70. *Nucleophilic Attacks on Carbon–Carbon Double Bonds. Part I. General Considerations: Arylmethylene Transfer and Cyclodimerisation.*

By SAUL PATAI and ZVI RAPPOPORT.

It is suggested that nucleophilic attack on activated carbon–carbon double bonds by a great variety of nucleophiles (Y), leading to widely differing final products, involves an intermediate carbanion of the general type $R^1R^2CY\cdot\bar{C}R^3R^4$. Seven possible reaction routes are summarised, and two of them, the transfer of an arylmethylene group from the $=CR^3R^4$ group to the $=CR^5R^6$ group, and the cyclodimerisation of compounds containing activated double bonds to the corresponding cyclobutane derivatives, are discussed and illustrated by several examples. A detailed mechanism is proposed for the last two reactions.

Introduction to a Series of Papers.—Carbon–carbon double bonds, activated by electron-attracting substituents, are readily attacked by a variety of nucleophilic reagents, giving a wide variety of products.

We shall try to show in the present series of papers that, apart from allylic S_N2' rearrangements,[1] the primary nucleophilic attack is always on the positively polarised (β-)carbon atom of the double bond, giving an unstable carbanion of the same general type in all cases. The further fate of this carbanion is determined by the type and nature of its constituent groups, and the nature of the solvent and other molecules present in the solution and participating in the reaction in its subsequent stages.

The various types of nucleophilic attacks and their products are summarised in Chart 1. The seven reaction routes in the Chart can be divided into two main categories. In the first four reactions the nucleophilic reagent or part of it remains attached to the products; while in the last three reactions the reagent acts only as a catalyst and does not appear in the products.

Path (a), addition, as exemplified by the Michael and the cyanoethylation reaction, has been well documented [2,3] and although only a few kinetic studies are available [4] the mechanism given by Ingold [5] is generally accepted.

Nucleophilic replacement of one of the substituents attached to the doubly bonded carbon atoms (path b) was studied by Miller and Yonan,[6] by Modena,[7] and recently by Vernon and his co-workers.[8] These authors verified the addition-elimination route for this reaction, *i.e.*, a carbanion is formed and elimination of one of the substituents then gives the product. Alternatively, an addition product (path a) is first formed, and elimination of a molecule gives the final product.[9]

By path (c), examples of which are found in the literature,[10] the arylmethylene group

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[1] Wheland, " Advanced Organic Chemistry," John Wiley and Sons, Inc., New York, 1951, p. 539; Fried and Miller, *J. Amer. Chem. Soc.*, 1959, **81**, 2078.

[2] Bergmann, Ginsburg, and Papo, " Organic Reactions," John Wiley and Sons, Inc., New York, 1959, Vol. X, p. 179.

[3] Bruson, " Organic Reactions," John Wiley and Sons, Inc., New York, 1949, Vol. V, p. 79.

[4] Jones, *J.*, 1914, **105**, 1547; Kamlet and Glover, *J. Amer. Chem. Soc.*, 1956, **78**, 4556; Ogata, Okano, Furuya, and Tabushi, *J. Amer. Chem. Soc.*, 1956, **78**, 5426; Hine and Kaplan, *J. Amer. Chem. Soc.*, 1960, **82**, 2915; Schmidt and Kubitzek, *Ber.*, 1960, **93**, 866.

[5] Ingold, " Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, 1953, p. 692.

[6] Miller and Yonan, *J. Amer. Chem. Soc.*, 1957, **79**, 5931.

[7] Modena, *Ricerca Sci.*, 1958, **28**, 341; Maioli and Modena, *Gazzetta*, 1959, **89**, 854; Modena and Todesco, *ibid.*, p. 856; Modena, Todesco, and Tanti, *ibid.*, p. 878.

[8] Jones, Morris, Vernon, and White, *J.*, 1960, 2349.

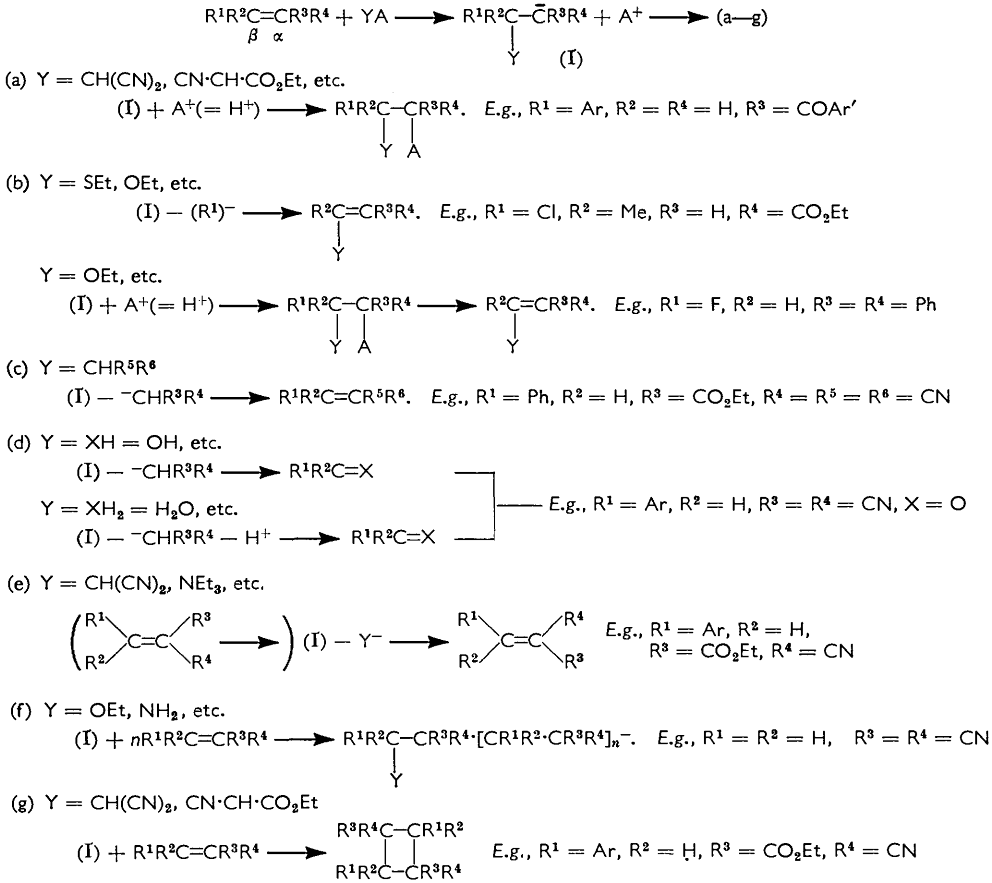
[9] Silversmith and Smith, *J. Org. Chem.*, 1958, **23**, 427.

[10] Vorlander and Knoetzsch, *Annalen*, 1897, **294**, 317; Dornow and Boberg, *Annalen*, 1952, **578**, 101.

attached to the group $=CR^3R^4$ is transferred to a different group $=CR^5R^6$. Some examples of this " arylmethylene transfer " will be discussed in the present paper and it will be suggested that the product is formed by a one-step reaction from the intermediate carbanion.

Path (d) is a solvolysis [of which (c) is a special case]. The products are the same, irrespective of whether the nucleophilic reagent is a neutral molecule (H_2O, etc.) or its conjugated base (OH^-, etc.). Solvolyses of these types have been studied kinetically, *e.g.*, the base-catalysed hydrolysis of nitrochalcones by Walker and Young[11] and the hydrolysis of piperonylidene- and vanillylidene-nitromethane in water by Crowell and Francis[12] and Stewart.[13] In Parts II and III of the present series we present a kinetic study demonstrating path (d) by use of ethylenes with widely differing substituents.

CHART 1. *Generalised modes of nucleophilic attacks on activated carbon–carbon double bonds.*



$$\underset{\beta\ \ \alpha}{R^1R^2C{=}CR^3R^4} + YA \longrightarrow \underset{\substack{|\\ Y}}{R^1R^2C}{-}\bar{C}R^3R^4 + A^+ \longrightarrow (a\text{—}g) \qquad (I)$$

(a) $Y = CH(CN)_2,\ CN{\cdot}CH{\cdot}CO_2Et$, etc.

$$(I) + A^+(=H^+) \longrightarrow \underset{\substack{|\\ Y}}{R^1R^2C}{-}\underset{\substack{|\\ A}}{CR^3R^4}. \quad E.g.,\ R^1 = Ar,\ R^2 = R^4 = H,\ R^3 = COAr'$$

(b) $Y = SEt,\ OEt$, etc.

$$(I) - (R^1)^- \longrightarrow \underset{\substack{|\\ Y}}{R^2C}{=}CR^3R^4. \quad E.g.,\ R^1 = Cl,\ R^2 = Me,\ R^3 = H,\ R^4 = CO_2Et$$

$Y = OEt$, etc.

$$(I) + A^+(=H^+) \longrightarrow \underset{\substack{|\\ Y}}{R^1R^2C}{-}\underset{\substack{|\\ A}}{CR^3R^4} \longrightarrow \underset{\substack{|\\ Y}}{R^2C}{=}CR^3R^4. \quad E.g.,\ R^1 = F,\ R^2 = H,\ R^3 = R^4 = Ph$$

(c) $Y = CHR^5R^6$

$$(I) - {}^-CHR^3R^4 \longrightarrow R^1R^2C{=}CR^5R^6. \quad E.g.,\ R^1 = Ph,\ R^2 = H,\ R^3 = CO_2Et,\ R^4 = R^5 = R^6 = CN$$

(d) $Y = XH = OH$, etc.

$$(I) - {}^-CHR^3R^4 \longrightarrow R^1R^2C{=}X$$

$Y = XH_2 = H_2O$, etc.

$$(I) - {}^-CHR^3R^4 - H^+ \longrightarrow R^1R^2C{=}X$$

E.g., $R^1 = Ar,\ R^2 = H,\ R^3 = R^4 = CN,\ X = O$

(e) $Y = CH(CN)_2,\ NEt_3$, etc.

$$\left(\begin{matrix}R^1 & & R^3\\ & C{=}C & \\ R^2 & & R^4\end{matrix} \longrightarrow \right)(I) - Y^- \longrightarrow \begin{matrix}R^1 & & R^4\\ & C{=}C & \\ R^2 & & R^3\end{matrix} \quad E.g.,\ R^1 = Ar,\ R^2 = H,\ R^3 = CO_2Et,\ R^4 = CN$$

(f) $Y = OEt,\ NH_2$, etc.

$$(I) + nR^1R^2C{=}CR^3R^4 \longrightarrow \underset{\substack{|\\ Y}}{R^1R^2C}{-}CR^3R^4{\cdot}[CR^1R^2{\cdot}CR^3R^4]_n^-. \quad E.g.,\ R^1 = R^2 = H,\ R^3 = R^4 = CN$$

(g) $Y = CH(CN)_2,\ CN{\cdot}CH{\cdot}CO_2Et$

$$(I) + R^1R^2C{=}CR^3R^4 \longrightarrow \begin{matrix}R^3R^4C{-}CR^1R^2\\ |\qquad\ \ |\\ R^1R^2C{-}CR^3R^4\end{matrix} \quad E.g.,\ R^1 = Ar,\ R^2 = H,\ R^3 = CO_2Et,\ R^4 = CN$$

Examples of path (e) (*cis–trans*-isomerisation) in the presence of nucleophiles are given by Vernon and his colleagues[8] and by Miller and Yonan;[6] this reaction will be studied in some detail in Part IV.

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[11] Walker and Young, *J.*, 1957, 2045.

[12] Crowell and Francis, jun., *J. Amer. Chem. Soc.*, 1961, **83**, 591.

[13] Stewart, *J. Amer. Chem. Soc.*, 1952, **74**, 4531.

The anionic polymerisation of vinylidene cyanide, nitroethylene, and similar compounds by nucleophilic reagents is again well documented,[14] and path (f) is generally accepted for the initiation and propagation steps.

The dimerisation to cyclobutane derivatives (path g) is a special case of (f). This reaction has hitherto been studied only photochemically. In the present paper we show that it may also take place by nucleophilic catalysis.

Present Results.—Reactions of ethyl α-cyano-β-*o*-methoxyphenylacrylate (Ia of Chart 2) and related compounds were studied in 95% ethanol. With malononitrile they gave arylmethylenemalononitrile (path c) or cyclobutane derivatives (path g).

"*Arylmethylene transfer.*" Ethyl *p*-methoxy-, *o*-methoxy-, and unsubstituted α-cyano-β-phenylacrylate were attacked by malononitrile in 95% ethanol, and arylmethylene transfer took place, *i.e.*, the arylmethylene group became attached to the malononitrile residue in place of the ethyl cyanoacetate residue, giving the respective arylmethylenemalononitriles:

$$\text{(1)}\quad \mathrm{Ar{\cdot}CH{:}C(CN){\cdot}CO_2Et} + \mathrm{CH_2(CN)_2} \longrightarrow \mathrm{Ar{\cdot}CH{:}C(CN)_2} + \mathrm{CN{\cdot}CH_2{\cdot}CO_2Et}$$

As a rule no cyclobutane derivative or normal Michael adduct was found in the reaction mixture. The spectra of the initial compounds and the products are generally too similar to permit spectrophotometric kinetic experiments. However, from measurements with the *cis*-o-isomer * of (Ia) with malononitrile (see Part IV) it will be deduced that no intermediate of Michael adduct type is hidden in the reaction mixture.

The reversibility of the reaction was investigated by the reaction of 2-methoxybenzylidenemalononitrile (Va) with an excess of ethyl cyanoacetate. No acrylate could be detected and the starting material was recovered unchanged.

Formation of cyclobutane derivatives (*cyclodimerisation*). A cyclobutane derivative was obtained as a by-product in low yields in several cases and under different experimental conditions from ethyl *trans*-α-cyano-β-*o*-methoxyphenylacrylate (*trans*-Ia) with malononitrile in ethanol. This by-product was identical with that obtained by Baker and Howes [15] by photodimerisation of the same compound and was proved by them to have structure (VIIIa). The dimerisation catalysed by malononitrile was extremely sensitive to the experimental conditions, so that even when the procedures given in the experimental part were followed closely the results were irreproducible and in many cases no cyclobutane derivative could be separated.

Attempts to obtain the cyclobutane by using low concentrations of base (sodium hydroxide or triethylamine) as the nucleophile, failed.

Ultraviolet absorption spectra of mixtures of acrylate (Ia) (*trans*-isomer) with various concentrations of malononitrile were measured. In all cases the absorption of the solution fell rapidly at the beginning of the measurements and later slowly, to a constant value. At this stage the spectrum of the solution corresponded to that of only 75—80% of that of the arylmethylenemalononitrile (Va). Although no product analysis was possible owing to the very low concentrations used, it is probable that the difference in the material balance is due to the formation of the cyclobutane (VIIIa) which has practically no absorption in the range measured.

When solutions of the cyclobutane were heated with malononitrile, ethyl cyanoacetate, or base, no absorption corresponding to an ethylenic compound appeared and accordingly the reaction seems to be practically irreversible.

A dimeric by-product was observed, but not characterised, by Corson and Staughton [16] on condensation of aromatic aldehydes with malononitrile.

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* Here *cis* and *trans* refer to the Ar and CO_2Et groups.

[14] Wieland and Sakellarios, *Ber.*, 1919, **52**, 898; Gilbert, Miller, Averill, Schmidt, Stewart, and Trumbell, *J. Amer. Chem. Soc.*, 1954, **76**, 1074; Grodizinski, Katchalsky, and Vofsi, *Makromol. Chem.*, 1961, **44—46**, 591.

[15] Baker and Howes, *J.*, 1953, 119.

[16] Corson and Staughton, *J. Amer. Chem. Soc.*, 1928, **50**, 2825.

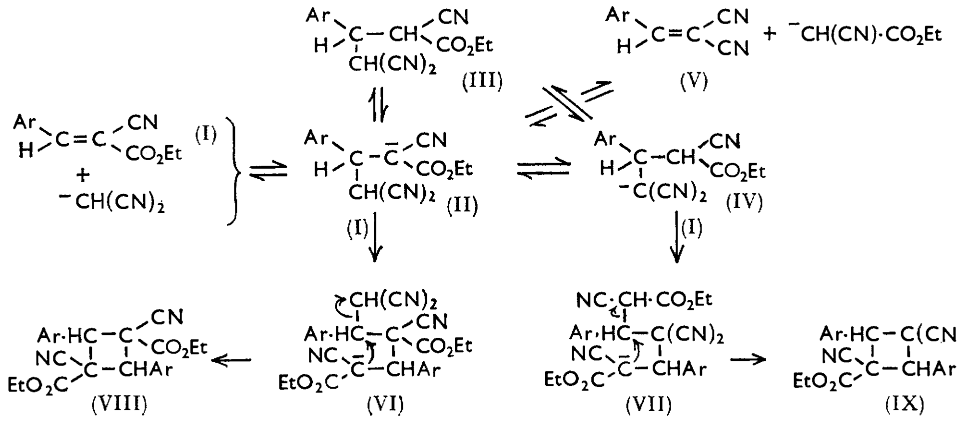
Twenty-four arylmethylene derivatives of malononitrile, ethyl cyanoacetate, and cyanoacetamide were subjected to irradiation in order to obtain cyclobutane derivatives. The acrylate (Ia) gave quantitative yields; the malononitrile (Vc) gave only traces of a compound with high melting point and infrared spectra corresponding to a cyclobutane; none of the other compounds underwent any reaction.

In all cases when active methylene compounds (malononitrile, ethyl cyanoacetate, cyanoacetamide) were used as nucleophilic reagents for various reactions with compounds containing active carbon–carbon double bonds, only one normal Michael adduct was formed. At low temperature (0°) salicylaldehyde and malononitrile[15] gave an almost quantitative yield of the Michael adduct, salicylidenedimalononitrile, if an excess of the active methylene compound was used. Even this compound decomposed already at room temperature in ethanol or tetrahydrofuran solution, affording salicylidenemalononitrile Salicylaldehyde is also known to give a relatively stable diadduct with ethyl cyanoacetate;[17] with other aromatic aldehydes the reaction gives arylmethylene derivatives and no subsequent Michael addition.

Infrared absorption of cyclobutane derivatives. Reid and Sack[18] examined eight fully substituted cyclobutanes and found characteristic absorption between 868 and 888 cm.$^{-1}$. Appearance of peaks in the 852—895 region in our compounds is not inconsistent with the cyclic nature of our dimer.

Discussion.—We believe that in both the " arylmethylene transfer " and the cyclodimerisation, the first step is attack of the malononitrile anion on the positively polarised (β-)carbon atom of the double bond (Chart 2). The resulting anion (II) can be protonated by the medium to give the normal Michael adduct (III), it can give the isomeric anion (IV) by intramolecular proton transfer, or it can attack another molecule giving a new anion (VI).

CHART 2. *Proposed mechanism for " arylmethylene transfer " and cyclodimerisation.**



* In the text, a, b, and c after a Roman numeral denote Ar = o-MeO·C_6H_4, p-MeO·C_6H_4, and Ph, respectively.

As no Michael adduct could be isolated in our experiments, it is probable that if the compound (III) exists at all in the reaction mixture, it is present only in minor proportions. We reach the same conclusion by inspecting the final products of dimerisation, by the following argument:

It would be expected, that if compound (III) is one of the intermediates of the main reaction path, at least some of the cyclobutane derivatives should have structure (IX), *i.e.*, contain the $>$C(CN)$_2$ group. If it exists, the intermediate (III) could lose either one

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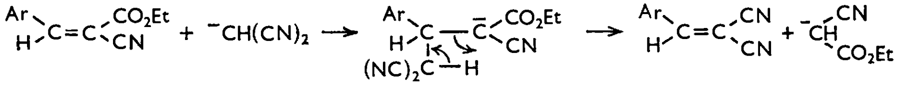
[17] Migrdichian, " Organic Synthesis," Reinhold Publ. Corp., New York, 1957, 215.

[18] Reid and Sack, *J. Amer. Chem. Soc.*, 1951, **73**, 1985.

of two protons, giving the anion (II) or (IV). In accord with Pearson and Dillon's and our results[19] for malononitrile and ethyl cyanoacetate, ionisation of the proton bound to the $C(CN)_2$ group is both faster and more complete than that of a proton bound to the $C(CN){\cdot}CO_2Et$ group. Accordingly, formation of ion (IV) should be preferred, giving (*via* VII) the cyclobutane (IX) as the final product. Exclusive formation of the isomer (VIII) in the cases when a cyclobutane could be obtained seems to be strong evidence that this reaction does not go through ester (III).

The presence of ester (III) as an intermediate cannot be excluded *a priori* in the formation of arylmethylenemalononitriles. On the other hand, spectrophotometric investigation failed to disclose a hidden intermediate in the reaction of malononitrile with the *cis*-acrylate (Ia) and there exists a *direct* route from the anion (II) to the arylmethylenemalononitrile, by a four-centre reaction, such as (Ia).

(Ia)



Migration of the proton from the carbon bearing two cyano-groups is made easier by the negative charge on the α-carbon atom and the initial intramolecular proton transfer is followed by cleavage of the αβ-carbon–carbon bond. The formation of arylmethylenemalononitrile seems to be thermodynamically more favoured than that of the corresponding arylmethylenecyanoacetate, since arylene transfer takes place in this direction and not the other.

The formation of the two types of product discussed above depends on the life of the intermediate carbanion (II). Its decomposition resulting in arylmethylene transfer is a unimolecular process; its reaction with another molecule of the starting material is necessarily bimolecular and, moreover, only one special conformation of the carbanion (VI) can give the desired cyclobutane.

It seems that the dimerisation has very special requirements as regards the constitution of the reacting molecule, for only two of twenty-four compounds of the general type Ar·CH:CXY (X, Y = CN, CO_2Et, or $CO{\cdot}NH_2$) underwent photodimerisation in the conditions used by Baker and Howes[15] or by us, and similarly only one of ten compounds gave the same reaction on catalysis by malononitrile.

There is a resemblance in behaviour between aromatic aldehydes on the one hand and arylmethylene-malononitriles and -cyanoacetates on the other (*e.g.*, both form addition compounds with hydrogen cyanide or sodium hydrogen sulphite[16]). This resemblance applies also in the dimerisation of ethyl benzylidenecyanoacetates, as compared with the benzoin condensation. Both reactions take place by an initial nucleophilic attack, followed by the attack of the anion so produced on a second molecule, and the reaction is completed by expulsion of the "catalyst" with formation of a "dimeric" product. Only the rearrangement of the anion in the benzoin condensation has no parallel in the cyclobutane formation.

Regarding the stereochemistry of the cyclobutanes produced, our only information is that of several possible isomers the same one is obtained by the photochemical method and by our catalytic method. This isomer may have a preferred configuration, probably each pair of aryl and ester groups *trans* to each other, as in the starting material.

EXPERIMENTAL

Materials.—Commercial malononitrile (B.D.H.), ethyl cyanoacetate ("AnalaR"), and ethanol were purified by distillation. Ethyl α-cyano-β-phenylacrylate and its *o*- and *p*-methoxy-derivatives were prepared as described in the literature.[15, 20]

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[19] Pearson and Dillon, *J. Amer. Chem. Soc.*, 1953, **75**, 2439; Patai, Zabicky, and Israeli, *J.*, 1960, 2038.

[20] Zabicky, *J.*, 1961, 683.

" Arylmethylene Transfer."—Ethanolic solutions of malononitrile and the ethyl arylmethylenecyanoacetates were left at room temperature for several hours. Most of the solvent was evaporated *in vacuo* and the residue crystallised. The arylmethylenemalononitriles obtained (see Table) were identified by mixed m. p.s and by their ultraviolet spectra.

Preparation of arylmethylenemalononitriles from ethyl β-aryl-α-cyanoacrylates and malononitrile in 95% ethanol at 25°.

$CH_2(CN)_2$ (g.)	Acrylate Ar	g.	Solvent (ml.)	Reaction (hr.)	Yield of $Ar{\cdot}CH{:}C(CN)_2$ (%)	M. p.	Cryst. solvent	Ref.
4	p-MeO·C_6H_4	6	100	25 *	91	113°	EtOH	16
1·5	o-MeO·C_6H_4	2	25	4	81	84	EtOH	15
1·5	Ph	2	30	3	71	83	EtOH/H_2O	16

* The undissolved starting material (2 g.) was filtered off after 1 hr.

" Cyclodimerisation: " Diethyl 1,3-Dicyano-2,4-di-o-methoxyphenylcyclobutane-1,3-dicarboxylate (VIIIa).—(a) *With malononitrile.* (1) To a solution of the acrylate (Ia) (210 mg.) in ethanol (50 ml.) malononitrile (130 mg.) was added. After 1 day at 40°, most of the solvent was removed at reduced pressure, and 40 mg. (18%) of a white solid, m. p. 162°, were obtained.

(2) Malononitrile (2 g.) was added to the acrylate (Ia) (5 g.) in ethanol (150 ml.) and the solution was stirred for 1 hr. In the first 15 min. white crystals of the cyclobutane derivative were precipitated, with simultaneous dissolution of the yellow starting material. The precipitate (200 mg., 4%) crystallised from propan-2-ol, then melting at 162·5—163°.

(b) *With ethyl cyanoacetate.* A solution of acrylate (Ia) (5 g.) and ethyl cyanoacetate (5 g.) in ethanol (25 ml.) was stirred for 4 hr. After cooling, crystals, m. p. 162° (320 mg., 6·4%), appeared. Recrystallisation from ethanol gave a product of m. p. 163°.

(c) *Photodimerisation.* The solid acrylate (Ia) (2 g.) was kept in direct sunlight for a total of 72 hr. A quantitative yield of ester (VIIIa) was obtained as needles, m. p. 163° (yield by Baker and Howes's procedure [15] 55%).

All the products were identified by mixed m. p. with a sample obtained by Baker and Howes's method. The product obtained by procedure (a2) (Found: C, 67·1; H, 5·8; N, 6·0. Calc. for $C_{26}H_{26}N_2O_6$: C, 67·5; H, 5·6; N, 6·1%) had an infrared absorption spectrum identical with that of a sample obtained by Baker and Howes's method (characteristic peaks at 858 and 880 cm.$^{-1}$). The ultraviolet absorption spectra were identical for all the samples, with $\lambda_{max.}$ 280 mμ (ε 6200).

The above procedures, but with ethanolic solutions of sodium hydroxide (0·001M) or triethylamine (0·01M), gave no cyclobutane in 72 hr.

Attempts to follow spectrophotometrically the formation of the cyclobutane (VIIIa) from the acrylate (Ia) and malononitrile were made with a Beckman DU spectrophotometer, the absorption at 359 mμ being measured (the maximum for the starting material). In all cases studied with various concentrations of the reactants, there was a fast initial decrease in the optical density, after which the absorption remained practically constant at a value corresponding to the formation of about 75—80 moles % of malononitrile derivatives (Va).

Preparation of Salicylidenedimalononitrile.—To salicylaldehyde (30 g.) in ethanol (100 ml.) were added malononitrile (30 g.) and piperidine (one drop). The mixture was kept for 4 hr. at 0°. The white *product* (50 g., 96%) that separated recrystallised from tetrahydrofuran–water; it became yellow at 120° and melted with decomposition at 145° (Found: C, 65·6; H, 3·7. $C_{13}H_8N_4O$ requires C, 65·7; H, 3·4%). Solutions of the compound in tetrahydrofuran or ethanol, when kept for some days (even at 0°), gave yellow crystals of salicylidenemalononitrile, m. p. 167°, identified by m. p., mixed m. p., and infrared spectra with a sample [15] from salicylaldehyde and malononitrile.

Spectra.—The infrared spectra were taken in the solid state with a potassium bromide prism in a Baird Associates spectrophotometer.

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