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

Arylation of Unsaturated Systems by Free Radicals. III. The Action of Radical Generators upon Coumarin[1]

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Coumarin is arylated by free radicals from benzoyl peroxide, N-nitrosoacetanilide, 1-phenyl-3,3-dimethyltriazene and the correspondng *p*-nitro compounds. The 3-arylcoumarins are formed in much lower yields than when the arylating agent is a diazonium salt promoted by cupric chloride (Meerwein reaction). Acrylonitrile and acrylic acid are not arylated by N-nitrosoacetanilides nor 1-phenyl-3,3-dimethyltriazene, although the Meerwein reaction gives good yields. These results imply that *free* radicals are not intermediates in the Meerwein reaction.

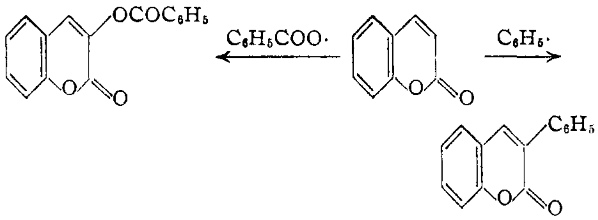
Aromatic rings are arylated by several different reagents, notably benzoyl peroxides, N-nitrosoacetanilides, 1-aryl-3,3-dimethyltriazenes and diazonium salts in alkaline medium.[3] These reagents are thought to decompose to free aryl radicals which then attack the aromatic ring. Quinones are arylated by diazonium salts, often in high yields.[4] Still less aromatic systems, such as found when olefinic double bonds are conjugated with vinyl, aryl, carbonyl and cyano groups, are attacked by diazonium salts in the presence of cupric chloride at *p*H 3 with substitution of aryl for hydrogen or addition of aryl and halide groups to the conjugated system.[1,5] This so-called Meerwein reaction has been regarded as a free-radical process,[6] though others have stated that carbonium ions are involved.[5,7-9]

To distinguish these possibilities, it was of interest to decompose known free radical generators in the presence of an olefinic double bond known to undergo the Meerwein reaction. Many of the common unsaturated systems, such as acrylonitrile and acrylic acid, are polymerized by benzoyl peroxide and N-nitrosoacetanilide.[10] Therefore, coumarin was selected for this study since it is not readily polymerized and since it also affords an opportunity to compare aromatic ring arylation with double-bond arylation. The less reactive radical generators also were tried with acrylonitrile and acrylic acid.

Aroyl Peroxides.—Meerwein[5] obtained a 26% yield of 3-phenylcoumarin and a 50% yield of 3-*p*-nitrophenylcoumarin from the corresponding diazonium salts in acetone solvent.[11] We obtained lower yields of 3-arylcoumarins when benzoyl and *p*-nitrobenzoyl peroxides were decomposed in the presence of coumarin in acetone, butanone, acetonitrile and ethyl acetate; the yield in glycol dimethyl ether solvent was nil.

A benzoxycoumarin was a by-product from benzoyl peroxide decompositions.[12] After the reaction product had been freed from the benzoic acid normally formed in peroxide decompositions, it exhibited bands in the infrared at 7.82, 8.45, 9.40 and 13.02 μ, in addition to the complete spectrum of 3-phenylcoumarin. The first two mentioned are said to be characteristic of benzoate esters.[13] These four bands disappeared upon alkaline hydrolysis, and an additional quantity of benzoic acid was formed; 3-phenylcoumarin was reformed upon acidification, but 3-hydroxycoumarin (or its tautomer) was not isolated. The benzoxy group is assumed to be in position 3, since this appears to be the most reactive site in the coumarin molecule for free radical attack. No evidence was obtained for any isomeric phenylcoumarins, hence the conjugated unsaturated "side chain" is more reactive toward radicals than the aromatic ring. The quantity of benzoate ester was larger when the decompositions were carried out in the higher-boiling

$$(C_6H_5COO)_2 \longrightarrow C_6H_5COO\cdot \longrightarrow C_6H_5\cdot$$



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[1] Paper II, C. S. Rondestvedt, Jr. and O. Vogl, THIS JOURNAL, **77**, 2313 (1955).

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[3] For references, see C. S. Rondestvedt, Jr., and H. S. Blanchard, THIS JOURNAL, **77**, 1769 (1955).

[4] D. E. Kvalnes, *ibid.*, **56**, 2478 (1934); K. Schimmelschmidt, *Ann.*, **566**, 184 (1950).

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

[6] C. F. Koelsch and V. Boekelheide, THIS JOURNAL, **66**, 412 (1944).

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

[8] F. Bergmann and D. Schapiro, *J. Org. Chem.*, **12**, 57 (1947), and previous papers.

[9] P. L'Ecuyer and C.-A. Olivier, *Can. J. Research*, **28B**, 648 (1950), and previous papers.

[10] A. T. Blomquist, J. R. Johnson and H. J. Sykes, THIS JOURNAL, **65**, 2446 (1943).

[11] C. S. Rondestvedt, Jr. and O. Vogl, *ibid.*, in press, have noted that solvents with no unsaturation are decidedly inferior.

[12] Benzoxylation frequently occurs when benzoyl peroxides are decomposed in the presence of reactive molecules. For example, P. D. Bartlett and S. G. Cohen, *ibid.*, **65**, 543 (1943), have observed incorporation of benzoxy groups into polymer molecules, although more commonly aryl groups are introduced [C. C. Price, R. W. Kell and E. Krebs, *ibid.*, **64**, 2508 (1942)]. Highly reactive aromatic systems are benzoxylated, rather than phenylated; R. L. Dannley and M. Gippin, *ibid.*, **74**, 332 (1952), obtained a mixture of α- and β-naphthyl benzoates by decomposition of benzoyl peroxide in naphthalene.

[13] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, Chapter 11.

solvents butanone and acetonitrile than when performed in acetone. No 3-*p*-nitrobenzoxycoumarin was observed with *p*-nitrobenzoyl peroxide.

1-Aryl-3,3-dimethyltriazenes.—These triazenes decompose in the presence of acetic acid or hydrogen chloride at 80–100° to form free radicals which arylate aromatic rings.[3,14] It appears that dimethylamine is displaced from the initially protonated triazene by the anion A to form a covalent diazo acetate or chloride which then decomposes homolytically

$$\mathrm{ArN{=}NN(CH_3)_2 + HA \longrightarrow}$$
$$\mathrm{[ArN{=}NA] + HN(CH_3)_2{\cdot}HA \dashrightarrow Ar\cdot + N_2 + A\cdot}$$
$$\mathrm{A = OAc,\ Cl}$$

Coumarin was not attacked by 1-*p*-nitrophenyl-3,3-dimethyltriazene in boiling glycol dimethyl ether solvent in the presence of stoichiometric quantities of acetic acid or perfluorobutyric acid, and only a trace of 3-*p*-nitrophenylcoumarin was obtained using hydrogen chloride in this solvent. However, a 25% yield of 3-*p*-nitrophenylcoumarin was obtained, together with substantial amounts of nitrobenzene, on heating the triazene and coumarin in acetic acid solvent overnight. Lower yields were obtained in formic or propionic acids. A purple dye also was formed in these experiments (azo coupling?). No 3-phenylcoumarin could be isolated from similar reactions with 1-phenyl-3,3-dimethyltriazene, and most of the coumarin was recovered.

In an experiment with 1-*p*-nitrophenyl-3,3-dimethyltriazene and acrylic acid in acetic acid solvent, no *p*-nitrocinnamic acid was detected[15]; only a little polyacrylic acid was formed.

N - Nitrosoacetanilides.—N - Nitrosoacetanilide produced no 3-phenylcoumarin when allowed to decompose in the presence of coumarin in *t*-butyl alcohol solution. N-Nitroso-*p*-nitroacetanilide, with the same conditions, formed 3-*p*-nitrophenylcoumarin in 21% yield. Other solvents were less satisfactory (see Experimental). An attempt to promote the reaction with a small amount of cupric acetate caused extensive denitrosation, and the yield of product was much lower. N-Nitrosoacetanilides are relatively inefficient and slow catalysts for polymerization,[10] but they arylate aromatic rings with great speed.[3] N-Nitroso-*p*-nitroacetanilide was allowed to decompose in acetone solutions of acrylonitrile or acrylic acid. Neither *p*-nitrocinnamonitrile nor *p*-nitrocinnamic acid could be detected. It is unlikely that appreciable quantities of either compound would have escaped detection, in view of their solubilities. Small amounts of polyacrylonitrile or polyacrylic acid were formed. However, a substantial amount of *p*-nitroacetanilide was recovered, indicating that denitrosation had taken place in solution. In all of these experiments, substantial amounts of purple dye were formed; its structure was not investigated.

Discussion

From our results it appears that "free" aryl radicals of the type involved in arylation of aromatic rings do not enter into the Meerwein reaction. In aromatic arylations, peroxides usually give the best yields and alkaline diazonium salts the worst. Further, cupric salts are not effective catalysts. In arylations of conjugated unsaturated systems, the diazonium salts (plus cupric chloride) are far superior to peroxides, triazenes and N-nitrosoacetanilides. This difference is particularly noticeable with the aliphatic compounds acrylic acid and acrylonitrile, where diazonium salts give satisfactory yields but the other reagents give none at all, either owing to polymerization or to the dominance of competitive side reactions. The absence of addition polymerization in the Meerwein reactions described in the literature, even with readily polymerized systems, argues strongly against the participation of "free" radicals.

For these reasons, a simple free-radical mechanism[6,16] does not fully explain the Meerwein reaction. On the other hand, the carbonium ion mechanism is inconsistent with the direction of addition of the supposed aryl cation to compounds such as acrylates, cinnamates, etc., since the normal polarization of these systems $\overset{\delta^+}{\mathrm{C}}{=}\mathrm{C}{-}\mathrm{C}{=}\overset{\delta^-}{\mathrm{O}}$ would require the opposite orientation. Since Koelsch's mechanism,[6] involving addition to form the more stable free radical intermediate, accurately accounts for all known orientation phenomena, we feel that the homolytic character of the reaction is established, but that the reaction is "radicaloid" rather than "free" radical. An intermediate complex such as that suggested previously[1] could accommodate these facts and explain the Meerwein reaction.[17] A more detailed formulation of this complex will be presented at the close of experimental work now in progress.

Experimental[18]

Benzoyl Peroxide and Coumarin. Acetone.—Benzoyl peroxide (7.5 g.) and coumarin (4.5 g.) were boiled with 70 ml. of acetone for 5 days. The acetone was evaporated, and the residue was taken up in ether and shaken several times with sodium bicarbonate solution. The residue from the ether layer (7.4 g.) was distilled. Unreacted coumarin (1.4 g.) was collected below 140° (0.01 mm.), followed by 2.0 g. of a yellow, viscous oil from 150–200°. The residue weighed 4.0 g.

The oil was crystallized from alcohol, yielding 0.30 g. (4.5%) of 3-phenylcoumarin, m.p. 138–140°, identical with 3-phenylcoumarin prepared by Meerwein's procedure.[5]

Butanone.—The above procedure was followed with the same quantities of materials in 70 ml. of butanone. Following the coumarin fraction, 3.0 g. of a yellow oil distilled from 140–210° (0.01 mm.) (mostly 170–180°), leaving a residue of 3.2 g. The oil, which could not be crystallized readily, was hydrolyzed with 1 *N* aqueous alcoholic alkali by refluxing for 2 hr. The solution was concentrated, diluted with water, and acidified to cause cyclization of the coumaric acids. The mixture was extracted thoroughly with ether, and the ether solution was extracted with sodium bicarbonate solution. From the bicarbonate solution was isolated 0.35 g. of benzoic acid by acidification, extraction with ether, distillation and recrystallization.

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[14] J. Elks and D. H. Hey, *J. Chem. Soc.*, 441 (1943).

[15] J. Rai and K. B. L. Mathur, *J. Indian Chem. Soc.*, **24**, 413 (1947), obtained a 60% yield of *p*-nitrocinnamic acid from acrylic acid and *p*-nitrobenzenediazonium chloride under Meerwein's conditions (without acetone).

[16] *Cf.* E. Müller, *Angew. Chem.*, **61**, 179 (1949); also see reference 15 and previous papers cited therein.

[17] A similar complex is suggested for free-radical aromatic arylation; C. S. Rondestvedt, Jr., and H. S. Blanchard, manuscript in preparation.

[18] Melting points are uncorrected. Distillations were carried out in a short-path bulb tube heated in an air-bath; boiling points recorded are bath temperatures. Infrared curves were taken by M. Yoshimine.

The ether solution of neutral materials was distilled, giving 0.30 g. of additional coumarin and 0.25 g. (4%) of 3-phenylcoumarin, m.p. 139–140° after crystallization. The recovery is low partly because of decomposition and isomerization of the coumaric acids in alkaline medium. 3-Hydroxycoumarin was not isolated.

Glycol Dimethyl Ether.—From a similar reaction in boiling glycol dimethyl ether, no 3-phenylcoumarin could be isolated.

Ethyl Acetate.—From a similar experiment in ethyl acetate solvent, 0.21 g. (3%) of 3-phenylcoumarin was obtained by distillation and crystallization. Hydrolysis of the residue afforded 0.05 g. of benzoic acid.

Acetonitrile.—The same quantities were boiled for 5 days in 75 ml. of acetonitrile. The solvent was evaporated, and the residue was dissolved in ether and extracted with sodium carbonate solution to yield 3.3 g. of benzoic acid. The ether solution was distilled, giving 3.5 g., b.p. 110–180° (0.1 mm.), and 4.0 g. of residue. The distillate was redistilled, yielding 1.6 g. of coumarin, b.p. 120–135° (0.1 mm.), and 1.8 g. of a solid, b.p. 145–160° (0.1 mm.). The solid was recrystallized from alcohol. The first crop, 0.2 g., m.p. 166–170°, was not investigated further. The second crop, 0.72 g., m.p. 123–125°, could not be purified further by crystallization. The third crop, 0.35 g. (5%), m.p. 137–138°, was 3-phenylcoumarin.

Microanalysis of the second crop gave low values for carbon and hydrogen, and its infrared spectrum showed the presence of benzoate esters. The mixture was heated with 25% aqueous sodium hydroxide until it just dissolved, then cooled and acidified. The mixture was extracted with ether, and the benzoic acid was separated by bicarbonate extraction. The ether extract was evaporated and the residue was crystallized from alcohol, giving pure 3-phenylcoumarin (36% recovery), m.p. 137–138.5°, whose spectrum was identical with that of an authentic sample. The total yield was thus 9%.

***p*-Nitrobenzoyl Peroxide and Coumarin. Butanone.**—A solution of 5.1 g. of *p*-nitrobenzoyl peroxide and 2.3 g. of coumarin in 50 ml. of butanone was boiled for 4 days. On chilling, the solution deposited 0.58 g. (14%) of 3-*p*-nitrophenylcoumarin, m.p. 259–263°. It was crystallized from boiling anisole, m.p. 262–263°. The residue from evaporating the butanone filtrate was completely soluble in acetone. (Advantage was taken of the fact that 3-*p*-nitrophenylcoumarin is practically insoluble in cold acetone, while the by-products are readily soluble.) The residue, after evaporation of the acetone, yielded 2.6 g. of *p*-nitrobenzoic acid, m.p. 234–236°, through bicarbonate separation.

Acetone.—A similar experiment in acetone solvent yielded 0.71 g. (17%) of 3-*p*-nitrophenylcoumarin, m.p. 243–255°; recrystallized from anisole, m.p. 261–263°. After removal of *p*-nitrobenzoic acid from the acetone-soluble fraction, distillation afforded 1.5 g. of coumarin and 1.4 g. of residue.

Glycol Dimethyl Ether.—A similar reaction in this solvent produced no detectable 3-*p*-nitrophenylcoumarin.

Acetonitrile.—A mixture of 10.3 g. of *p*-nitrobenzoyl peroxide and 4.5 g. (0.03 mole) of coumarin in 120 ml. of acetonitrile was boiled for 4 days. The solvent was removed and the residue was allowed to stand at 0° overnight with 100 ml. of acetone; 1.52 g. of yellow crystals, m.p. 253–256°, were insoluble. After recrystallization from 20 ml. of anisole, there remained 1.40 g., m.p. 260–262°. The acetone was evaporated and the residue was partitioned between ether and potassium carbonate solution. The ether layer was filtered, dried and evaporated, leaving 4.85 g. of brownish oil which deposited an additional 0.09 g. of 3-*p*-nitrophenylcoumarin (total 1.61 g., 20%) when treated with 20 ml. of cold acetone. The filtrate was distilled, giving 2.16 g. of nearly pure coumarin and 2.07 g. of residue. The carbonate solution yielded 6.3 g. of *p*-nitrobenzoic acid when acidified.

1-Phenyl-3,3-dimethyltriazene and Coumarin. Acetic Acid.—A solution of 7.5 g. of the triazene and 7.5 g. of coumarin was boiled in acetic acid for 7 hours. The solvent was removed and the residue was poured into ice-cold 2% sodium hydroxide solution. The crystalline coumarin (6.1 g.) was removed, but no 3-phenylcoumarin could be isolated.

1-*p*-Nitrophenyl-3,3-dimethyltriazene and Coumarin. Acetic Acid.—A solution of the triazene (3.01 g.) and coumarin (2.3 g.) in acetic acid was heated on the steam-bath for 12 hr. The solvent was removed at reduced pressure, and the residue was triturated with acetone. The crude 3-*p*-nitrophenylcoumarin, m.p. 250–255°, was stirred with fresh acetone, leaving 0.82 g. (25%) of 3-*p*-nitrophenylcoumarin which, after crystallization from anisole, melted at 261–263°. When the acetone-soluble portion was distilled, 0.8 g. of impure nitrobenzene was collected, leaving 3.15 g. of brown, oily residue.

Formic Acid.—A similar experiment, in which double quantities of the reagents were boiled in formic acid for 18 hr., gave 0.82 g. of 3-*p*-nitrophenylcoumarin (12%) and 0.55 g. of impure nitrobenzene.

Propionic Acid.—In boiling propionic acid for 9 hr., the same procedure afforded 0.55 g. of 3-*p*-nitrophenylcoumarin (16%) and 0.55 g. of impure nitrobenzene from 3.01 g. of triazene and 2.3 g. of coumarin.

Glycol Dimethyl Ether.—When the reagents were boiled overnight with an equivalent quantity of acetic acid in glycol dimethyl ether, both starting materials were recovered. With perfluorobutyric acid in this solvent, reaction took place but 3-*p*-nitrophenylcoumarin was not isolated. When dry hydrogen chloride was passed through the boiling solution of 6.0 g. of the triazene and 4.5 g. of coumarin in this solvent for 12 hr., only 0.3 g. of 3-*p*-nitrophenylcoumarin, m.p. 240–245°, was obtained, together with 1.85 g. of nitrobenzene; very little coumarin was recovered.

1-*p*-Nitrophenyl-3,3-dimethyltriazene and Acrylic Acid.—When 6.0 g. of triazene and 2.6 g. of acrylic acid were boiled for 12 hr. in acetic acid solvent, no *p*-nitrocinnamic acid was formed, but a little polyacrylic acid appeared.

N-Nitroso-*p*-nitroacetanilide and Coumarin.—*p*-Nitroacetanilide was nitrosated with nitrosyl chloride by the method of DeTar.[19] The nitroso derivative from 17.0 g. of *p*-nitroacetanilide was stirred with 14.6 g. of coumarin in 200 ml. of *t*-butyl alcohol. Nitrogen evolution commenced in 10 min. The temperature rose gradually from 25–35° during 1 hr. After 3 hr., evolution of nitrogen had ceased, but the mixture was stirred overnight at room temperature. The solvent was removed *in vacuo* and the residue was poured into water. After chilling, the water was decanted and the residue treated with acetone. The acetone-insoluble 3-*p*-nitrophenylcoumarin weighed 5.3 g., m.p. 255–258°. An additional 0.3 g. was recovered from the acetone mother liquor by concentration; total yield, 21%. The acetone was concentrated further, and addition of ether precipitated 4.5 g. of a purple dye; an additional 0.8 g. of dye was obtained by concentration. Evaporation to dryness and addition of anhydrous ether left 2.0 g. of a brown solid.

The nitroso derivative from 10 g. of *p*-nitroacetanilide was dissolved in 100 ml. of ethylene glycol dimethyl ether containing 8.0 g. of coumarin. With stirring, 5 ml. of 1 *N* aqueous cupric acetate was added. Stirring was continued overnight. The mixture was concentrated and poured into water. After chilling, the solid was dissolved in acetone, leaving 0.45 g. (4%) of 3-*p*-nitrophenylcoumarin. From the acetone, 7 g. of pure *p*-nitroacetanilide was recovered.

N-Nitrosoacetanilide and Coumarin.—The nitroso derivative[19] from 9.0 g. of acetanilide was stirred with a solution of 10 g. of coumarin in 100 ml. of *t*-butyl alcohol overnight. The insoluble purple precipitate (2.5 g., m.p. 145–150°) was removed. No 3-phenylcoumarin could be isolated from the filtrate, although a great deal of coumarin was present.

N-Nitroso-*p*-nitroacetanilide and Acrylonitrile.—The nitroso derivative from 18 g. of *p*-nitroacetanilide in 200 ml. of acetone was treated with 5.3 g. (0.1 mole) of acrylonitrile in 80 ml. of acetone. After stirring overnight, the mixture was evaporated and extracted with chlorobenzene. No *p*-nitrocinnamonitrile could be detected, though 5.2 g. of *p*-nitroacetanilide was recovered.

N-Nitroso-*p*-nitroacetanilide and Acrylic Acid.—From 10 g. of *p*-nitroacetanilide and 4.0 ml. of acrylic acid in acetone, there was obtained 3.0 g. of purple dye, m.p. 185–200°. No *p*-nitrocinnamic acid was found.

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[19] D. F. DeTar, THIS JOURNAL, **73**, 1448 (1951).