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

Arylation of Unsaturated Systems by Free Radicals. II. Arylation of Maleimide by Diazonium Salts[1,2]

BY CHRISTIAN S. RONDESTVEDT, JR., AND O. VOGL

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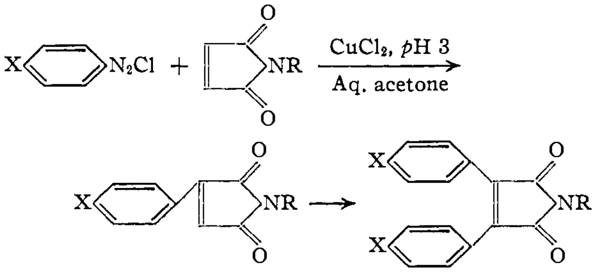
Maleimide and N-substituted maleimides are arylated by diazonium salts in aqueous acetone at *p*H 3 in the presence of cupric chloride (Meerwein reaction). α-Arylmaleimides are formed in 20–55% yield. The yield is lowest with unsubstituted phenyl and it increases with the introduction of either electron-attracting or electron-releasing substituents into the *para* position. This variation is attributed to a change in mechanism. The arylmaleimides can be hydrolyzed readily and recyclized to arylmaleic anhydrides, making available a simple, general synthetic method for these compounds. *p*-Anisyldiazonium chloride is much more reactive toward maleimide than toward other unsaturated systems. Maleimide is readily diarylated by *p*-anisyldiazonium chloride and, to a slight extent, by *p*-bromobenzene- and *p*-toluenediazonium chloride.

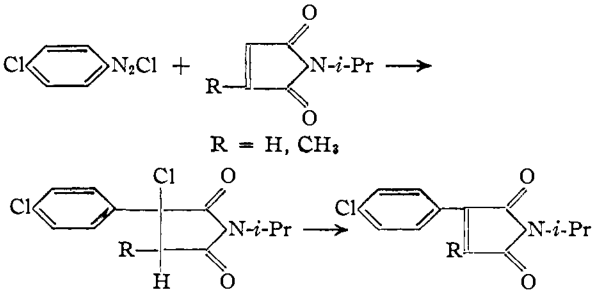
Diazonium salts arylate conjugated unsaturated systems in aqueous acetone at *p*H 3–5 in the presence of cupric salts (Meerwein reaction). For example, methyl fumarate,[3] methyl maleate,[4] butadiene,[5] acrylic acid,[6] acrylonitrile[7–9] and coumarin[3] have been converted into aryl substitution products or their hydrogen chloride addition compounds.

As part of a systematic investigation of the scope and mechanism of the Meerwein reaction, we studied the arylation of maleimide and its N-substituted derivatives[10] by *p*-substituted benzenediazonium chlorides. α-Arylmaleimides were formed in 20–55% yields. In some cases, the low yields resulted from purification difficulties. N-Phenyl-, N-ethyl- and N-isopropylmaleimide reacted similarly with *p*-chlorobenzenediazonium chloride. The structures of the products were established by alkaline hydrolysis and recyclization to arylmaleic anhydrides which, in several cases, could be compared with authentic materials. Elementary analysis and infrared spectra were consistent with the assigned structures.



I II

N-Isopropylcitraconimide reacted with *p*-chlorobenzenediazonium chloride to form N-isopropyl-α-*p*-chlorophenyl-α-chloro-α′-methylsuccinimide (III, R = CH_3), together with a small amount of N-isopropyl-α′-*p*-chlorophenylcitraconimide (IV, R = CH_3). The former was converted to the latter in high yield by brief treatment with 2,6-lutidine. N-Isopropylmaleimide behaved similarly. The formation of the hydrogen chloride addition products is not unexpected, since many examples have been reported when other unsaturated systems are arylated in the Meerwein reaction.[3] The hydrochloride addition products were not encountered with the other Meerwein reactions reported in the present paper, but they have appeared with certain other diazonium salts.[11]



III IV

p-Anisyldiazonium chloride reacted with an equimolar amount of maleimide to form not only α-*p*-anisylmaleimide (I, X = OCH_3) but also α,α′-di-*p*-anisylmaleimide (II, X = OCH_3). The latter was characterized by analysis and by conversion to α,α′-di-*p*-anisylmaleic anhydride. The relative yields of the two imides could be controlled somewhat by varying the molar ratios of the reactants. With two moles of maleimide, the yield of II dropped to about 5%; with 2 moles of *p*-anisyldiazonium chloride, II was formed in 35% yield. A small amount of di-*p*-bromophenylmaleimide was isolated from an experiment with equimolar amounts of *p*-bromoaniline and maleimide. *p*-Toluenediazonium chloride in excess produced a small amount of II (X = CH_3) which could not be isolated as such, but it was obtained when the entire crude product was converted to a mixture of anhydrides which was separated by distillation and crystallization. Diarylation was not detected with other *p*-substituted diazonium salts.

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[1] Paper I, C. S. Rondestvedt, Jr., and H. S. Blanchard, THIS JOURNAL, **77**, 1769 (1955).

[2] Presented before the American Chemical Society Meeting, September, 1954.

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

[4] E. C. Taylor, Jr., and E. J. Strojny, THIS JOURNAL, **76**, 1872 (1954).

[5] E. C. Coyner and G. A. Ropp, *Org. Syntheses*, **31**, 80 (1951).

[6] J. Rai and K. B. L. Mathur, *J. Indian Chem. Soc.*, **24**, 413 (1947).

[7] C. F. Koelsch, THIS JOURNAL, **65**, 57 (1943); C. F. Koelsch and V. Boekelheide, *ibid.*, **66**, 412 (1944).

[8] S. Malinowski, *Roczniki Chem.*, **26**, 85 (1952); *C. A.*, **48**, 620 (1954).

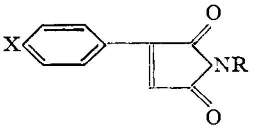
[9] W. Brunner and H. Perger, *Monatsh.*, **79**, 187 (1948); W. H. Brunner and J. Kustatscher, *ibid.*, **82**, 100 (1951).

[10] Maleic anhydride was thought to be unsuitable since it is readily hydrolyzed in aqueous medium to maleic acid; the latter is reported to form cinnamic acids under Meerwein's conditions; *cf.* J. Rai and K. B. L. Mathur, *J. Indian Chem. Soc.*, **24**, 383 (1947).

[11] C. S. Rondestvedt, Jr., and O. Vogl, unpublished experiments.

TABLE I

α-ARYLMALEIMIDES



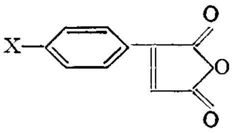
X	R	M.p., °C.	Yield, %	Crystn. solvents[a]	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
NO_2	H	212–213	36	Me_2CO	$C_{10}O_6O_4N_2$	55.05	55.02	2.77	2.85	12.84	13.10
Br	H	199–200	47	Et_2O	$C_{10}H_6O_2NBr$	47.65	47.63	2.40	2.42	5.56	5.52
Br[b]	H	210–212	..	Et_2O	$C_{16}H_9O_2NBr_2$	47.32	47.08	2.23	2.32	3.45	3.19
Cl	H	187–188	37	Et_2O; Me_2CO–P	$C_{10}H_6O_2NCl$	57.85	57.59	2.91	2.89	6.75	6.99
Cl	C_6H_5	153–154	33	EtOH	$C_{16}H_{10}O_2NCl$	67.77	67.62	3.55	3.63	...	...
Cl	C_2H_5	118–119	27	EtOH; Et_2O–P	$C_{12}H_{10}O_2NCl$	61.16	61.14	4.28	4.32	5.95	6.31
Cl	i-C_3H_7	102–104	51	Et_2O–P	$C_{13}H_{12}O_2NCl$	62.53	62.63	4.84	4.94	...	...
H	H	167–168	21	CH_2Cl_2–P	$C_{10}H_7O_2N$	69.36	69.45	4.07	4.12	8.09	8.23
CH_3	H	186–187	28	EtOH; Et_2O–P	$C_{11}H_9O_2N$	70.58	70.54	4.85	5.13	...	...
CH_3O	H	189–190	45[e]	Me_2CO–P; Et_2O	$C_{11}H_9O_3N$	65.02	64.93	4.46	4.81	...	...
CH_3O[c]	H	240–241	35[e]	Me_2CO	$C_{18}H_{15}O_4N$	69.89	69.90	4.89	4.89	4.53	4.89
Cl[d]	i-C_3H_7	78–79	56	Et_2O–P	$C_{14}H_{14}O_2NCl$	63.72	63.83	5.35	5.37	5.32	5.62

[a] P = petroleum ether (60–75°). [b] Di-*p*-bromophenylmaleimide; being less soluble than *p*-bromophenylmaleimide, it is concentrated in the first crops during crystallization. [c] Di-*p*-anisylmaleimide. [d] N-Isopropyl-α′-*p*-chlorophenylcitraconimide (IV, R = CH_3). [e] See Experimental.

The results of these experiments are presented in Tables I and II.

TABLE II

ARYLMALEIC ANHYDRIDES



X	M.p., °C.	B.p., °C.	B.p., Mm.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
CH_3O	143–144	150	0.1	$C_{11}H_8O_4$	64.70	64.50	3.95	4.13
CH_3O[a]	170–171	175	.1	$C_{18}H_{14}O_5$	69.67	69.65	4.55	4.75
CH_3	108–109	140	.1	$C_{11}H_8O_3$	70.21	69.98	4.29	4.31
CH_3[b]	167–169	155	.1	$C_{18}H_{14}O_3$	77.68	77.63	5.07	5.06
[c]	116–117	165	.2	$C_{14}H_8O_3$	74.99	75.00	3.60	3.67
[d]	167–168	160	.1	$C_{14}H_8O_3$	74.99	74.68	3.60	3.71

[a] Di-*p*-anisylmaleic anhydride. [b] Di-*p*-tolylmaleic anhydride. [c] 1-Naphthylmaleic anhydride. [d] 2-Naphthylmaleic anhydride.

Discussion

The most unusual result of the present experiments is the surprising reactivity of *p*-anisyl- and *p*-toluenediazonium salts toward maleimide. The literature indicates that the yield in a Meerwein reaction is best when the diazonium salt is substituted with electron-attracting groups, and it decreases markedly (for a given unsaturated substituent) descending the series $NO_2 > Hal > H > Alkyl > CH_3O$.[6,9,12] This descending series, typical of an electrophilic reaction, has been used as an argument in support of a carbonium-ion mechanism.[3,9,12a] With maleimide, on the contrary, *p*-methoxy and *p*-methyl substituents actually are "activating," so much so that diarylation becomes a prominent side reaction in the former case.

We will defer a detailed discussion of the mechanism of the Meerwein reaction to a later paper, when more experimental work has been completed. Both carbonium-ion and free radical[6,7,10,13] mechanisms have been advanced. A third mechanism also must be considered: an intermediate complex may form at *p*H 3 among diazonium salt, cupric chloride and the unsaturated system, favorably influenced by the solvent acetone.[14] The complex then decomposes by internal one-electron shifts to form products.

NOTE ADDED IN PROOF.—Recently Denivelle and Razair[14a] reported the arylation of maleic acid at *p*H 1. They obtained some of the same mono- and diaryl-maleic anhydrides, with physical properties agreeing with ours. The difference between their results and those of Rai and Mathur[10] at *p*H *ca.* 3 points out the importance of *p*H in the Meerwein reaction.

Experimental[15]

Arylation of Maleimides. General Procedure.—The amine (0.1 mole) was dissolved in 30 ml. of concd. hydrochloric acid and 20 ml. of water by warming. The solution was cooled rapidly to 0–5° with stirring, 20 g. of ice was added, and the suspension was diazotized with 30% sodium nitrite solution with vigorous stirring at 0–5°. (The yield and quality of the product depend on the care taken during diazotization.) The filtered diazonium solution was added all at once to an ice-cold suspension of 0.1 mole of the maleimide derivative in 30 ml. of acetone (in some cases, excess maleimide was used), and the mixture was brought to *p*H 3 by addition of concd. sodium acetate solution or crystalline sodium acetate trihydrate. To the resulting suspension was added 2.55 g. (0.015 mole) of cupric chloride dihydrate and enough more acetone to make a homogeneous solution. Evolution of nitrogen began almost immediately in most cases. After 0.5 hour at 0–5°, the mixture was warmed to 35–40° with continuous stirring and there maintained for 3 hours or overnight.

The two-phase mixture was stripped of acetone *in vacuo* without heating. The solid precipitate was collected, washed with water, and dried. The crude product usually represented a high yield, but it often was recrystallized only with difficulty. Sublimation at 0.1 mm. was sometimes helpful for preliminary purification of the crude material. The pure arylmaleimides (I) were yellow, and usually nicely crystalline. Additional details are given below and in Table I.

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[12] (a) P. L'Ecuyer and C. A. Olivier, *Can. J. Research*, **28B**, 648 (1950); (b) F. Bergmann and D. Schapiro, *J. Org. Chem.*, **12**, 57 (1947).

[13] E. Müller, *Angew. Chem.*, **61**, 179 (1949).

[14] The effects of solvent, *p*H and metal salt catalyst will be discussed in a subsequent paper, now in preparation.

[14a] L. Denivelle and D. Razair, *Compt. rend.*, **237**, 570 (1953); *C.A.*, **48**, 12038 (1954).

[15] Microanalyses by Anna Griffin in these laboratories. Melting points are uncorrected. Boiling points, except where noted, are air-bath temperatures. Distillations were conducted in a short-path bulb tube heated by an air-bath. The maleimides were generously donated by the U. S. Rubber Co.

***p*-Anisyldiazonium Chloride and Maleimide.**—The crude product from 0.1 mole each of *p*-anisidine and maleimide was treated with acetone. There remained 3.8 g. (16%) of yellow crystals of di-*p*-anisylmaleimide (II, X = OCH_3) which were practically insoluble in acetone, benzene, ether, alcohol or chloroform. They were crystallized from a large volume of acetone. A portion of the I (X = OCH_3) was recovered from the acetone-soluble fraction by dilution with petroleum ether (60–75°). The filtrate and the crystalline material were sublimed separately at 160° (0.1 mm.). The combined solid sublimates were crystallized; yield of pure I, 29%. With two moles of *p*-anisidine per mole of maleimide, the yield of II was 35%.

In another experiment with 1.5 moles of maleimide per mole of *p*-anisidine, the crude product was hydrolyzed directly (see below) and the anhydrides were separated by distillation-sublimation. The yield of *p*-methoxyphenylmaleic anhydride was 45% and of di-*p*-methoxyphenylmaleic anhydride 6%.

***p*-Toluenediazonium Chloride and Maleimide.**—The runs with a 1:1 mole ratio are described in Table I. With 0.1 mole of *p*-toluenediazonium chloride and 0.05 mole of maleimide, the di-*p*-tolylmaleimide (II, X = CH_3) could not be isolated, since its solubility was similar to that of I (X = CH_3). Accordingly, the entire crude product was hydrolyzed (see below) and recyclized by heating for 15 min. at 150–160°. The mixed anhydrides were distilled and then fractionated. The first fraction, b.p. to 145° (0.1 mm.), was *p*-tolylmaleic anhydride. The fraction boiling 145–170° (0.1 mm.) was crystallized once from methylene chloride–petroleum ether. The distillation and crystallization operations were repeated three times, giving finally 0.15 g. of pure di-*p*-tolylmaleic anhydride.

***p*-Chlorobenzenediazonium Chloride and N-Isopropylcitraconimide.**—From 0.1 mole of each reagent, the general procedure yielded 22 g. of an oily product. The oil was dissolved in ether, washed several times with water to remove acetic acid, dried and distilled. After a little forerun of unchanged N-isopropylcitraconimide, an orange-yellow oil distilled at 160–163° (0.1 mm.) (vapor temp.). Analysis of a center cut of redistilled material showed that the product was mostly N-isopropyl-α-methyl-α′-*p*-chlorophenyl-α-chlorosuccinimide (III, R = CH_3). Five grams of this product was heated briefly with 20 ml. of 2,6-lutidine near its boiling point; precipitation of 2,6-lutidine hydrochloride was rapid. The mixture was partitioned between water and ether, the excess lutidine was removed by washing with dilute acid and water, and the ether layer was dried and again distilled, b.p. 150–155° (0.1 mm.). The solid distillate (IV, R = CH_3) was recrystallized from ether–petroleum ether.

***p*-Chlorobenzenediazonium Chloride and N-Isopropylmaleimide.**—The general procedure yielded 25 g. of an oil from 0.1 mole of each reactant. The product decomposed on attempted distillation. Five grams was treated with 15 ml. of 2,6-lutidine as above and diluted with 25 ml. of benzene, giving 1.65 g. of 2,6-lutidine hydrochloride (calcd. for pure N-isopropyl-α-*p*-chlorophenyl-α′-chlorosuccinimide (III, R = H), 2.5 g.); the oil is evidently a mixture of the latter product with I (X = Cl, R = C_3H_7). The benzene solution was partitioned between ether and water, washed free of lutidine with acid and water, dried and evaporated. The I crystallized directly and was recrystallized from ether–petroleum ether. The crystals and the mother liquors were distilled (b.p. 135–140° (0.1 mm.)) separately, combined and recrystallized.

Since the N-isopropyl derivatives are readily distilled, it may be desirable to use N-isopropylmaleimide instead of maleimide to facilitate separation from the inevitable tars. The yield of pure material seems to be enhanced.

2-Naphthalenediazonium Chloride and Maleimide.—The tarry residue obtained from 0.05 mole each of 2-naphthylamine and maleimide by the general procedure was hydrolyzed immediately with 80 ml. of 25% NaOH. After cyclization at 160–170°, the 2-naphthylmaleic anhydride was distilled. Pure 2-naphthylmaleimide was not isolated. The experiment with 1-naphthylamine was similar.

Saponification of Arylmaleimides. Arylmaleic Anhydrides.—The maleimide (either purified material or the crude product directly from the reaction) was boiled for 4–6 hours with excess 25% sodium hydroxide solution. In some cases, a little alcohol was added. After the evolution of ammonia had ceased, the mixture was diluted with water, extracted with ether and acidified with sulfuric acid. The arylmaleic acid was collected by filtration or, when quite water-soluble, by continuous ether extraction. There was no significant amount of isomerization to the arylfumaric acid[4] during these procedures. The crude arylmaleic acid was cyclized by heating above its melting point for 10–30 min. or by refluxing for 30 min. with excess acetic anhydride followed by vacuum evaporation of the acetic acid and anhydride. If a crude maleimide was used, the anhydride was then distilled before crystallization, but this was unnecessary when starting with purified maleimide. The anhydrides were crystallized from methylene chloride–petroleum ether (60–75°) or ether–petroleum ether. Difficulty was encountered in the hydrolysis of α-*p*-nitrophenylmaleimide. Details are given in Table II.

Phenylmaleic anhydride prepared in this way (m.p. 119–120°) was identical with samples prepared by other routes.[16] Our sample of *p*-chlorophenylmaleic anhydride (m.p. 149–150°) corresponded to that reported by Meerwein.[3] The *p*-methoxyphenylmaleic anhydride was identical with a sample later synthesized by Miller[17] by another route.

Acknowledgment.—We are indebted to the Horace H. Rackham Fund of the University of Michigan for a grant in support of this work.

ANN ARBOR, MICHIGAN

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[16] C. S. Rondestvedt, Jr., and A. H. Filbey, *J. Org. Chem.*, **19**, 119 (1954).

[17] We are indebted to Dr. L. E. Miller for making the comparison and for informing us of the progress of his synthesis.

[COMMUNICATION NO. 1705 FROM THE KODAK RESEARCH LABORATORIES, EASTMAN KODAK COMPANY]

The Structure of Certain Diphenylcyclopentenones

BY C. F. H. ALLEN AND J. A. VANALLAN

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The substance long believed to be 3,4-diphenyl-3-cyclopentenone has been shown to be the 2-cyclopentenone. Certain other related structures have been corrected, including several chloroketones about which there has previously been some uncertainty.

Many years ago, while attempting to elucidate the structure of anhydroacetonebenzil (I), Japp[1,2] carried out a reduction of the substance with hydrogen iodide, and obtained a product to which was assigned the structure 3,4-diphenyl-3-cyclopentenone (II). This formulation appears to have been accepted without question ever since, in spite of certain anomalous reactions. Most outstanding of these is ozonization, which gave desylacetic acid (III).[3] *A priori*, it would be expected that in a structure such as II, the two phenyl

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[1] F. R. Japp and C. I. Burton, *J. Chem. Soc.*, **51**, 420 (1887).

[2] F. R. Japp and G. D. Lander, *ibid.*, **71**, 123 (1897).

[3] H. Burton and C. W. Shoppee, *ibid.*, 567 (1939).