hours, no more alcohol was obtained as distillate, the mixture was cooled, acidified with acetic acid and agitated with water. The organic layer was washed free of acid and dried. Fractionation gave 31% (15 g.) recovered capronitrile and 54% (41 g.) ethyl α-cyanocaproate, b. p. 128–129° (23 mm.), n^{20}D 1.4262. A sample of the ester was hydrolyzed with alcoholic sodium hydroxide. The butylmalonic acid, crystallized from petroleum ether, melted at 102–103°.

Summary

A procedure is described for the condensation of alkyl carbonates with nitriles by means of metal alcoholates to give α-cyano esters, and the results of its application to a variety of nitriles are presented.

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Alkyl Carbonates in Synthetic Chemistry. IV. Alkylation of Malonic Esters by Alkyl Carbonates[1]

BY V. H. WALLINGFORD AND DAVID M. JONES

In a study of the carbalkoxylation of aliphatic esters reported recently[2] it was noted that in certain cases the metal derivatives of the resulting malonic esters were alkylated by diethyl carbonate. This interesting alkylation action of alkyl carbonates has now been studied further and applied to a number of mono-substituted malonic esters. The reaction is represented by eq. 1.

$$[R'C(COOR)_2]M + (RO)_2CO \longrightarrow$$
$$R'RC(COOR)_2 + RMCO_3 \quad (1)$$
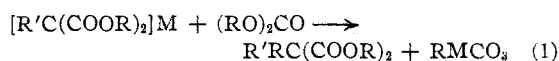
The only previous study of this type of reaction that has come to our attention is that of Noller and Dutton[3] who stated in 1933 that preliminary experiments with alkyl carbonates indicated that they are of no value as alkylating agents. The present work shows that in certain applications they are as useful in this respect as the well-known alkyl halides and sulfates, and the occasionally used alkyl esters of other inorganic acids. It is well known that alkyl esters of organic acids, including alkyl carbonates, act as alkylating agents in the Friedel–Crafts reaction, and Breslow and Hauser[4] were able to isopropylate ethyl acetoacetate with isopropyl acetate using boron trifluoride. Organic esters also react with metal phenolates[5] to give ethers. However, the alkylation of metal enolates by esters of organic acids appears to be new.

Most mono-substituted malonic esters were readily alkylated by heating their metal deriva-

tives with alkyl carbonates. Ethyl, butyl, isobutyl, isoamyl and benzyl groups were introduced by means of the corresponding carbonates into a variety of malonic esters. Secondary carbonates were poor alkylating agents. Malonic ester itself could not be alkylated since it gave tricarbalkoxymethane.[2] Alkylation of mono-substituted malonic esters was successful regardless of the length of the substituent chain provided it was a primary aliphatic group. When the substituent was a secondary aliphatic group, alkylation gave poor yields. Phenyl and benzyl substituted malonic esters were alkylated satisfactorily.

Little reaction took place in any case below 100° and the usual temperature range used was 125–175°. Diethyl phenylmalonate could only be alkylated at 225° in a bomb. Fluorene did not react at 150°, but at 200° both carbalkoxylation and alkylation occurred in the 9 position. Preliminary experiments with mono-alkyl α-cyanoacetic esters and acetoacetic esters gave negative results, but it is possible that these compounds may be forced to react at higher temperatures. A mono-substituted acetic ester may be used as starting material[2] since carbalkoxylation gives the metal derivative of a mono-substituted malonic ester. In such cases some mono-substituted malonic ester was found in the product.

Sodium and potassium derivatives of the esters react well, and the ethoxymagnesium derivative of diethyl ethylmalonate reacted when the temperature was raised to 225°. The metal derivatives were produced by the action of metal alcoholates on the malonic esters. The formation of the metal derivative was forced to completion by removing the alcohol by fractionation under

(1) Presented before the Division of Organic Chemistry at the Atlantic City Meeting of the American Chemical Society, September 9, 1941.

(2) Wallingford, Homeyer and Jones, THIS JOURNAL, **63**, 2056 (1941).

(3) Noller and Dutton, ibid., **55**, 424 (1933).

(4) Breslow and Hauser, ibid., **62**, 2611 (1940).

(5) King and Wright, J. Chem. Soc., 1168 (1939).

TABLE I

Starting material	Product	B. p., °C. (uncor.)	Mm.	nD	t, °C.	Yield, %	Recovered starting material, %
Ethyl butyrate	Diethyl diethylmalonate[a,b]	102–103	11	1.4240	20	36	[c]
Ethyl caproate	Diethyl butylethylmalonate[d]	122–124	12	1.4282	20	34	33
Ethyl δ-methylcaproate	Diethyl ethylisoamylmalonate[e,f]	130–135	16	1.4293	20	45	25
Ethyl isovalerate	Diethyl ethylisopropylmalonate[g]	112–114	18	..		10	[e]
Diethyl ethylmalonate	Diethyl diethylmalonate[b]	99–101	10	1.4240	20	54	24
Diethyl octylmalonate	Diethyl ethyloctylmalonate[h]	122	1.5	1.433	26	25	15
Diethyl s-butylmalonate	Diethyl s-butylethylmalonate	...	..	..	..	Poor	..
Dibutyl ethylmalonate[i,j]	Dibutyl butylethylmalonate[i,k]	117–119	1	1.4329	26.5	42	38
Dibutyl cetylmalonate[i,l]	Dibutyl butylcetylmalonate[i,d]	265–268	4	1.4500	20	83	..
Diisobutyl ethylmalonate[i,m]	Diisobutyl ethylisobutylmalonate[i,n]	175	30	1.4320	26.5	45	35
Diisoamyl ethylmalonate[i,o]	Diisoamyl ethylisoamylmalonate[i,p,s]	126–129	1	1.4351	26	60	..
Di-s-butyl s-butylmalonate[i,q]	Di-s-butyl di-s-butylmalonate[z]	...	..	..	..	Poor	50
Di-3-pentyl ethylmalonate[i,r]	Di-3-pentyl ethyl-3-pentylmalonate[i,s]	132–134	3	..	..	20[s]	..
Dibutyl benzylmalonate[i,t]	Dibutyl benzylbutylmalonate[i,u,s]	172	3	1.4770	25.5	80	..
Dibenzyl ethylmalonate[i,v]	Dibenzyl benzylethylmalonate[i,w]	245–247	2	1.5560	23.5	53	..
Diethyl phenylmalonate	Diethyl ethylphenylmalonate[x]	105	1	1.4905	20	30	..
Fluorene	Butyl 9-butyl-9-fluorenecarboxylate[y,s]	175–176	2	1.5550	28.5	45	5

[a] Diethyl ethylmalonate was also obtained in 18% yield. [b] Diethylmalonic acid, m. p. 126–128°. [c] Starting material not readily recoverable from Et₂CO₃. [d] See experimental part. [e] Diethyl isoamylmalonate was also obtained in 25% yield. [f] Ethylisoamylmalonic acid, m. p. 120–121°. [g] Diethyl isopropylmalonate was also obtained in 30% yield. [h] Ethyloctylmalonic acid, m. p. 82–83°. Neutral equivalent calcd., 122; found, 123. [i] New compound. [j] B. p. 98–99° (2 mm.), $n^{26.5}$D 1.4241. [k] Butylethylmalonic acid, m. p. 116–118°. [l] B. p. 255–260° (4–5 mm.) n^{26}D 1.4450. [m] B. p. 150° (28 mm.), $n^{27.3}$D 1.4204. [n] Ethylisobutylmalonic acid, m. p. 109–110°. Neutral equivalent calcd., 95; found, 94. [o] B. p. 96° (1 mm.), $n^{26.5}$D 1.4270. [p] Ethylisoamylmalonic acid, m. p. 120–121°. Neutral equivalent calcd., 101; found, 103. [q] B. p. 115° (3 mm.), $n^{20.2}$D 1.4282. [r] B. p. 168–169° (35 mm.), $n^{28.5}$D 1.4245. [s] Product was impure and yield was estimated. [t] B. p. 154° (1 mm.), n^{27}D 1.4760. [u] Benzylbutylmalonic acid, m. p. 105–107°. Neutral equivalent calcd. 125; found, 127. [v] B. p. 190° (2 mm.), $n^{24.4}$D 1.5300. [w] Benzylethylmalonic acid, m. p. 125–127°. Neutral equivalent calcd. 111; found 112. [x] M. p. −9 to −7°. Mixed m. p. showed no depression. Also obtained 50% yield of ethyl α-phenylbutyrate. [y] *Anal.* Calcd. for $C_{22}H_{26}O_2$: C, 82.0; H, 8.1. Found: C, 82.1; H, 8.1. The ester was hydrolyzed to 9-butyl-9-fluorenecarboxylic acid, m. p. 112–114°. Neutral equivalent calcd. 266; found, 262. [z] Potassium alcoholate used.

reduced pressure. This is important since metal alcoholates react with alkyl carbonates to form an ether and a metal alkyl carbonate. This undesired formation of ether may be regarded as the result of the alkylation of the metal alcoholate by the alkyl carbonate. In general, to avoid the mixed esters which might result from interchange, the alkyl carbonate, metal alcoholate and malonic ester should have the same alkoxy groups. However, in the case of dibenzyl ethylmalonate, sodium methylate was used without difficulty. Table I summarizes the experimental data. The alkyl carbonate used and consequently the alkyl group introduced was in each case derived from the same alcohol as the esterifying group of the product.

The authors wish to express their appreciation to Dr. A. Q. Butler and Mr. Robert A. Burdett for the analyses reported.

Experimental

General Procedure.—The apparatus for the alkylation of malonic esters with alkyl carbonates consisted of a three-necked flask arranged with a piano wire stirrer, dropping funnel and fractionating column.[2]

The metal derivative of the malonate was heated four to five hours with 5–10 molecular equivalents of the alkyl carbonate. When the starting material was a substituted acetic acid ester the preliminary carbalkoxylation was carried out as previously described.[2] When a malonic ester was used, the alcohol produced by the formation of the metal derivative was removed by fractionation under reduced pressure before the mixture was heated at atmospheric pressure to bring about the alkylation.

Diethyl Butylethylmalonate.—Sodium (11.5 g.) was reacted with ethyl alcohol (200 ml.) in a 500 cc. three-necked flask arranged as described above. The excess alcohol was distilled under reduced pressure until a white cake remained. This was cooled and broken up with a glass rod and diethyl carbonate (400 ml.) was added. The mixture was stirred and all of the remaining alcohol was removed by fractionation under reduced pressure. Care was taken that the bath temperature did not exceed 100°. Then, at atmospheric pressure, the mixture was heated to refluxing (150–155° bath temperature) and immediately ethyl caproate (72 g.), b. p. 166–167°, n^{20}D 1.4070, was added during one-half hour. Alcohol was slowly formed by the carbalkoxylation reaction and was removed continuously by fractionation. During three hours, 55 ml. of alcohol was obtained and then the formation of alcohol stopped.

The mixture was refluxed for four hours to complete the alkylation. The mixture was cooled and decomposed with acetic acid (30 ml.) and water. The organic layer was washed, dried and distilled. There were obtained 25 g. of diethyl butylethylmalonate, b. p. 124° (12 mm.), $n^{20}D$ 1.4282 and 41 g. of a mixture of this ester and diethyl butylmalonate, b. p. 122–124° (12 mm.), $n^{20}D$ 1.4250–1.4268. On the basis of refractive indices the yield of disubstituted ester was 34% and that of mono was 26%. Also, there was recovered 24 g. or 33% of the ethyl caproate. The diethyl butylethylmalonate was identified by hydrolyzing it to butylethylmalonic acid which melted at 116–118°.

Dibutyl Butylcetylmalonate.—Sodium (2.9 g.) reacted with butyl alcohol (125 ml.) and excess alcohol was vacuum distilled off until a mush containing some alcohol remained. The mixture was cooled and dibutyl carbonate (125 ml.) and dibutyl cetylmalonate (55 g.) were added. On stirring and warming to 90° the solid completely dissolved. The remaining excess alcohol and that produced by the formation of the enolate was removed by fractiona-tion at 20 mm. The mixture was then stirred at atmospheric pressure and heated to a bath temperature of 200–210°. Within one-half hour the mixture had set to a solid mass. Heating was continued for four and one-half hours. The mixture was then cooled and acetic acid (8 ml.) and water were added. The organic layer was washed, dried and distilled. There was obtained 52 g. (83%) of dibutyl butylcetylmalonate, b. p. 265–268° (4 mm.), $n^{20}D$ 1.4500. The ester was hydrolyzed with alcoholic sodium hydroxide and butylcetylmalonic acid, m. p. 96–98°, was obtained.

Summary

A method is described for the successful use of alkyl carbonates as alkylating agents. It has been applied to a variety of mono-substituted malonic esters for the introduction of primary alkyl and benzyl groups. Several new malonic esters have been prepared.


Alkyl Carbonates in Synthetic Chemistry. V. Alkyl Carbonates as Solvents for Metalation and Alkylation Reactions[1]

By V. H. Wallingford, Melvin A. Thorpe and August H. Homeyer

In an earlier paper[2] it was stated that alkyl carbonates are advantageous media for many organic reactions. The successful use of alkyl carbonates in the metalation and alkylation of a variety of malonic, β-keto and α-cyano esters is reported in this paper. By this method, cleavage of a carbalkoxyl group by alcoholysis is avoided and the formation of the metal derivative may be forced substantially to completion.

The ,new procedure is particularly useful in preparing certain alkyl derivatives of malonic esters. Esters containing a highly branched substituent such as the s-butyl group, are very difficult to alkylate further by the ordinary procedure using sodium alcoholate in alcoholic solution. The failure of such esters to readily undergo further alkylation was first observed by Fisher and Dilthey[3] and later by Shonle,[4] and Cope[5] and their associates. As pointed out by previous investigators, this failure to alkylate when alcohol

is used as a reaction medium is probably due to the incomplete formation of the sodio derivative according to eq. (1).

$$R'HC(COOR)_2 + NaOR \rightleftharpoons [R'C(COOR)_2]Na + ROH \quad (1)$$
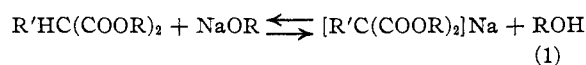
Consequently, when such a reaction mixture is treated with an alkyl halide a large part of the reaction which takes place involves the sodium alkoxide and the alkyl halide. Furthermore, the original malonic ester or the desired alkylated product may be in part decarboxylated by alcoholysis under the conditions of the reaction as represented by eq. (2).

$$R'R''C(COOR)_2 + ROH \xrightarrow{RONa} R'R''CHCOOR + (RO)_2CO \quad (2)$$
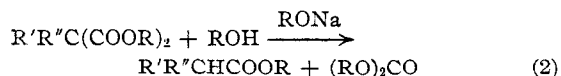
By substituting an alkyl carbonate for alcohol as a reaction medium, it is possible to complete the formation of the metal derivative (eq. 1) by distilling all alcohol from the reaction mixture. The metal derivative can then be treated with the alkylating agent with no fear of alcoholysis according to eq. 2.

We have used alkyl carbonates as media for the alkylation of representative members of the ma-

(1) Presented before the Division of Organic Chemistry at the Atlantic City Meeting of the American Chemical Society, September 9, 1941.

(2) Wallingford, Homeyer and Jones, This Journal. **63**, 2056 (1941).

(3) Fisher and Dilthey, *Ann.*, **335**, 337 (1904).

(4) Shonle, Keltch and Swanson, This Journal, **52**, 2440 (1930).

(5) Cope, Hartung, Hancock and Crossley, *ibid.*, **62**, 314 (1940).