Anal. Calcd. for $C_{34}H_{54}O_2$: C, 82.53; H, 11.00; mol. wt., 495. Found: C, 82.39; H, 10.89; mol. wt. (Rast, micro), 486.

Lithium Aluminum Hydride Reduction of the Isopropenylquinonemethide.—A five-gram sample of the quinonemethide V was reduced with lithium aluminum hydride according to the procedure of Brown.[11] After vacuum distillation the melting point and infrared spectrum were identical with a sample of 2,6-di-*t*-butyl-4-isopropylphenol.

Addition of Hydrogen Bromide to the Isopropenylquinonemethide (VII).—Anhydrous hydrogen bromide was bubbled through a petroleum ether solution of the quinone methide. On cooling a copious precipitate of white crystals, m.p. 102–111° dec., was formed. On standing in the air the crystals rapidly decomposed.

BURLINGTON, VERMONT

[11] W. G. Brown, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF MICHIGAN]

Arylation of Unsaturated Systems by Free Radicals. VI.[1] The Meerwein Reaction. IV.[2] The Stereochemistry of the Arylation of Maleic and Fumaric Acid Derivatives

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The Meerwein arylation of the methyl and butyl esters and nitriles of maleic and fumaric acid with *p*-chlorobenzenediazonium chloride gave mixtures of the corresponding derivatives of *p*-chlorophenylmaleic acid and *p*-chlorophenylfumaric acid in a ratio of 1:2. The ratio was independent of the geometry of the starting material. This result is explained by suggesting that the intermediate formed by the attack of the aryl radical on the double bond is incapable of retaining its configuration. A mechanism for the Meerwein reaction is proposed.

The arylation by diazonium salts of a carbon-carbon double bond conjugated with an "activating" group, initiated by cupric chloride,[3] is known as the Meerwein reaction.[4,5] The product is usually a mixture of addition and substitution compounds (types A and B, eq. 1)

$$\mathrm{ArN_2Cl + RCH{=}CRZ \xrightarrow{CuCl_2} \underset{A}{ArCR{=}CRZ} + \underset{B}{ArCHRC(R)ClZ}} \quad (1)$$

Only a few observations on the stereochemistry of the Meerwein reaction have been recorded to date. Bergmann, Dimant and Japhe[6] found that the two stereoisomeric forms of β-phenyl-β-*p*-bromophenylacrylic acid were converted to the same 1-phenyl-1-*p*-bromophenyl-2-*p*-nitrophenylethene upon reaction with *p*-nitrobenzenediazonium chloride, the yields being 30 and 11%. Taylor and Strojny[7] obtained 6% of phenylmaleic anhydride and 12% of phenylfumaric acid from benzenediazonium chloride and methyl maleate, although the alkaline hydrolysis may have caused partial isomerization of one form to the other.[4] Meerwein, Büchner and van Emster[4] used *p*-chlorobenzenediazonium chloride with methyl fumarate, but they demonstrated that their alkaline hydrolysis conditions caused isomerization so that the sole product was *p*-chlorophenylfumaric acid. In their parallel experiment with methyl maleate, the saponification conditions were selected so as not to cause isomerization, and they obtained 28% of *p*-chlorophenylfumaric acid and 19% of *p*-chlorophenylmaleic anhydride.

Since none of these experiments provides conclusive evidence about the stereochemistry of the Meerwein reaction, we have investigated the reaction of *p*-chlorobenzenediazonium chloride with three *cis-trans* pairs, the methyl and butyl esters and the nitriles of maleic and fumaric acids. This diazonium salt was selected on the basis of preliminary experiments which showed that it gave good yields of products with convenient physical properties.

The reactions were conducted according to standardized conditions developed previously.[2] The crude products (mixtures of types A and B) were treated with 2,6-lutidine or 2,4,6-collidine to convert type B into type A. The amount of chlorine thus eliminated was determined by weighing the amine hydrochloride formed, and checked by hydrolysis with alcoholic alkali; approximately one-third mole of eliminatable chlorine per mole of *p*-chloroaniline was found in each example.[8] The small amount of tarry by-product was removed by filtration through a column of activated alumina, and the eluate was evaporated under high vacuum to remove volatile impurities. A small amount of diarylated material (resulting from further arylation of type A product) was not removed by this treatment. The stereoisomer ratio in the residue was determined by infrared spectroscopy. The stereochemical results are given in Table I.

The pure stereoisomeric esters required for infrared comparison were prepared from the available[5] *p*-chlorophenylmaleic anhydride and *p*-chlorophenylfumaric acid; different methods of esterification gave the same esters, indicating that isomerization had not occurred. The stereoisomeric nitriles were isolated from a large-scale arylation of fumaronitrile, and their configurations were es-

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[1] Paper V, C. S. Rondestvedt, Jr., and H. S. Blanchard, *J. Org. Chem.*, **21**, 229 (1956).

[2] Paper III, C. S. Rondestvedt, Jr., and O. Vogl, THIS JOURNAL, **77**, 3401 (1955).

[3] See, however, J. K. Kochi, *ibid.*, **77**, 5090 (1955).

[4] H. Meerwein, E. Büchner and K. van Emster, *J. prakt. Chem.*, **152**, 237 (1939).

[5] The literature has been reviewed by C. S. Rondestvedt, Jr., and O. Vogl, THIS JOURNAL, **77**, 2313 (1955). See also ref. 3.

[6] F. Bergmann, E. Dimant and H. Japhe, *ibid.*, **70**, 1618 (1948).

[7] E. C. Taylor, Jr., and E. J. Strojny, *ibid.*, **76**, 1872 (1954).

[8] It is tempting to seek some significance in the constancy of the amount of eliminatable chlorine. However, since the yield of arylation product (see below) varies widely, it seems unwise to attempt to explain this possibly fortuitous coincidence in the absence of further evidence.

tablished by their melting points[9] and infrared spectra.

The infrared spectra of the pure methyl and butyl *p*-chlorophenyl-fumarates showed a very strong band at 1240 cm.$^{-1}$ which was absent from the spectra of the corresponding maleates. In *p*-chlorophenylfumaronitrile, this band is shifted to 1203 cm.$^{-1}$. Methyl and butyl *p*-chlorophenylmaleates exhibited characteristic strong bands at 1280–1285, 1340–1350 and 1408–1410 cm.$^{-1}$ which were absent from the fumarate spectra. *p*-Chlorophenylmaleonitrile has a strong band at 1320 cm.$^{-1}$ which is absent from the spectrum of its isomer.

Table I

Stereoisomers Formed from *p*-Chlorobenzenediazonium Chloride and Derivatives of Maleic and Fumaric Acid

Compound arylated	% *cis* isomer	% *trans* isomer
Methyl maleate	24	66
Methyl fumarate	29	55
Butyl maleate	32	62
Butyl fumarate	31	58
Maleonitrile	33	57
Fumaronitrile	30	62

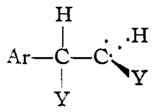
Discussion

The Meerwein reaction could be formulated in several stereospecific ways. For example, *cis* addition of Ar and Cl followed by *trans* elimination of HCl would give the isomer of the same configuration. *trans*-Addition and *trans* elimination would give the isomer of the opposite configuration. The process leading directly to the unsaturated product (type A) should give the product of opposite configuration if it were a direct "rear-side" displacement of hydrogen by aryl.

The actual reaction is not stereospecific, as indicated by the data in Table I. Regardless of the original stereochemistry, the product is the same mixture; the *trans* product is approximately twice as abundant as the *cis*. One may argue that the reaction itself is actually stereospecific but that the products themselves are isomerized by the reaction conditions into an equilibrium mixture of the composition found. This seems unlikely, *a priori*, because such *cis-trans* isomerizations usually proceed through an addition to the double bond, followed by elimination, and additions to these products should be strongly retarded by the profusion of electron-attracting groups attached to the double bonds. Experimental confirmation of this supposition was obtained by exposing *p*-chlorophenylmaleonitrile (m.p. 169–171°) to simulated Meerwein reaction conditions, and recovering the product quantitatively, unchanged (m.p. 169–171°). It is concluded, therefore, that the products retain their stereochemical identity, once formed.

Ionic additions to double bonds are highly stereospecific, in general, involving charged intermediates in which a precise geometry is maintained by a *quasi*-ring structure such as the well-known bromonium ion. Although radical additions may sometimes be stereospecific, notably with cyclic olefins,[10] with acyclic olefins they more often are not.[10b,c,d] The absence of stereospecificity then lends additional support to the radical-type mechanism for the Meerwein reaction.[2,5,11] A further argument on its behalf may be deduced from the observation (Table II) that the yields of mixed isomeric esters are greater from a *trans* starting material than from the corresponding *cis* isomer, whereas the yields are comparable from the *cis* and *trans* nitriles. Lewis and Mayo[12] have made exactly parallel observations on the rates of radical polymerization of these same compounds. The *trans* esters polymerize much faster than the *cis* esters, whereas the two nitriles polymerize at the same rate.

The intermediate resulting from attack by the aryl radical from the diazonium salt upon the olefin YCH=CHY must have such a long life that it becomes planar. It may resemble structure I. The conversion of this radical to products (type A and B) would be independent of the original stereochemistry.



I, Y = COOR, CN

The exact mechanism of conversion of I to products (A and B) has not been established. The simplest path, loss of a hydrogen *atom* or acquisition of a chlorine *atom*, is improbable because of the high energy of a neutral hydrogen atom and the shortage of free chlorine atoms in the solution. Koelsch proposed that the intermediate radical is oxidized by transfer of one electron to cupric chloride (eq. 2), giving a cation which readily loses a proton or acquires chloride anion.[11a] Dickerman, Weiss and Ingberman suggested that cupric chloride furnishes chlorine directly to the radical to give the type B product (eq. 3).[13] Their suggestion may be augmented (eq. 4) to account for the formation of type A product.

$$\text{Ar—C—C}\cdot + \text{Cu}^{++} \longrightarrow \text{Ar—C—C}^{+} + \text{Cu}^{+} \qquad (2)$$

$$\text{Ar—C—C}\cdot + \text{CuCl}_2 \longrightarrow \text{Ar—C—C—Cl} + \text{CuCl} \qquad (3)$$

$$\text{Ar—}\underset{\text{H}}{\underset{|}{\text{C}}}\text{—C}\cdot + \text{CuCl}_2 \longrightarrow \text{Ar—C=C} + \text{CuCl} + \text{HCl} \qquad (4)$$

The mechanism of formation of the radical intermediate is more intriguing than its subsequent fate.

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[9] W. F. Beech and H. A. Piggott, *J. Chem. Soc.*, 423 (1955), demonstrated by means of dipole moment measurements that phenylmaleonitrile was higher-melting, less volatile, and less soluble than phenylfumaronitrile. The same conclusion was reached independently by W. C. Schneider, This Journal, **77**, 2796 (1955), and D. W. Hein, *ibid.*, **77**, 2797 (1955). We therefore have assigned the structure *p*-chlorophenylmaleonitrile to the isomer m.p. 171° and the structure *p*-chlorophenylfumaronitrile to the isomer m.p. 98°.

[10] (a) H. L. Goering, P. I. Abell and B. F. Aycock, *ibid.*, **74**, 3588 (1952); (b) E. A. Shilov and I. V. Smirnov-Zamkov, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 32 (1951); *C.A.*, **45**, 7952 (1951); (c) K. N. Campbell, J. Shavel, Jr., and B. K. Campbell, This Journal, **75**, 2400 (1953); (d) P. S. Skell and R. C. Woodworth, *ibid.*, **77**, 4638 (1955).

[11] (a) C. F. Koelsch and V. Boekelheide, *ibid.*, **66**, 412 (1944); (b) E. Müller, *Angew. Chem.*, **61**, 179 (1949); (c) K. B. L. Mathur and co-workers, *J. Ind. Chem. Soc.*, **32**, 465 (1955), and previous papers; (d) O. Vogl and C. S. Rondestvedt, Jr., This Journal, **77**, 3067 (1955).

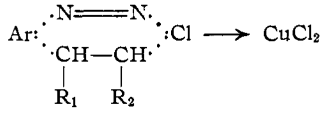
[12] F. M. Lewis and F. R. Mayo, *ibid.*, **70**, 1533 (1948).

[13] S. C. Dickerman, K. Weiss and A. K. Ingberman, *J. Org. Chem.*, **21**, 380 (1956).

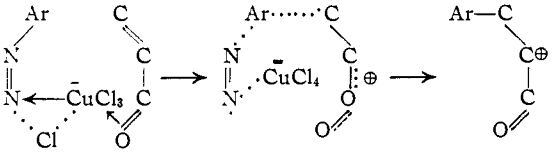
Most of the published mechanisms show the diazonium salt breaking down to an aryl radical by loss of nitrogen, with[3,13] or without[11] intervention of cupric or cuprous salt. It has been recognized,[5,11a,11d] however, that this proposal is oversimplified, because the rate of nitrogen evolution depends not only upon the structure of the diazonium salt but also very strongly on the nature of the unsaturated compound.[4,14] Therefore, some sort of intermediate complex has been suggested[11a,5] although not described in detail.

A possible form of this complex is now proposed, derived in part from suggestions by Allan and Muzhik[15] and Huisgen and Horeld[16] relative to the free-radical arylation of aromatic compounds by diazo compounds. They visualize an initial oxidation–reduction transfer of one electron from the aromatic hydrocarbon to the diazo compound, following which nitrogen is lost and the radicals associated to the product (a biaryl). A somewhat related type of one-electron transfer is found in Woodward's mechanism for the Diels–Alder reaction,[17] in which, however, the resulting oppositely charged radicals are held tightly together by electrostatic attraction.

The structure II tentatively proposed by Allan and Muzhik seems to require preferential *cis* addition of Ar and Cl with exclusive formation of the type B product. This conclusion being contrary to fact, we have revised and amplified their suggestion as shown by the accompanying formulas.



II



III IV V

An α,β-unsaturated carbonyl compound has been selected for this illustration, since it is well known that some unsaturated "activating" group must be attached to the olefinic double bond.[18] The fundamental concept in this portrayal is the transfer of one electron *from the electron-rich activating group* (not the electron-poor conjugated double bond) to the diazonium compound *with cupric copper*[19] *functioning as an intermediary.* Structure III is an attempt to show the pattern of electron transfer along the arrows. The result of the transfer is the cation radical and the diazonium radical (formula IV); the two are probably held together by the copper. Breakdown of the diazonium radical then gives an aryl radical which unites with the cation radical. The resulting cation V loses a proton or acquires chloride ion as discussed earlier.

This formulation is in harmony with the major features of the Meerwein reaction as they are now known. Hence it can serve as a working hypothesis subject to test by further experiments now in progress. A detailed discussion of the implications of this mechanism will be reserved for later papers.

Since the above mechanism makes explicit use of the oxidizing ability of *cupric* copper, a word is necessary about the recent statement by Kochi[3] that *cuprous* copper is the active catalyst. He showed that cupric copper reacted with acetone to form cuprous chloride and chloroacetone,[20] and that cuprous chloride could induce a Meerwein reaction between *p*-chlorobenzenediazonium chloride and styrene (in one case, with acrylonitrile). It is unwise to generalize from these few experiments that all Meerwein reactions are catalyzed by cuprous copper, especially in the light of much evidence to the contrary. First of all, Meerwein himself had commented that cuprous copper was a relatively poor or completely inactive catalyst for the reactions he studied, though unfortunately he did not give experimental details. Secondly, he showed that acetonitrile—which Kochi[20] showed did *not* reduce cupric chloride—was about as good a solvent as acetone in the few cases examined.[4] Furthermore, Mathur and his collaborators[11c] have observed numerous examples of Meerwein reactions which give markedly inferior yields *in the presence of acetone* (and therefore cuprous chloride). Finally, Kochi did not demonstrate that cupric chloride was *not* catalytically active, only that cuprous chloride could be active. In the light of all the evidence cited, we prefer to regard cupric chloride as the usual catalytic agent, although we recognize that cuprous chloride may be active in favorable cases, perhaps *via* a different mechanism.

Experimental[21]

Materials.—*p*-Chloroaniline and *p*-nitroaniline were recrystallized Eastman Kodak products. Fumaronitrile was generously supplied by Monsanto Chemical Co.; it was recrystallized before use. Maleonitrile was prepared by isomerization of fumaronitrile with dry hydrogen chloride in 15% yield.[12,22] Methyl maleate and butyl maleate were donated by Commercial Solvents Corp. Butyl fumarate was a gift from The Borden Co., Chemical Division. Methyl fumarate was prepared by esterification of fumaric acid.

***p*-Chloroaniline and Fumaronitrile.**—*p*-Chloroaniline (64 g., 0.5 mole) was diazotized at 0–5° in the presence of 150 ml. of concd. hydrochloric acid. The final volume was 500 ml. The filtered solution was adjusted to *p*H 3.00 (Beckman *p*H meter) with saturated sodium acetate solution, the temperature being maintained below 0°. This solution was added to 45 g. (0.58 mole) of fumaronitrile in 500 ml. of acetone, followed by 13 g. of cupric chloride dihydrate in 40 ml. of water. The temperature rose slowly to 25°. After about an hour, a brown layer was observed floating on the clear green lower layer. The acetone was evaporated at room temperature, and the yellow crystals which appeared were taken up in 800 ml. of benzene,

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(14) Ionic mechanisms have been considered previously[5] and rejected.

(15) Z. J. Allan and F. Muzhik, *Coll. Czech. Chem. Comm.*, **19**, 720 (1954).

(16) R. Huisgen and G. Horeld, *Ann.*, **562**, 137 (1949).

(17) R. B. Woodward, THIS JOURNAL, **64**, 3058 (1942).

(18) The only contradiction to this statement is the observation of Müller[11b] that simple olefins and acetylenes could be arylated in very low yield. No corroboration nor further study has been published yet.

(19) We do not intend to imply which form of cupric copper is catalytically active. It is shown as the anionic complex because of the high concentration of chloride ions necessarily[11b] present and because the negative charge should facilitate association with cations.

(20) J. K. Kochi, THIS JOURNAL, **77**, 5274 (1955).

(21) Microanalyses by Anna Griffin in this Laboratory. Melting points are uncorrected.

(22) H. Mommaerts, *Bull. Classe sci. Acad. roy. Belg.*, **27**, 579 (1941); *C. A.*, **38**, 3621 (1944).

washed and dried ($MgSO_4$). The brown solution was treated with 60 ml. of dry 2,6-lutidine (or 2,4,6-collidine). The solution warmed spontaneously and began to deposit crystals. After standing overnight, the mixture was filtered. The lutidine hydrochloride was washed with dry ether; 25.4 g., 36% yield.

The benzene filtrate was steam distilled until no more volatile material was removed. The brown oil remaining in the still pot solidified on cooling. The water layer was extracted with benzene which was evaporated and combined with the solid; crude yield 57 g. In another experiment, the benzene solution was extracted with dilute acid to remove excess collidine, and the volatile materials were evaporated at 100° (10 mm.); the crude yield was comparable.

A portion of the crude product (50 g.) was distilled at 0.6 mm. from a "sausage" flask, giving fraction A, 31.2 g., bath 135–160°, yellow oil which solidified, and fraction B, 10.8 g., bath 160–185°, yellow oil which solidified immediately. The residue was transferred to a bulb tube and distilled at 0.05 mm., giving fraction C, 4.5 g., bath 180–210°, pale yellow solid. The tarry residue weighed 3.5 g. Fraction C was redistilled, yielding 3.7 g. of distillate and 0.6 g. of residue.

Fraction C was recrystallized from benzene, yielding two crops of white crystals totaling 2.5 g. (4%), m.p. 189–190°. These were identical with di-*p*-chlorophenylmaleonitrile, prepared independently (see below).

The mother liquors were combined with fraction B and crystallized from benzene, giving three crops: 2.5 g., m.p. 170–171°; 4.0 g., m.p. 169–171°; 4.0 g., m.p. 150–155°. Fraction A gave two crops from benzene: 2.5 g., m.p. 97–98°; 11.4 g., m.p. 92–95°. The combined mother liquors yielded 6.5 g., m.p. 82–88°. The residue was quite low-melting; its infrared spectrum showed that it contained some *p*-chlorophenylfumaronitrile.

In another experiment, it was advantageous to boil the high melting fraction with cyclohexane (in which the *cis*-isomer is practically insoluble) to remove the low melting isomer. The low melting isomer could also be purified by crystallization from this solvent. No attempt was made in this work to effect a quantitative separation, though the ratio is roughly 1:2.

Di-*p*-chlorophenylmaleonitrile.—A solution of 15.2 g. of *p*-chlorobenzyl cyanide (Eastman Kodak) in 65 ml. of anhydrous methanol was mixed with a solution of 25.4 g. of iodine in 150 ml. of anhydrous ether.[23] To this well-stirred solution was added a solution of 4.6 g. of sodium in 70 ml. of anhydrous methanol during 20 min. The product was isolated by distillation at 185–195° (0.01 mm.); yield 9.4 g. (63%), m.p. 188–190°. The analytical sample crystallized from benzene as white prisms, m.p. 189–190°.

Anal. Calcd. for $C_{16}H_8N_2Cl_2$: C, 64.24; H, 2.70; N, 9.44. Found: C, 64.32, 64.47; H, 2.58, 2.69; N, 9.33, 9.20.

This material did not depress the melting point of that isolated from the Meerwein reaction above, and the infrared spectra were congruent.

***p*-Nitroaniline and Fumaronitrile.**—The reaction was effected according to the above procedure on a 0.1 mole scale. The crude brown solid was boiled twice with 150-ml. portions of ether, yielding 7.2 g. (36%), of deep yellow fluffy product, m.p. 260–265° (dec., blackening). Fractional crystallization from acetone yielded two products. The first, m.p. 268° dec., is soluble in hot acetone to the extent of 3%; the second, m.p. 300° (dec., blackening), is soluble to the extent of 0.1%. The low melting product predominates by a 3:1 ratio.

Consistent analytical results could not be obtained with either compound; weighing proved to be very difficult because of a persistent electrostatic charge on the crystals.

Heller[24] reported that di-*p*-nitrophenylmaleonitrile melted at 268–269°. A sample was prepared by his method, but it depressed the melting point of the lower melting product, and the infrared spectra were markedly dissimilar.

The 268° product was hydrolyzed by heating at 180° (sealed tube) for 4 hr. with acetic acid–concd. hydrochloric acid. The known[24] di-*p*-nitrophenylmaleic anhydride, which was also prepared from the authentic di-*p*-nitrophenylmaleonitrile, could not be isolated, however.

In another run using 0.13 mole of dry *p*-nitrobenzenediazonium sulfate[25] with added sodium chloride, the yield of mixed product after treatment with ether was 9.6 g. (37%), m.p. 260–263° dec.

Preparation of Mixtures for Analysis.—*p*-Chlorobenzenediazonium chloride was allowed to react with methyl and butyl maleate and fumarate, and with fumaronitrile and maleonitrile. The same procedure was followed with all these compounds to prepare the unknown mixture for infrared analysis. One run is given as an example.

p-Chlorobenzenediazonium chloride (prepared from 6.4 g., 0.05 mole, of *p*-chloroaniline as described above) was brought to *p*H 3.00 (*p*H meter) and added to a solution of 12.0 g. (0.055 mole) of butyl maleate in 150 ml. of acetone and an aqueous solution of 1.7 g. of cupric chloride dihydrate was added. The flask was placed in a water-bath at 20°. Nitrogen evolution ceased in about 1.5 hr. The acetone was evaporated at reduced pressure, the residue was extracted with 300 ml. of benzene in portions, and the extracts were washed and dried. About 15 ml. of 2,4,6-collidine was added and the solution was concentrated at reduced pressure to about 75 ml. and allowed to stand overnight. The mixture was then refluxed for 0.5 hr., cooled, diluted with 100 ml. of benzene, and filtered. The collidine hydrochloride was dried and weighed. The filtrate was extracted with dilute sulfuric acid and water, dried and concentrated. The solution was passed through a 10–11 cm. column of 30 g. of alumina and developed with 400 ml. of benzene. The product was contained in the first 200 ml. of eluate, mostly in the fraction 50–100 ml. A narrow tarry band was retained at the top of the column, and the eluate was clear yellow.

An aliquot (one-fifth) of the eluate was evaporated to dryness and kept in an evacuated bulb tube at 0.05 mm. for 1 hr. at the temperature specified. This treatment was shown in control experiments to remove unreacted starting material quantitatively with no loss of product. For products from the methyl esters, the temperature was 100°; from the butyl esters, 125°; from the nitriles, 110°. From the weights of these aliquots the yields of mixed isomers were calculated.

To serve as a check on the collidine method for determining chlorine incorporated during the reaction, the crude products from separate runs with methyl and butyl maleates and fumaronitrile were refluxed with excess 2 *N* methanolic potassium hydroxide for 2 hr. The methanol was evaporated, water was added, the mixture was extracted with benzene, acidified with dilute nitric acid, and again extracted with benzene. The resulting aqueous solution was titrated for ionic chloride by the Volhard method.

The data from the various runs are summarized in Table II.

Table II

Meerwein Reaction of *p*-Chlorobenzenediazonium Chloride with Derivatives of Maleic and Fumaric Acids

Product from	% $Cl^{a,b}$ eliminated by		Yield of isomer mixture, %[c]
	Collidine	KOH	
Me maleate	22	31	26
Me fumarate	32	. .	48
n-Bu maleate	24	32	40
n-Bu fumarate	23	. .	62
Maleonitrile	27	. .	45
Fumaronitrile	25	32	52

[a] Calculated on aromatic amine. [b] The small but constant difference between the percentages of chlorine removed by the amine and by KOH suggests that the type B product is a mixture of racemates, only one of which is dehydrohalogenated rapidly by the weak base. [c] Calculated as *p*-chlorophenylmaleate ester or nitrile; some diarylated product may be present.

Preparation of Pure Stereoisomers for Infrared Comparison.—Pure *p*-chlorophenylmaleic anhydride and *p*-chlorophenylfumaric acid were available from previous work.[5]

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[23] Procedure of L. Chalanay and E. Knoevenagel, *Ber.*, **25**, 288 (1892).

[24] G. Heller, *Ann.*, **332**, 279 (1904).

[25] N. Kornblum, G. D. Cooper and J. E. Taylor, This Journal, **72**, 3013 (1950).

TABLE III

PROPERTIES OF ESTERS AND NITRILES OF *p*-CHLOROPHENYLMALEIC AND -FUMARIC ACIDS

	Compound	B.p., °C. (mm.)	M.p., °C.	*n*D (*T*, °C.)	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found	Anal. frequencies, cm.$^{-1}$
1	Me *p*-chlorophenylmaleate	150–155(0.05)	55–57	1.5690(25.0)[a]	$C_{12}H_{11}O_4Cl$	56.59	56.70	4.35	4.13	...	...	1285, 1350; 1410
2	Me *p*-chlorophenylfumarate	140–145(0.05)	.....	1.5438(24.5)	$C_{12}H_{11}O_4Cl$	56.59	56.41	4.35	4.26	...	...	1240
3	*n*-Bu *p*-chlorophenylmaleate	155–160(0.05)	.....	1.5291(25.0)	$C_{18}H_{23}O_4Cl$	63.81	63.83	6.84	6.75	...	...	1280, 1340; 1408
4	*n*-Bu *p*-chlorophenylfumarate	150–155(0.05)	.....	1.5076(24.5)	$C_{18}H_{23}O_4Cl$	63.81	63.56	6.84	6.85	...	...	1240
5	Benzyl *p*-chlorophenylmaleate	....	134–136	....	$C_{24}H_{19}O_4Cl$	70.85	70.64	4.70	4.74	...	...	..
6	*p*-Chlorophenylmaleonitrile	....	170–171	....	$C_{10}H_5N_2Cl$	63.68	63.81	2.67	2.65	14.85	14.90	1320
7	*p*-Chlorophenylfumaronitrile	....	97–98	....	$C_{10}H_5N_2Cl$	63.68	63.78	2.67	2.67	14.85	15.00	1203

[a] Determined on supercooled melt.

Several different procedures were used for esterification to insure that no isomerization had taken place.

Method A.—The silver salts were prepared by dissolving the anhydride (or the acid) in the calculated amount of 1 *N* aqueous potassium hydroxide. A considerable excess of silver nitrate solution was added, and the white silver salt which precipitated was collected, washed with distilled water and methanol and dried in a vacuum desiccator.

The silver salts were boiled with a slight excess of alkyl halide. Benzyl chloride in boiling xylene (0.5 hr.) gave about 40% yield of the two benzyl esters (the fumarate was not obtained pure). Butyl bromide in boiling toluene (2 hr.) gave about 30% yield of the two butyl esters.

Method B.—*p*-Chlorophenylmaleic anhydride was refluxed with methanol for 0.5 hr.; though the anhydride was not soluble in cold methanol, it dissolved rapidly with reaction when heated. The methanol was evaporated, and trituration with petroleum ether gave white crystals of the half ester, crude m.p. 145°. It was dissolved in dry ether and treated with one equivalent of ethereal diazomethane. The methyl *p*-chloromaleate was isolated by distillation as a colorless oil which crystallized on standing; yield 80%.

When two equivalents of diazomethane were added to *p*-chlorophenylfumaric acid, a white semi-solid was obtained. Though some of the desired ester was doubtless present, it appears that diazomethane had also reacted to some extent with the double bond.

Method C.—*p*-Chlorophenylmaleic anhydride was boiled with butanol. The alcohol was evaporated and the residue was dissolved in ether. The half-ester was extracted with bicarbonate, liberated with dilute acid, taken into ether, washed, dried, evaporated and esterified with butanol containing a little sulfuric acid. The butyl *p*-chlorophenylmaleate was isolated by distillation; yield 70%.

Method D.—*p*-Chlorophenylfumaric acid, methanol and thionyl chloride were mixed at −5° in a weight ratio of 1:25:1.2.[26] After 40 hr. at 0°, the mixture was evaporated at room temperature at reduced pressure, dissolved in ether, washed with bicarbonate and water, dried and distilled.

When *p*-chlorophenylfumaric acid was boiled in benzene with excess thionyl chloride, the acid dissolved completely in 1 hr. and the solution became yellow. The volatile materials were evaporated at reduced pressure with slight warming, and excess methanol or butanol was added. After standing overnight, the mixture was evaporated, dissolved in ether, washed with bicarbonate, and concentrated. Addition of petroleum ether (40–60°) precipitated about 20% of *p*-chlorophenylmaleic anhydride, identified by mixture m.p. and infrared spectrum. The colorless mother liquors were distilled, giving the desired esters.

The properties of the esters prepared by the various methods agreed very closely, showing that contamination by isomers were very unlikely. The data are recorded in Table III, together with the characteristics of the pure *p*-chlorophenylmaleonitrile and *p*-chlorophenylfumaronitrile isolated from the Meerwein reaction described above. The unique infrared frequencies used for analysis are also given.

Stereomutation.—A solution of 1.00 g. of *p*-chlorophenylmaleonitrile in 150 ml. of acetone was added to a solution of 5 ml. of concd. hydrochloric acid, 6 g. of sodium chloride and 1.7 g. of cupric chloride dihydrate in 75 ml. of water which had been adjusted to *p*H 3 with sodium acetate. This clear green homogeneous solution was kept at room temperature for 3 hr., then the acetone was evaporated in an air jet. The precipitated solid was recovered by filtration, washed with water and dried; 1.00 g. was isolated. The melting points of the starting and recovered materials were identical (169–171°), and a mixture of the two also melted at the same temperature.

Infrared Determination of Isomer Ratios.—Known mixtures of the stereoisomers were prepared and the infrared spectra were recorded. Carbon disulfide was used as solvent for the esters. The nitriles were too insoluble in carbon disulfide, hence acetonitrile was used. Its broad band centered at 1400 cm.$^{-1}$ overlapped somewhat the maleic frequency at 1320 cm.$^{-1}$, but this could be compensated by matched cells. The solubility of *p*-chlorophenylmaleonitrile in acetonitrile was about 2.5%, of *p*-chlorophenylfumaronitrile about 11%.

The optical densities at the absorption maxima were plotted against composition, giving straight lines.[27] The points tended to scatter slightly, but no curvature was observed. The compositions of the unknown mixtures were estimated from the working curves and checked by preparing artificial mixtures of the calculated compositions. The error of a percentage in Table I is estimated not to exceed 5%, except for *p*-chlorophenylmaleonitrile which may be twice as great because of the low solubility and the band overlap. The percentages in Table I do not total 100, indicating the presence of roughly 10% of impurity, perhaps the diarylated product.

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