	$C_{13}H_{22}O_4$	64.42	64.69	9.16	9.34
Isopropyl	Isopropyl iodide	5	10	114–116	10	1.4381	.9872	65.09	64.59	$C_{13}H_{22}O_4$	64.42	63.99	9.16	9.47
Butyl	Butyl iodide	10	59	137–138	13	1.4419	.9768	69.71	69.58	$C_{14}H_{24}O_4$	65.58	65.58	9.42	9.69
Isobutyl	Isobutyl bromide	58	40	131–132	12	1.4422	.9792	69.71	69.46	$C_{14}H_{24}O_4$	65.58	65.80	9.42	9.51
Amyl	Amyl bromide	9	50	147–148.5	12	1.4438	.9689	74.33	74.27	$C_{15}H_{26}O_4$	66.62	66.73	9.70	9.71
Isoamyl	Isoamyl bromide	25	36	140–141	11	1.4430	.9667	74.33	74.32	$C_{15}H_{26}O_4$	66.62	66.75	9.70	9.86

[a] The first three reaction mixtures were neutral after refluxing for the number of hours indicated; the remainder were from 70 to 90% neutralized. [b] We are indebted to Miss Corris Hofmann for these analyses.

with the ether. The oil-bath was removed and 101.6 g. (0.66 mole) of diethyl sulfate added during ten minutes. The oil-bath was then replaced and heated to 135°. After refluxing for one hour the reaction mixture was neutral. It was cooled in ice and washed with two portions of cold water. The washings were extracted with ether, and the ether and toluene distilled off in vacuum. The residue was shaken for twelve hours with 200 cc. of concentrated aqueous ammonia at room temperature. The ester layer was separated and the ammonia solution extracted twice with ether. The ether and ester were washed with water and the product was distilled in vacuum.

Variations of this procedure are less convenient but may be used in some cases. Ether or benzene may be employed as inert solvents. After the sodamide is formed, the inert solvent may be added and the excess ammonia expelled before adding the ester. This procedure is as convenient as that described above if the inert solvent is ether, but the ester reacts slowly with sodamide in benzene or toluene, probably due to the insolubility of both sodamide and the ester enolate. The methylation with dimethyl sulfate proceeds satisfactorily in ether, but the other alkylating agents require temperatures higher than the boiling point of ether for reaction at a satisfactory rate. With the higher alkyl halides, the reaction mixtures never become neutral. It is convenient in such cases to remove 2-cc. aliquots from time to time and determine the percentage reaction by titration with standard acid. If the reaction time is prolonged above that recorded in Table I, the yields are increased slightly in some cases, but in others increased amounts of high boiling material are formed. When the reaction mixtures do not become neutral, they should be neutralized with dilute hydrochloric acid before washing with water. Larger amounts of aqueous ammonia should be used to purify the product in such cases, and the treatment with aqueous ammonia may be prolonged to three or four days. In the alkylations giving poorer yields, it is convenient to distil the crude ester before shaking with ammonia in order to eliminate high boiling material. The esters were redistilled through a Widmer column. The yields of purified products, their physical constants and pertinent data concerning the preparations are recorded in Table I.

B. Sodium Procedure.—One-half mole of sodium was powdered under xylene and rinsed into a 1-liter, three-necked flask with 500 cc. of dry ether. Ethyl isopropylidene malonate (100 g. or 0.5 mole) was added during ten minutes with stirring and cooling in an ice-bath. The solution refluxed during the addition of the ester. The solution was stirred and refluxed for twelve hours, after which the alkylating agent was added and the reaction mixture treated as in part A. Methylation with dimethyl sulfate required two hours, and ethylation with diethyl sulfate twenty-four hours at the boiling point of ether. It is advantageous to replace the ether with benzene or toluene if less active alkylating agents are used. The sodium derivative may be prepared by this method in benzene or toluene, but, whereas in ether the sodium derivative separates as a flour-like solid and all of the sodium eventually reacts, in benzene and toluene stiff gels are formed and mechanical difficulties result.

C. Sodium Ethoxide Procedure.—In the methylation procedure described by Kon and Speight,[2] a large amount of the product is decomposed by alcoholysis, due to the long contact of the alkylated ester with alcoholic sodium ethoxide. The yields are improved if the ethyl isopropylidene malonate is treated once with sodium ethoxide and methyl iodide, and the unalkylated ester removed by shaking with aqueous ammonia as described in part A. Higher alkyl groups are not introduced in good yield by the sodium ethoxide procedure, even under conditions designed to minimize alcoholysis, as may be illustrated by the synthesis of ethyl butyl isopropenyl malonate.

A solution of sodium ethoxide was prepared in a 500-cc. three-necked flask by dissolving 5.75 g. (0.25 mole) of sodium in 200 cc. of absolute alcohol. The solution was cooled to −5° and 50 g. (0.25 mole) of ethyl isopropylidene malonate added with stirring at −5 to −10°. After stirring for thirty minutes at this temperature, 56 g. (0.30 mole) of *n*-butyl iodide was added in one portion and the solution was heated rapidly to the boiling point. After the vigorous reaction had subsided, the mixture was refluxed until neutral (one and one-half hours). The solution was cooled, diluted with water, and the ester extracted with benzene. Distillation gave 49 g. of crude ester, b. p. 110–128° (9 mm.), but after purification by shaking with concentrated ammonia for two days and redistilling, only 12 g. (19%) of ethyl isopropenyl *n*-butyl malonate was obtained.

Purity of the Alkylation Products.—The purity of the esters produced by the sodamide procedure (A) is indicated by the close correspondence of calculated and observed molecular refractions recorded in Table I. Several of the esters were hydrogenated quantitatively and the reduction products characterized as further proof of their purity and identity. The esters (0.01 to 0.03 mole) in 20 cc. of alcohol were hydrogenated at atmospheric pressure in the presence of 1 g. of palladinized charcoal,[5] containing 100 mg. of palladium. The reductions were carried out at room temperature in a 100-cc. mechanically shaken bottle attached to a large gas buret. Under these conditions the methyl, ethyl and allyl substituted isopropenyl malonic esters (described in Table I) absorbed 99.3, 99.6 and 97.8% of the theoretical quantity of hydrogen. The reductions required approximately one-half hour. The reduced esters were obtained in 85–90% yield by filtering the catalyst and distilling in vacuum. Ethyl methylisopropylmalonate, b. p. 100–102° (11 mm.), was identified by condensation with urea in the presence of alcoholic sodium ethoxide to give 5-methyl-5-isopropylbarbituric acid, m. p. 188–188.5°,[6] and by saponification with 10% barium hydroxide to methyl isopropylmalonic acid, m. p. 123.5–124.5°.[7] Ethyl ethylisopropylmalonate, b. p. 108–110° (11 mm.), was identified in a similar manner by conversion to 5-ethyl-5-isopropylbarbituric acid, m. p. 201.5–202.5°.[8]

The higher isopropenyl alkyl malonic esters are reduced very slowly with palladium at room temperature, but may be reduced rapidly and quantitatively at 150° over Raney nickel in the micro bomb described by Adkins.[9] Thus 0.02 mole of ethyl butyl isopropenyl malonate in 15 cc. of ethyl alcohol absorbed 99.7% of the theoretical quantity of hydrogen using 1 g. of catalyst. Ethyl butyl isopropyl malonate, b. p. 131–132° (11 mm.), was isolated as the reduction product in 90% yield by filtering and distilling in vacuum.

The esters obtained by the sodium alkylation procedure (B) contain a saturated impurity, which is presumably the corresponding isopropyl alkyl malonic ester, since it is not removed by long shaking with concentrated aqueous ammonia or by fractional distillation. Thus over palladium catalyst as previously described the methyl and ethyl substituted isopropenylmalonic esters prepared by sodium alkylation absorbed only 76 and 72% of the theoretical quantity of hydrogen, respectively.

Summary

Ethyl isopropylidene malonate, $(CH_3)_2C{=}C(COOEt)_2$, forms a sodium derivative (formula I) almost quantitatively by reaction with sodamide in liquid ammonia solution or in inert solvents. By alkylation of this sodium derivative in inert solvents, eight new isopropenyl alkyl malonic esters, $CH_2{=}C(CH_3)C(R)(COOEt)_2$, have been prepared. The sodium derivative has also been prepared by reaction of ethyl isopropylidene malonate with powdered sodium in inert solvents, but about 25% of the ester is reduced during the reaction.

If the sodium derivative is prepared and alkylated in alcoholic solution, the yields of alkylated esters are poor, due to extensive alcoholysis which occurs during the synthesis.

Bryn Mawr, Penna. Received August 9, 1938

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(5) Hartung, This Journal, 50, 3372 (1928).

(6) Preiswerk, *Helv. Chim. Acta*, 6, 192 (1923).

(7) Van Romburgh, *Rec. trav. chim.*, 5, 236 (1886).

(8) Thorp, U. S. Patent 1,255,951: *C. A.*, 12, 977 (1918).

(9) Adkins, This Journal, 55, 4272 (1933).

[Contribution from the Daniel Sieff Research Institute]

Interaction between Grignard Compounds and Maleic Acid Derivatives

By Ch. Weizmann and F. Bergmann

Recently, Tarbell[1] reported on reactions between maleic and dimethylmaleic anhydrides with phenylmagnesium bromide: maleic anhydride reacted with two and three mols of the Grignard compound, respectively, giving phenylbenzoylpropionic acid (I) and desylacetophenone (II, $R = C_6H_5$). As we have studied some time ago the action of various Grignard compounds on maleic anhydride and dimethyl maleate, in continuation of previous work on other dicarboxylic acid anhydrides, we may be allowed to describe briefly our results. In accordance with Tarbell's results, neither ethylmagnesium bromide nor butylmagnesium bromide or benzylmagnesium chloride gave the expected unsaturated keto acids, $RCOCH{=}CHCOOH$, even when the organometallic compound was added to the anhydride; the keto acids formed apparently react more quickly with the Grignard compounds than maleic anhydride (or dimethyl maleate). The experiments to be described have been carried out, using a large excess (8 mols) of the magnesium derivatives.

Dimethyl maleate reacted under these conditions with 3 mols of each Grignard compound. The reacting products are 1,4-diketones of the general formula (II): they are saturated, do not contain hydroxyl groups, as shown by their negative response to the Zerewitinoff test, and give the pyrrole reaction characteristic for 1,4-diketones. The keto groups, although resistant against the attack of semicarbazide in aqueous ethyl alcohol solution, react upon phenylmagnesium bromide: 6-butyl-5,8-diketododecane (II, $R = C_4H_9$) gave a crystalline diol (IV), while the corresponding

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(1) Tarbell, This Journal, 60, 215 (1938).