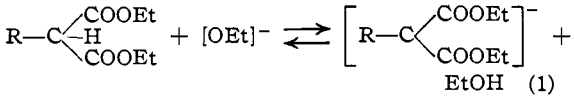
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, GENERAL MILLS, INC.]

Addition of Alkylmalonic Esters to Acrylonitrile[1,2]

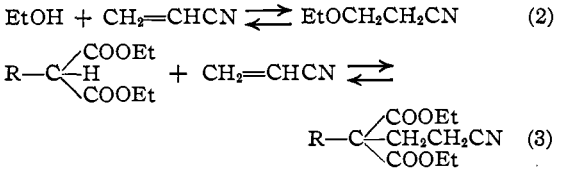
BY DON E. FLOYD

The addition reactions of a large number of active hydrogen systems, including certain substituted malonic esters, to acrylonitrile, have been described by Bruson and Riener.[3] Numerous other investigators have contributed to our knowledge of the Michael reaction.[4,5,6,7,8] The present study was undertaken in order to discover under what conditions alkylmalonic esters, particularly those with large substituents, would form addition products with acrylonitrile. Additions with ethyl and *n*-butyl substituted malonic esters had been reported previously.[3]

The alkylmalonate additions to acrylonitrile reported here were conducted under various reaction conditions, using different catalysts and solvents. It was expected that ethanol would be unsuitable as a solvent because of two inhibitory effects. The first of these expected effects was the suppression of alkylmalonate anion formation (mass action), according to the equation.



Anion formation is the first step in this addition reaction. The other expected inhibitory effect was the competition of ethanol for the acrylonitrile.



Koelsch[7] reported that acrylonitrile formed addition products with alcohols with exceptional rapidity. When attempts were made by him to add benzyl cyanide to acrylonitrile in alcohol solution, only β-alkoxypropionitriles were obtained. However, in the present study, ethanol was found to be a very useful solvent; addition of the alkylmalonate to acrylonitrile was rapid and very nearly complete when it was used. Formation of β-ethoxypropionitrile was apparently negligible. It was concluded, therefore, that (1) the concentration of alkylmalonate anion in ethanol was great enough for ready addition to acrylonitrile, (2) the alkylmalonic ester almost completely displaced the ethanol in the competition for acrylonitrile, and (3) the reaction rates and equilibria in the steps of the addition subsequent to that shown in equation 1 were favorable for alkylmalonate addition.

On the other hand, the reaction in benzene when catalyzed by sodium alkoxide was slow unless alcohol was added. It may be that since the sodium alkoxide is virtually insoluble in benzene the rate of alkylmalonate anion formation is slow; whereas the high solubility of the catalyst in alcohol leads rapidly to a state of equilibrium in which the alkylmalonate anion is present. This view is substantiated by experiments in which there was added to systems containing either benzene or no solvent, an amount of alcohol sufficient to cause the sodium alkoxide to dissolve. The striking improvement evidenced by rapid evolution of heat and increased yield of addition product indicated the effect of this small amount of alcohol. At the same time, the use of large amounts of alcohol as reaction media did not adversely affect the rate or yield and little or no addition of alcohol to the acrylonitrile was noted.

When the alkylmalonic ester was allowed to react with a catalytic amount of sodium metal in an inert solvent, such as benzene, the reaction product underwent rapid reaction with acrylonitrile. This emphasizes that the solubility of the alkylmalonate anion (or base capable of forming the anion) is of great importance. Here the anion is formed in benzene and is soluble in benzene (without alcohol) and the addition reaction occurs readily in contrast to previously mentioned experiments in benzene solution with alcohol-free sodium alkoxide catalyst where low solubility of the catalyst led to slow reactions.

When the reaction medium consisted of benzene, or when no alcohol was present, a solid acrylonitrile polymer was formed at temperatures above 40°. However, when the reaction was conducted in alcohol, formation of this solid polymer did not occur even at temperatures as high as 70°. As expected, in 95% ethanol no noticeable addition reaction occurred. Piperidine was found to be a rather inactive catalyst; yields were only about 10% even after refluxing the reagents for six hours in either alcohol or benzene with this base. No addition at all was observed when a similar reaction mixture was allowed to stand at room temperature for eighteen hours.

All of the alkylmalonic esters studied reacted with acrylonitrile very rapidly under the conditions used. In contrast to the experience of Kohler[9] and Connor and Andrews[5] with other Michael

(1) Paper No. 93, Journal Series, Research Department, General Mills, Inc.

(2) Presented at the Fall, 1948, meeting of the American Chemical Society at St. Louis, Missouri.

(3) Bruson and Riener, THIS JOURNAL, **65**, 23 (1943).

(4) Michael, *J. prakt. Chem.*, **35**, 349 (1887).

(5) Connor and Andrews, THIS JOURNAL, **56**, 2713 (1934).

(6) Hauser and Abramovitch, *ibid.*, **62**, 1763 (1940).

(7) Koelsch, *ibid.*, **65**, 437 (1943).

(8) Connor and McCellan, *J. Org. Chem.*, **3**, 570 (1938).

(9) Kohler, THIS JOURNAL, **44**, 843 (1922).

reactions it was not found that increasing the size of the alkyl substituent caused a noticeable diminishing of reactivity. This was true even when the substituent was as large as hexadecyl. Only low yields of the expected addition products were obtained using the procedure described by Bruson and Riener[3] for additions with ethyl or *n*-butyl substituted malonates. Furthermore, reactions under these conditions were slow.

Experimental

The alkylmalonic esters used in this study were prepared as described in an earlier paper.[10] The experiments described in the following paragraphs typify the different procedures used. Numerical data are given in Table I.

TABLE I

ADDITION OF ALKYLMALONIC DIETHYL ESTERS TO ACRYLONITRILE

Alkyl substituent	Method and % yield	B. p.[a] adduct, °C. (1 mm.)	$n^{25}D$ of adduct	Nitrogen, % Calcd.	Found
n-Butyl	A 87	133–134[b]	1.4413	5.19	5.16
n-Hexyl[c]	A 82	149–150	1.4436	4.70	4.61
n-Octyl[c]	B 90	163–165	1.4460	4.31	4.43
n-Decyl[c]	A 89	173–174	1.4482	3.96	3.86
n-Dodecyl[c]	B 92	182–183	1.4491	3.67	3.50
n-Tetradecyl[c]	D 86	189–190	1.4511	3.41	3.28
Cetyl[c]	C 89	M. p. 45°	Solid[d]	3.19	3.07

[a] Boiling points are uncorrected; determined in an alembic still at a distillation rate of 2–3 drops per second. A 6-inch indented column was used to prevent superheating. [b] Bruson and Riener give the boiling point of this adduct as 145–150° (1 mm.). [c] These adducts are new compounds. [d] Colorless needles.

Addition of Ethyl *n*-Butylmalonate to Acrylonitrile

Method A (in Alcohol).—A solution of 0.1 g. of metallic sodium in 20 ml. of absolute ethanol was prepared. To it was added 21.6 g. (0.1 mole) of ethyl *n*-butylmalonate and the solution was mechanically stirred while 8 g. of acrylonitrile was added slowly. The heat of the reaction caused the temperature to rise rapidly and it was maintained at about 70° by adjusting the rate of addition of the acrylonitrile. The reaction mixture was allowed to stand for about two hours after which it was acidified to litmus with glacial acetic acid and the solvent was evaporated off under reduced pressure. The residual liquid was taken up in ether, washed and dried over sodium sulfate. The addition product was distilled under reduced pressure after removal of the ether. No low-boiling fraction was obtained.

Addition of Ethyl *n*-Dodecylmalonate to Acrylonitrile

Method B (in Benzene).—A solution of ethyl *n*-dodecylmalonate (0.1 mole) in dry benzene was prepared and to it was added 0.05 g. of sodium metal. Using the usual apparatus, acrylonitrile (0.11 mole) was slowly added to the yellow solution. The temperature of the reaction mixture was maintained at 30–40° during the reaction by means of a cooling bath and no solid acrylonitrile polymer was formed under these conditions. The reaction mixture was processed and the reaction product distilled under reduced pressure.

Addition of Ethyl Cetylmalonate to Acrylonitrile

Method C (in Benzene).—Ethyl cetylmalonate (30 g.) was dissolved in dry benzene and to the solution was added 0.1 g. of sodium methoxide dissolved in 1 ml. of ethanol. Then acrylonitrile (5 g.) was added slowly to the solution at such a rate that the reaction temperature did not rise above 70°. A small amount of yellow solid (acrylonitrile polymer) settled out of the solution. An additional three grams of acrylonitrile was added to replace that lost in polymer formation. After acidification and concentration of the filtrate there was obtained a solid product melting at 45°. Recrystallization from 80% ethanol did not alter the melting point of the crystals.

Addition of Ethyl *n*-Tetradecylmalonate to Acrylonitrile

Method D (No Solvent).—A solution of 0.05 g. of sodium ethoxide in 0.5 ml. of absolute ethanol was prepared and to it was added ethyl *n*-tetradecylmalonate (0.05 mole), followed by acrylonitrile (0.055 mole). The reaction temperature was maintained at 60–70° by adjusting the rate of addition of the acrylonitrile. The reaction mixture was processed as before, the product isolated by ether extraction and distilled under reduced pressure.

Summary

The addition reactions of a series of alkylmalonic esters with acrylonitrile and the physical properties of the adducts have been described. The influence of various solvents and bases on the reaction have been discussed on the basis of the present theory of addition of active hydrogen systems to acrylonitrile.

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(10) Floyd and Miller, THIS JOURNAL, **69**, 2354 (1947).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Some 6-Quinolyl Sulfides and Sulfones

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As a result of the high antistreptococcal activity of 4,4′-diaminodiphenyl sulfone[1b] and the inhibitory effect of this compound on experimental tuberculosis in animals,[2] together with the indicated antimalarial activity of certain of its derivatives,[3] a series of quinoline analogs of this compound has been prepared.

It is known that the dinitro and diaminodiphenyl sulfides and sulfones have therapeutic effects similar to that of sulfanilamide,[1,4,5] but are generally more toxic, [6,7] and since the introduction of some heterocycles in sulfanilamide adds desirable features, it was thought that certain sulfides and sulfones of quinoline might have therapeutic value.

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(1b) Buttle, Stephenson, Smith, Dewing and Foster, *Lancet*, **1**, 1331 (1937).

(2) Rist, Block, and Hamon, *Ann. Inst. Pasteur*, **64**, 203 (1940).

(3) (a) Heymann and Fieser, THIS JOURNAL, **67**, 1979 (1945); (b) Heymann and Heidelberger, *ibid.*, **67**, 1986 (1945).

(4) Fourneau, J. and Mme. J. Trefouel, Nitti and Bovet, *Bull. acad. med.*, **118**, 210 (1937); *Compt. rend.*, **204**, 1763 (1937).

(5) Bauer and Rosenthal, *U. S. Pub. Health Rpts.*, **53**, 40 (1938).

(6) Welch, *J. Pediatrics*, II, no. 2, 159 (1937).

(7) Raiziss, Clemence, Severae and Moetsch, THIS JOURNAL, **61**, 2763 (1939).