[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

The Condensation of Aromatic Nitro Compounds with Arylacetonitriles.[1,2] III. Some *ortho*- and *meta*-Substituted Nitrobenzenes

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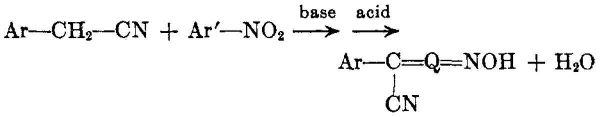
A number of substituted nitrobenzenes containing methyl, methoxy and chloro groups in positions *ortho* and *meta* to the nitro group and also 1-nitronaphthalene condense with some arylacetonitriles to yield new arylacetonitriles having quinone-like substituents in the position alpha to the cyano group. Evidence bearing on the structures of the products is presented. Some observations are made concerning the reaction conditions.

It has been found that some aromatic nitro compounds condense with arylacetonitriles in methanolic potassium hydroxide solution, yielding products having quinone-like structures. When nitrobenzene is used in such reactions, the *para* position is the preferred position of attack, and the products are compounds which we referred to as arylcyanomethylenequinone oximes.[3] (It has subsequently been called to our attention that these compounds are more properly named as derivatives either of cyclohexadienone or of acetonitrile.[4] For example, the compound which we referred to as phenylcyanomethylenequinone oxime[3] is correctly named 4-α-cyanobenzylidene-2,5-cyclohexadien-1-one oxime or 4-oxo-α-phenyl-2,5-cyclohexadiene-Δ^1,α-acetonitrile oxime. The latter is preferred for indexing by Chemical Abstracts.) When *p*-halonitrobenzenes are employed in similar reactions, attack occurs preferentially at a position *ortho* to the nitro group, and the products are 3-aryl-5-haloanthranils.[2] We undertook the present investigation in order to determine whether *ortho*- and *meta*-substituted nitrobenzenes condense with arylacetonitriles, and if so, to determine the nature of the products.

This investigation has revealed that monosubstituted nitrobenzenes containing a chloro, methoxy, or methyl group either *ortho* or *meta* to the nitro group react much in the same manner as nitrobenzene[3]; that is, they condense with arylacetonitriles in methanolic potassium hydroxide solution to yield new arylacetonitriles having quinone-like substituents in the position alpha to the cyano group. We have prepared the corresponding quinoid compounds from the reactions of *o*- and *m*-chloronitrobenzene, *o*- and *m*-nitrotoluene, and *o*- and *m*-nitroanisole with phenylacetonitrile and *p*-chlorophenylacetonitrile. It has likewise been found that disubstituted nitrobenzenes containing a chloro, methoxy, or methyl group *ortho* to the nitro group and a second chloro, methoxy, or methyl group *meta* to the nitro group condense with arylacetonitriles to produce similarly substituted acetonitriles. The corresponding quinoid compounds have been prepared from the reactions of 2-chloro-6-nitrotoluene, 2,3-dichloronitrobenzene, 1,4-dichloro-2-nitrobenzene, 1,4-dimethoxy-2-nitrobenzene, 1,4-dimethyl-2-nitrobenzene, 4-chloro-2-nitroanisole, 4-chloro-2-nitrotoluene and 4-chloro-3-nitrotoluene with phenylacetonitrile, *p*-chlorophenylacetonitrile, and *p*-methoxyphenylacetonitrile. In addition, naphthoquinone-like substituted acetonitriles have been prepared from the reactions of phenylacetonitrile, *p*-chlorophenylacetonitrile and *p*-methoxphenylacetonitrile with 1-nitronaphthalene, which may be considered as a 2,3-disubstituted nitrobenzene.

While the scope and limitations of the condensation reaction between aromatic nitro compounds and arylacetonitriles have not been completely investigated, nevertheless, we have acquired evidence indicating the reaction has some of the characteristics of a general or type reaction. The following equation, in which =Q= represents a *p*-quinoid structure derived from the aromatic nitro compound employed, may be used to illustrate one aspect of the general reaction:



$$Ar{-}CH_2{-}CN + Ar'{-}NO_2 \xrightarrow{\text{base}} \xrightarrow{\text{acid}} Ar{-}\underset{\displaystyle CN}{\underset{|}{C}}{=}Q{=}NOH + H_2O$$

The only limitation that may be stated at this time for the above equation is that the aromatic nitro compound, Ar'—NO_2, must be unsubstituted in the position *para* to the nitro group, thus enabling the aryl group, Ar'—, to be transformed to the *p*-quinoid group, =Q=.

Table I lists the substituted acetonitriles synthesized in the present investigation. They were synthesized following procedures similar to the method described for preparing phenylcyanomethylenequinone oxime.[3] However, when solid nitro compounds were used in the syntheses, the solids were dissolved in a minimum of methanol prior to their introduction to the reaction mix-

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(1) Research project supported in part by National Science Foundation grant, NSF-G10030.

(2) Previous paper, *J. Org. Chem.*, **25**, 1884 (1960).

(3) R. B. Davis, L. C. Pizzini, and J. D. Benigni, *J. Am. Chem. Soc.*, **82**, 2913 (1960).

(4) Private communication from J. H. Fletcher, Committee on Organic Nomenclature, American Chemical Society.

TABLE I SUBSTITUTED ACETONITRILES

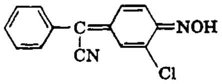
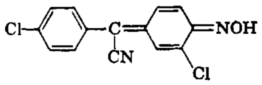
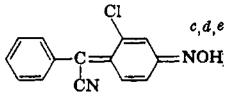
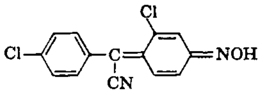
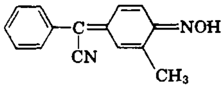
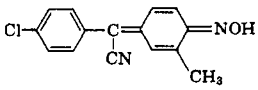
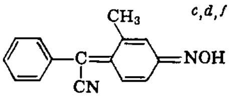
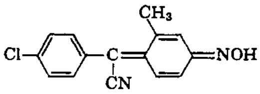
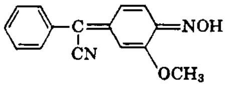
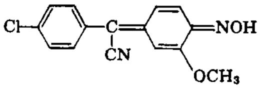
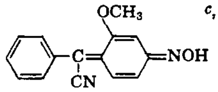
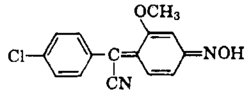
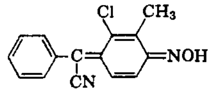
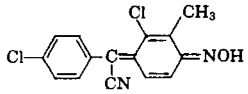
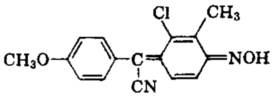
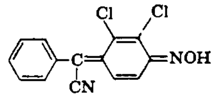
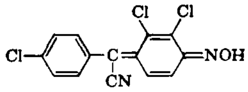
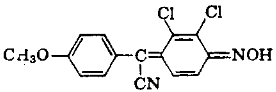
$\mathrm{Ar{-}C(CN){=}Q{=}NOH}$	M.P., dec.[a]	Yield, %	Carbon, %[b]		Hydrogen, %		Nitrogen, %	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
	180	92	65.50	65.92	3.35	3.77		
	190	100	57.75	57.60	2.77	2.86	9.62	9.62
 [c,d,e]	144	53	65.50	65.62	3.53	3.81		
	177	100	57.75	57.81	2.77	2.75	9.62	9.46
	161	72	76.25	76.04	5.08	5.33	11.86	11.63
	192–193	60	66.55	66.23	4.09	3.93	10.35	10.56
 [c,d,f]	121–122	76	76.25	76.16	5.12	5.25		
	173	33	66.55	66.51	4.10	4.23	10.35	10.47
	186	87	71.41	71.28	4.80	4.69	11.11	11.23
	205	80	62.83	62.82	3.78	4.23	9.77	9.80
 [c,g]	146–147	25	71.41	71.54	4.80	5.01	11.11	10.91
 [h]	188–189	89	62.83	63.22	3.78	4.17		
	146	82	66.55	66.77	4.09	4.10		
	183	80	59.04	59.31	3.30	3.60		
	175	80	63.90	63.98	4.36	4.37		
	168	53	57.76	58.01	2.77	3.04		
	185	92	51.65	52.00	2.17	2.40		
	180	65	56.10	56.26	3.14	3.21		

TABLE I (*continued*)

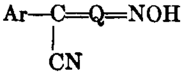
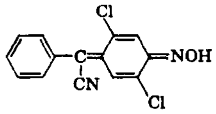
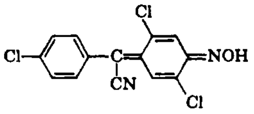
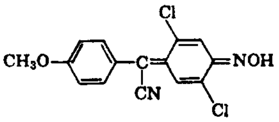
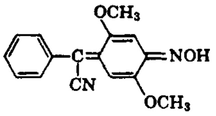
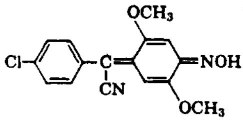
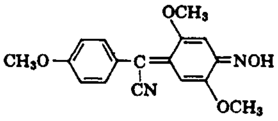
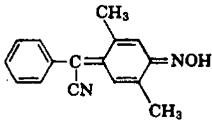
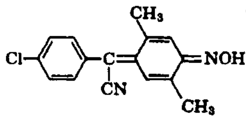
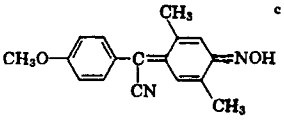
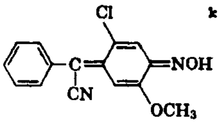
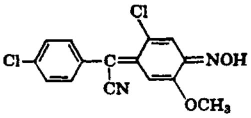
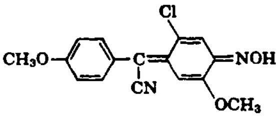
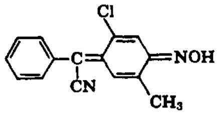
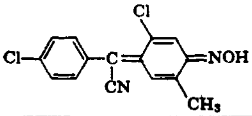
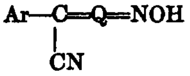
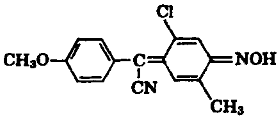
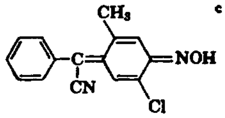
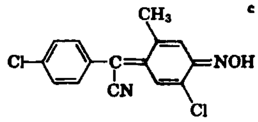
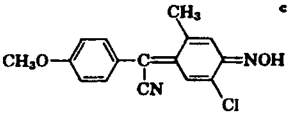
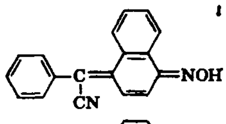
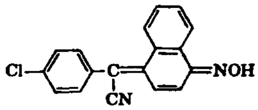
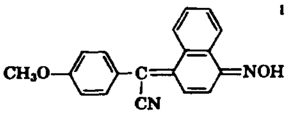
 $\mathrm{Ar{-}\underset{\displaystyle CN}{\underset{\vert}{C}}{=}Q{=}NOH}$	M.P., dec.[a]	Yield, %	Carbon, %[b]		Hydrogen, %		Nitrogen, %	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
	170	93	57.76	57.60	2.77	2.89		
	184	94	51.65	51.96	2.17	2.11		
	178	91	56.10	56.43	3.14	3.17		
	198	88	68.08	67.86	5.00	5.30	9.92	9.94
 [c]	200	80	60.67	60.50	4.14	4.15	8.84	8.82
	199	65	65.38	65.26	5.16	5.30	8.97	8.67
 [c]	164	53	76.78	76.61	5.64	5.80	11.19	11.15
 [c]	181	43	67.49	67.70	4.60	4.76		
 [c]	168	69	72.84	73.04	5.75	6.00	9.99	10.04
 [k]	170	82	62.83	63.06	3.87	3.97		
	168	81	56.10	56.22	3.14	3.34		
	173	84	60.67	60.77	4.14	4.23		
	155	92	66.55	66.90	4.09	4.29		
	171	87	59.04	59.17	3.30	3.44		

TABLE I (*continued*)

 $\mathrm{Ar{-}C(CN){=}Q{=}NOH}$	M.P., dec.[a]	Yield, %	Carbon, %[b]		Hydrogen, %		Nitrogen, %	
			Calcd.	Found	Calcd.	Found	Calcd.	Found
	156	88	63.90	63.58	4.36	4.55	9.31	9.00
 [c]	162	77	66.55	66.56	4.09	4.18	13.10	12.81
 [c]	173	77	59.04	58.64	3.30	3.45		
 [c]	163	80	63.90	64.25	4.36	4.48		
 [l]	182–183	33	79.39	79.44	4.44	4.54	10.29	10.32
	195–196	88	70.48	70.25	3.61	3.68	9.13	9.45
 [l]	193–194	36	75.48	75.54	4.67	4.74	9.27	9.24

[a] All melting points are uncorrected. [b] Analyses by Midwest Microlab, Inc., Indianapolis, Ind. [c] Prepared by reaction at room temperature. [d] The usual treatment with boiling benzene was omitted, and the product was recrystallized from ethylene chloride. [e] Reaction in the usual manner at 50–55° gave 4% yield of product. [f] Reaction in the usual manner at 50–55° gave 7% yield of product. [g] Reaction in the usual manner at 50–55° gave 8% yield of product. [h] Per cent of chlorine, calcd.: 13.10, found: 13.21. [i] Per cent of chlorine, calcd.: 24.36, found: 24.59. [j] Per cent of chlorine, calcd.: 24.26, found: 24.27. [k] Per cen of chlorine, calcd.: 12.37, found: 12.57. [l] Reaction conducted in 4.5*M* potassium hydroxide in methanol. When the reaction was conducted in the usual manner (3.0*M* potassium hydroxide in methanol), the yield of product was much lower.

tures. During the course of some of the reactions, additional methanol was added in order to impart some degree of fluidity to the reaction mixtures.

That the compounds reported in this investigation have *p*-quinone-like structures is evident from their method of preparation, from their similarity in physical and chemical properties to the known quinoid compounds,[3] and from other evidence. These compounds were prepared from reactions of arylacetonitriles with aromatic nitro compounds unsubstituted in the position *para* to the nitro group, following procedures similar to the method described for preparing phenylcyanomethylenequinone oxime.[3] All the reaction mixtures turned deep red.[3] Upon acidification of the reaction mixtures, yellow or orange solids were obtained.[3] Upon treating the yellow or orange solids with potassium hydroxide solution, deep red colors were produced.[3] All the compounds melted with decomposition,[3] ranging from 121° to 205°. The infrared spectra of the products were very similar to those of known arylcyanomethylenequinone oximes,[3] particularly in regard to absorption bands at 4.52 to 4.57 μ, characteristic of a cyano group that is part of a conjugated system more extended than one double bond.[5] Finally, that the products are *p*-quinoid oximes and not the corresponding *o*-quinoid oximes was concluded from evidence gathered in our previous investigations. For nitrobenzene we found that the preferred position of attack by arylacetonitriles is at the position *para* to the nitro group.[2,3] When the position *para* to the nitro group is blocked such as in *p*-chloronitrobenzene and *p*-bromonitrobenzene, the arylacetonitriles can and do attack an *ortho* position. However, the products are not the corresponding *o*-quinoid oximes but rather 3-aryl-5-haloanthranils.[2]

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(5) R. D. Kitson and N. E. Griffith, *Anal. Chem.*, **24**, 334 (1952).

There are a large number of factors which influence the yields of the *p*-quinoid oximes. The more pertinent factors are the nature of the aromatic nitro compound, the nature of the arylacetonitrile, the reaction time, the reaction temperature, the amount of potassium hydroxide, the amount of methanol, the relative solubilities of the potassium salts of the quinoid oximes in the reaction mixtures, the relative solubilities of the quinoid oximes in benzene, and the relative stabilities of the quinoid oximes. We do not have quantitative data to demonstrate the influence of each of these factors on the yields. However, we do have quantitative evidence for some of these factors in specific cases. Phenylcyanomethylenequinone oxime was prepared in four reactions following the procedure previously described[3] with the exception that the reaction time was varied. The yields obtained were: 30% for one hour, 42% for two hours, 77% for four hours, and 74% for six hours. The same quinoid oxime was prepared in another series of reactions following the described procedure[3] with the exception of the reaction temperature. The yields obtained were: 57% at 35–40°, 77% at 50–55°, 73% at 55–60°, and 66% at 60–65°. It should be pointed out that the reactions were exothermic, and in the early stages the reaction mixtures were actually cooled for a time in order to maintain the indicated temperatures. While 50–55° seems to be an ideal temperature in this case, nevertheless it is not the ideal temperature for the preparation of all the quinoid oximes as is pointed out in Table I. The amount of potassium hydroxide was varied in a third series of controlled reactions for the preparation of phenylcyanomethylenequinone oxime. The yields obtained were: 8% for $1M$ potassium hydroxide in methanol, 42% for $2M$ potassium hydroxide in methanol, and 77% for $3M$ potassium hydroxide in methanol.[3] Table I reveals that as high as $4.5M$ potassium hydroxide in methanol was used in the preparation of some of the quinoid oximes. It is our opinion that large amounts of potassium hydroxide are not necessary to effect the condensation because we have noted that a deep red color is produced when nitrobenzene and phenylacetonitrile are added to warm methanol containing a small amount of potassium hydroxide or potassium cyanide. It is our opinion that the function of the large amounts of potassium hydroxide is to ensure precipitation of the potassium salts of the quinoid oximes. We have observed that best yields of the quinoid oximes are obtained when copious precipitation of their potassium salts results shortly after the reagents are mixed, thus preventing subsequent reaction. That subsequent reaction can occur was demonstrated by refluxing a solution of phenylcyanomethylenequinone oxime in methanol containing a small amount of potassium hydroxide. Upon dilution with water and acidification with acetic acid, a viscous material was obtained which did not solidify upon seeding with phenylcyanomethylenequinone oxime.

EXPERIMENTAL

Condensation of aromatic nitro compounds with arylacetonitriles. The following general procedure was used for the condensation reactions. Variations from this general procedure are listed under Table I.

The arylacetonitrile (0.069 mole) and the aromatic nitro compound (0.063 mole) were added to a solution of 25 g. of potassium hydroxide (assay 85%, 0.38 mole) in 100 ml. of methanol at room temperature. The mixture was then heated with stirring, maintaining a temperature of 50–55° for 4 hr. During this time the reaction mixture turned deep red in color, and a large amount of deep red solid precipitated. After cooling to room temperature, 250 ml. of water was added with stirring. The reaction mixture was then acidified by adding a solution of 45 g. of acetic acid (assay 98%, 0.74 mole) in 50 ml. of water with stirring. During the acidification, the deep red color gradually disappeared, and a yellow-orange solid precipitated. The yellow-orange product was isolated by filtration, washed with water-methanol and air dried. The product was then introduced into 100 ml. of benzene, and the mixture was heated to boiling for 15 min. After cooling, the product was again isolated by filtration and dried in a vacuum desiccator. The yield was determined, and a portion of the product was then recrystallized from benzene.

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