sired strength. With potassium hydroxide solutions of less than 40% strength, up to ten hours of heating with strong mechanical stirring had no effect, the carbinols being recovered to the extent of 95%.

In 50% solution two hours of heating was sufficient for complete reaction; actually this was much longer than necessary in most cases. An arrangement for partial condensation permitted hexyne and volatile ketones to distil off as formed. The distillate and organic material in the reaction flask were then combined, washed, dried, and carefully fractionated. Inspection of Table III shows the results obtained. Ketones were characterized by derivatives; hexyne by its mercury derivative, and by isolation of hexanone-2 semicarbazone. No effort was made to determine gaseous acetylene; its presence could always be shown by precipitation of silver acetylide from the gases evolved during decomposition of ethynyl carbinols. With dihexynyl carbinols it was possible to obtain hexyne in good yields but the residue in the reaction flask invariably was resinified.

Summary

A number of acetylenic tertiary carbinols have been prepared, with different alkynyl radicals. The effect of the alkynyl residue upon the decomposition of the carbinols over commercial alumina has been studied. Two types of decomposition have been observed, cleavage to ketone and acetylene derivative being favored by ethynyl and phenylethynyl substituents, and simple dehydration by alkylethynyl substituents. These results contrast with the decomposition with aqueous potassium hydroxide solution which invariably causes cleavage of the acetylenic group. Further studies are in progress to evaluate relative effects of groups.


[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE MALLINCKRODT CHEMICAL WORKS]

Alkyl Carbonates in Synthetic Chemistry. III. Condensation with Nitriles. Synthesis of α-Cyano Esters[1]

BY V. H. WALLINGFORD, DAVID M. JONES AND AUGUST H. HOMEYER

Previous papers in this series described the condensation of alkyl carbonates with organic esters to give malonic esters[2] and with ketones to give β-keto esters.[3] Similarly, alkyl carbonates may be condensed with nitriles to give α-cyano esters as illustrated by eq. (1).

$$R'CH_2CN + (RO)_2CO + MOR \longrightarrow$$
$$[R'C(CN)CO_2R]M + 2ROH \quad (1)$$
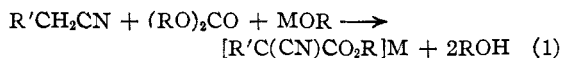
Earlier work on this reaction was devoted to the condensation of diethyl carbonate with phenylacetonitrile. Hessler[4] first prepared ethyl α-cyanophenylacetate in 55% yield by adding phenylacetonitrile to a mixture of diethyl carbonate, ether and sodium. The same result was obtained by Nelson and Cretcher,[5] who repeated Hessler's method and also tried other condensing agents. Sodamide gave a 30% yield in benzene and 70% in ether. Sodium ethylate in alcohol gave 55%. Ruggli, Caspar and Hegedus[6] carried out the carbethoxylation in toluene by

means of sodium ethylate, and added o-nitrobenzoyl chloride directly to the reaction mixture. The yield of ethyl α-cyano-α-(o-nitrobenzoyl)-phenylacetate was 57%. Adickes and Hinderer[7] attempted to force the condensation further to completion by the use of alcohol-free sodium ethylate, a reaction medium of xylene, and distillation of alcohol from the reaction medium. The yield of ethyl α-cyanophenylacetate was 63%. p-Methoxyphenylacetonitrile, the only other nitrile tried successfully in this reaction that has come to our attention, was carbethoxylated in ether by means of sodium giving a 55% yield.[8]

While previous workers obtained fair results with the reaction in the case of phenylacetonitriles, none has indicated that the method was generally applicable for the synthesis of α-cyano esters. By employing the technique described in earlier papers[2,3] a carbalkoxyl group has been introduced into a variety of nitriles as shown in Table I. The method consists in heating the nitrile with a metal alcoholate and a large excess of alkyl carbonate. Thus the use of sodium metal, sodamide and mixed solvents is avoided. Alcohol introduced with the metal alcoholate and that

(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) Wallingford, Homeyer and Jones, ibid., **63**, 2252 (1941).

(4) Hessler, Am. Chem. J., **32**, 119 (1904).

(5) Nelson and Cretcher, THIS JOURNAL, **50**, 2758 (1928).

(6) Ruggli, Caspar and Hegedus, Helv. Chim. Acta, **20**, 250 (1937).

(7) Adickes and Hinderer, J. prakt. Chem., [2] **150**, 89 (1938).

(8) Niederl, Roth and Plentl, THIS JOURNAL, **59**, 1901 (1937).

TABLE I

Starting material	Product	Yield, %	B. p., °C. (mm.) Uncor.	n_D (°C.)
Acetonitrile	Ethyl cyanoacetate[a]	10	106–107 (22)	
Butyronitrile	Ethyl α-cyanobutyrate[c]	40	109–110 (24)	1.418 (20)
Isovaleronitrile	Ethyl α-cyanoisovalerate[d]	47	111–113 (22)	1.422 (20)
Capronitrile	Ethyl α-cyanocaproate[e]	54	128–129 (23)	1.426 (20)
Isocapronitrile[b]	Propyl α-cyanoisocaproate[f]	72	78– 80 (1.5)	1.4262 (25)
Stearonitrile	Ethyl α-cyanostearate[g]	75	167–180 (2)	1.446 (27)
Phenylacetonitrile	Ethyl α-cyanophenylacetate[h]	78	125–126 (2–3)	1.5017 (24)
p-Iodophenylacetonitrile	Ethyl α-cyano-p-iodophenylacetate[i]	50	160 (2)	
p-Methylphenylacetonitrile	Ethyl α-cyano-p-methylphenylacetate[j]	87	120–121 (1)	1.5047 (20.5)

[a] Reaction time two hours. The sodium derivative separated as a solid from the reaction mixture. The solvent was decanted and the solid was washed with ether. It was suspended in ether and acidified with hydrochloric acid. The ether solution was dried and distilled. The product reacted with ammonia giving cyanoacetamide, m. p. 119–121°. [b] Potassium propylate and dipropyl carbonate were used; propyl alcohol was distilled at 100 mm. pressure. [c] Ethylmalonic acid, m. p. 112–113°. [d] Isopropylmalonic acid, m. p. 85–88°. [e] Butylmalonic acid, m. p. 102–103°. [f] α-Cyanoisocaproamide, m. p. 101–103°. [g] M. p. 14–18°; α-cyanostearic acid, m. p. 82–83°. [h] Anal. Calcd. for $C_{11}H_{11}NO_2$: N, 7.4. Found: N, 7.6. α-Cyanophenylacetamide, m. p. 148–149°. [i] Anal. Calcd. for $C_{11}H_{10}INO_2$: I, 40.3; N, 4.4. Found: I, 40.5; N, 4.4. [j] Anal. Calcd. for $C_{12}H_{13}O_2N$: C, 70.8; H, 6.4; N, 6.9. Found: C, 70.9; H, 6.5; N, 7.0.

produced in the reaction is preferably removed by distillation. It is clear from eq. (1) that these conditions favor the formation of the desired products by mass action. Likewise the reverse reaction observed by Cope and Hancock,[9] cleavage of the α-cyano ester by alcoholysis to an alkyl carbonate and a nitrile, is avoided. The resulting α-cyano ester is present in the reaction mixture as the metal derivative and may be subjected directly to a further reaction such as alkylation.

The method has been applied to a variety of aliphatic nitriles and aryl acetonitriles. The yields of α-cyano esters given in Table I probably do not represent the highest obtainable under optimum conditions. In most cases the method is suitable for preparative purposes, but a few exceptions may be noted. Vinylacetonitrile and p-nitrophenylacetonitrile appeared to be too reactive and resulted in tars. On the other hand, no reaction was obtained with α-phenylbutyronitrile. Nelson and Cretcher[5] likewise were unable to condense α-substituted phenylacetonitriles with diethyl carbonate.

The method of carbalkoxylation described in this and previous papers[2,3] appears to be usually applicable to esters, ketones and nitriles having two alpha hydrogen atoms. Lower members of each series gave poor yields of carbalkoxylated products either because the low boiling point prevented forcing the reaction, or because of polymerization. Unsaturated compounds such as benzalacetone and vinylacetonitrile formed tars under the con-

(9) Cope and Hancock, THIS JOURNAL, 61, 96, 776 (1939).

ditions tried. Sodium and potassium alcoholates were equally satisfactory as condensing agents but magnesium and aluminum alcoholates were not effective. All primary alkyl carbonates have reacted satisfactorily, but the use of secondary carbonates has not been practical.

Experimental

General Procedure.—The apparatus for condensing alkyl carbonates with nitriles was similar to that previously described[2] for carbalkoxylation of esters. It consisted of a three-necked flask fitted with a piano wire stirrer, dropping funnel and fractionating column.

The nitrile was heated with an equimolar amount of sodium ethylate and 4–8 molecular equivalents of diethyl carbonate. The alcohol concentration during the reaction was maintained as low as possible by fractionating from the mixture both the alcohol accompanying the sodium alcoholate and the alcohol produced by the reaction. The condensation of aliphatic nitriles was slow, requiring several hours at the boiling point of the mixture at atmospheric pressure. The condensation of phenylacetonitriles, however, was more rapid and was accomplished at the lower temperature obtained by distilling at 150 mm. pressure.

Ethyl α-Cyanocaproate.—Sodium (11.5 g.) was dissolved in anhydrous ethyl alcohol (300 ml.) in a 1-liter three-necked flask arranged as described above. The solution was distilled to dryness and the residue heated at reduced pressure until the sodium ethylate was substantially free of alcohol. After cooling, diethyl carbonate (300 ml.) was added and the cake of sodium ethylate was disintegrated. Capronitrile (47.5 g.) was added, the reaction mixture was stirred and heated, and alcohol was fractionally distilled at atmospheric pressure. When, after five

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.

$$[R'C(COOR)_2]M + (RO)_2CO \longrightarrow$$
$$R'RC(COOR)_2 + RMCO_3 \quad (1)$$
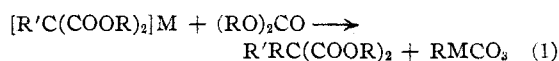
The only previous study of this type of reaction that has come to our attention is that of Noller and Dutton[3] who stated in 1933 that preliminary experiments with alkyl carbonates indicated that they are of no value as alkylating agents. The present work shows that in certain applications they are 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).