ments were made on a Beckman spectrophotometer Model DK2, using isopropyl alcohol as a solvent. Values are given for the crystalline material from mountain hemlock, m.p. 119° followed by those for a reference sample of matairesinol in brackets. λ_{max} 231 mμ (log ϵ 4.13) (log ϵ 3.84); λ_{min} 253–254 mμ (λ_{min} 255 mμ); λ_{max} 282 mμ, (log ϵ 3.84) (log ϵ 3.77).

Infrared measurements were made on a Baird atomic infrared recording spectrophotometer Model KM-1. Identical spectra were obtained using the potassium bromide pellet method from both the mountain hemlock crystals, m.p. 119°, and the reference sample of matairesinol. The following wave lengths are quoted in cm.$^{-1}$: 3400 s, 2925 m, 2000 w, 1870 w, 1770 s, 1610 m, 1520 s, 1460 m, 1440 w, 1380 m, 1355 w, 1272 s, 1240 w, 1208 w, 1150 w, 1125 w, 1080 w, 1020 s, 965 w, 940 w, 922 w, 890 w, 870 m, 850 w, 830 m, 792 w, 782 w, 750 m, 720 w, 680 w, 650 w. The lower melting point material, m.p. 66–67°, differed only in having broad peaks between 1725–1760 and 1360–1380 cm.$^{-1}$

Optical rotation. Optical rotation in acetone using the 4-decimeter tube gave the following: $[\alpha]^{25°}_{D}$ (m.p. 66–67°) = −42.2° (2.0 g./100 ml.); $[\alpha]^{25°}_{D}$ (m.p. 119°) = −45.0° (2.0 g./100 ml.); literature,[8] $[\alpha]^{25°}_{D}$ = −45.0° (4.2 g./100 ml.).

Stability of matairesinol to sulfite cooking. The stability of matairesinol to both neutral and acid sodium bisulfite was determined by three separate experiments:

(a) Matairesinol (80 mg.) was refluxed with 5 ml. of water containing 250 mg. of sodium bisulfite for 4 hr.

(b) Matairesinol (200 mg.) was cooked in a stainless steel bomb with 1.6 ml. of a 6% sodium bisulfite solution at 130° for 6 hr. Shaking was maintained during the heating.

(c) Matairesinol (200 mg.) was cooked in a stainless steel bomb with 2.0 ml. of 6% sodium bisulfite saturated with sulfur dioxide at 130° for 6 hr. Shaking was maintained during the heating.

Chloroform extracts of each cook as well as of commercial waste sulfite liquor were examined by means of reversed phase paper chromatography. In the case of the three cooks only unchanged matairesinol was detected. No other lignan was found to be present. In the case of waste sulfite liquor extract, matairesinol, conidendrin, and some unknowns were clearly present.

Acknowledgment. We are indebted to Dr. K. Freudenberg for the reference sample of matairesinol and to MacMillan, Bloedel, and Powell River Company for a sample of commercial waste sulfite liquor.

VANCOUVER LABORATORY
FOREST PRODUCTS RESEARCH BRANCH
DEPARTMENT OF FORESTRY OF CANADA
VANCOUVER 8, B. C., CANADA

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[7] H. Hergert and O. Goldschmidt, private communication.

[8] K. Freudenberg and L. Knof, *Chem. Ber.*, **90**, 2857 (1957).

Reaction of the Cyclic Chloride of o-Benzoylbenzoic Acid with Diethyl Ethoxymagnesiomethylmalonate

MELVIN S. NEWMAN[1]

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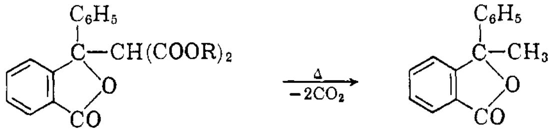
During a study of the reaction of methyl o-benzoylbenzoate with diethyl sodiomalonate, a compound, m.p. 100–101°, was isolated.[2] This compound was proved to be diethyl 3-phenylphthalidylmalonate, I$_A$, by hydrolysis to the malonic acid, I$_B$, followed by decarboxylation of the latter to 3-methyl-3-phenylphthalide, II.



I$_A$ (R = C_2H_5)
$_B$ (R = H)

II

A compound, III, m.p. 77–79°, claimed to have the structure I$_A$, had been prepared by reaction of the pseudo acid chloride of o-benzoylbenzoic acid with diethyl ethoxymagnesiomalonate.[3] However, Koelsch[4] proposed that this compound is the enol form of ethyl o-benzoylmalonate, III$_A$,[5] since authentic I$_A$, m.p. 100–102°, was prepared by reaction of diethyl sodiomalonate with ethyl o-benzoylbenzoate.[4]

Before Koelsch's publication,[4] we had attempted to prepare the compound described by Yost and Burger.[3] However, due to a mislabeled reagent bottle, diethyl methylmalonate was used instead of diethyl malonate. A compound, m.p. 106–107°, was obtained to which the structure IV was assigned since it absorbs strongly at 5.65 μ (five-membered lactone) and 5.80 μ (ester). Furthermore the NMR

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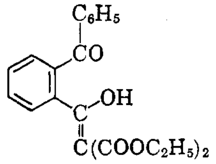
[1] This research was supported by Grant 356-A and in part by Grant 588-C of the Petroleum Research Fund of the American Chemical Society.

[2] A small amount of the same compound was obtained when pseudo methyl o-benzoylbenzoate, H. Meyer, *Monatsh.*, **25**, 475 (1904), was treated with diethyl sodiomalonate.

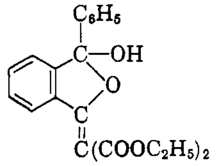
[3] W. L. Yost and A. Burger, *J. Org. Chem.*, **15**, 1113 (1950).

[4] C. F. Koelsch, *J. Org. Chem.*, **25**, 642 (1960).

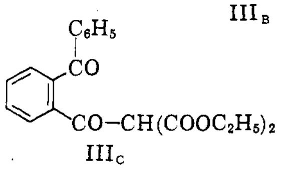
[5] In our hands, different preparations of III melt unsharply over about 10° ranges. For example, a sample of III sent by Professor Koelsch melted over the range 80–88°. Recrystallization from benzene–petroleum ether afforded samples which melted over ranges from 80–90° to 92–102°. These samples gave essentially identical infrared spectra in potassium bromide pellets. Probably III is a mixture of the forms III$_{A,B,C}$ whose composition varies with the crystallization media.



III$_A$



III$_B$



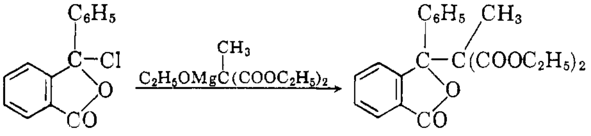
III$_C$

As none of the fractions had a band in the 5.6–5.7-μ region, lactonic structures are ruled out. We are not doing further work with III.

spectral analysis is in agreement with this structure.[6]

All attempts to hydrolyze IV to the malonic acid failed. Under both alkaline and acidic conditions either unchanged IV was recovered or *o*-benzoylbenzoic acid was obtained. The cleavage of IV under hydrolytic conditions stands in marked contrast to the ready hydrolysis of I to the malonic acid or to the half ester.[4]

It is also noteworthy that the ethoxymagnesium derivative of diethyl malonate reacts with the pseudo acid chloride of benzoylbenzoic acid by attack at the carbonyl group[4] to yield III whereas the ethoxymagnesium derivative of diethyl methylmalonate reacts by displacement of the chlorine atom to yield IV.



IV

EXPERIMENTAL[7]

Diethyl 3-phenylphthalidylmalonate, I$_A$. To a solution of 20 g. of diethyl malonate in 50 ml. of ether and 100 ml. of bis-2-ethoxyethyl ether was added 2.3 g. of sodium in small pieces. When solution was complete 24.0 g. of methyl *o*-benzoylbenzoate in 25 ml. of bis-2-ethoxyethyl ether was added, the ether distilled and the mixture refluxed for 6.5 hr. The cooled reaction mixture was poured on ice and dilute hydrochloric acid. The neutral fraction of the products was distilled to yield 14.0 g. of methyl *o*-benzoylbenzoate, b.p. b.p. 170–190° at 0.5 mm. and 12.0 g. of a yellow viscous product, b.p. 230–245° at 0.5 mm. On crystallization of the high boiling fraction from alcohol there was obtained 5.8 g. (16%) of colorless crystals of I$_A$, m.p. 95.0–98.6°. Recrystallization afforded a pure sample,[4] m.p. 100.4–101.8°.

In a similar experiment except that excess diethyl malonate was the solvent and the heating period was 7 hr. at 100±5° a smaller yield (10%) of I$_A$ was obtained.

3-Phenylphthalidyl malonic acid, I$_B$. A small amount of I$_A$ in aqueous ethanol was heated with a small excess of sodium hydroxide for 3 min. The reaction mixture was acidified with hydrochloric acid. This solution was allowed to evaporate to dryness and the solid residue was extracted with absolute alcohol. The filtered extracts were evaporated to dryness and the residue triturated with boiling benzene. The benzene-insoluble crystals were washed with water, collected, and dried to yield colorless crystals of I$_B$, m.p. 160° dec.[4]

Anal. Calcd. for $C_{17}H_{12}O_6$: C, 65.4; H, 3.9. Found[8]: C, 65.1; 65.3; H, 4.0, 3.9.

3-Methyl-3-phenylphthalide. An authentic sample of 3-methyl-3-phenylphthalide, m.p. 76.8–78.0°, was prepared essentially as described.[9] The crude phthalide was purified by alkaline hydrolysis to remove a persistent impurity of methyl *o*-benzoylbenzoate. The pure phthalide had a strong carbonyl band at 5.65 μ.

On heating a small amount of I$_B$ at 200–205° for 20 min. followed by vacuum distillation of the product, a good yield of 3-methyl-3-phenylphthalide, m.p. 76.8–78.0°, mixed melting point with above sample not depressed, was obtained. The infrared spectra were identical.

Diethyl 3-phenylphthalidylmethylmalonate, IV. A solution of the acid chloride prepared from 50.0 g. of *o*-benzoylbenzoic acid, prepared as described,[4] in 100 ml. of dry ether was added to the ethoxymagnesium salt of diethyl methylmalonate, prepared as described for diethyl malonate,[9] using 5.4 g. of magnesium and 38.0 g. of diethyl methylmalonate. The reaction mixture remained clear even after refluxing for 1 hr. or for longer periods up to 12 hr. The cooled mixture was treated with dilute hydrochloric acid and the products taken into ether-benzene. It was necessary to keep the separatory funnels used warm to prevent crystallization of the product. After washing with sodium carbonate solution, the ether-benzene solution was concentrated. The product, IV, was obtained in three crops, m.p. 103–107°, in 81–86% yield. The analytical sample, m.p. 106–107°, was obtained with little loss by recrystallization from alcohol.

Anal. Calcd. for $C_{22}H_{22}O_6$: C, 69.1; H, 5.8. Found[8]: C, 68.9; H, 5.7.

Many attempts at hydrolysis of IV were made. These included among others the following: (a) heating at reflux with aqueous alcoholic sodium hydroxide for 1 hr.; (b) heating at reflux for 12 hr. in acetic acid containing a small amount of concentrated sulfuric acid; (c) refluxing in 88% formic acid for several hours; (d) refluxing acetic acid solutions containing large amounts of sulfuric acid; (e) holding a solution of 3.0 g. of IV in 25 ml. of acetic acid containing 5 ml. of 48% hydrobromic acid at 50 ± 5° for 33 days; (f) heating for various times with insufficient alkali for complete hydrolysis. The results of the above experiments are summarized as follows: (*a*) *o*-benzoylbenzoic acid in high yield; (b,c,e) recovery of almost all of IV unchanged; (d) recovery of IV (mainly) plus small amounts of *o*-benzoylbenzoic acid; (f) recovery of *o*-benzoylbenzoic acid and of IV.

One attempt at catalytic hydrogenation of IV in ethyl acetate over a rhodium-on-alumina catalyst at room temperature and 50 p.s.i. of hydrogen for 90 min. failed, as no uptake of hydrogen occurred and IV was recovered almost quantitatively.

Evans Chemical Laboratory
The Ohio State University
Columbus, Ohio

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(6) I am indebted to Dr. Gideon Fraenkel for the NMR analysis. Significant features are the sharp unsplit CH_3 band at 8.362 τ units which indicates that the methyl group is on a carbon which has no hydrogen attached to an adjacent carbon. The fact that the ethyl groups are not equivalent indicates that freedom of rotation is restricted.

(7) All melting points are uncorrected.

(8) Microanalyses by the Galbraith Laboratories, Knoxville, Tenn.

(9) E. Bergmann, *J. Org. Chem.*, **4**, 1 (1939).

(9) H. G. Walker and C. R. Hauser, *J. Am. Chem. Soc.*, **68**, 1386 (1946).

Synthesis of Potential Anticancer Agents. XIII. Alkyleniminoquinoxalines[1,2]

W. R. Vaughan and M. S. Habib

Received July 27, 1961

The established anticancer activity of the ethylenimine (aziridine) group attributed to its "alkylating" action[3] prompted us to prepare a number of

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(1) Previous paper in this series, R. C. Elderfield and T.-K. Liao, *J. Org. Chem.*, **26**, 4994 (1961).

(2) This work supported by a Research Grant (CY-2961) from the National Cancer Institute to The University of Michigan.

(3) R. B. Ross, *J. Chem. Ed.*, **36**, 368 (1959). *Cf. Ann. New York Acad. Sci.*, **68**, 657 (1958).