The Reaction of Cyanide Ion with Carbonyl Compounds in Dipolar Aprotic Solvents[1]

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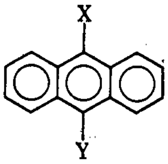
Dimethylformamide solutions of 9-benzoylanthracene and sodium cyanide at 80° give intensely blue solutions from which 9-cyanoanthracene, 9,10-dicyanoanthracene, 9,10-dihydroanthracene, anthracene, and benzoic acid can be isolated. Addition of the mild oxidizing agent sodium 9,10-anthraquinone-1-sulfonate to the blue solutions yields as major products only 9,10-dicyanoanthracene and benzoic acid. Similar treatment of 9-acetyl-, 9-benzoyl-, 9-chlorocarbonyl-, 9-formyl-, or 9-carbomethoxyanthracene also yields 9,10-dicyanoanthracene. 2,3,9,10-Tetracyanoanthracene is obtained from 9,10-dicyanoanthracene and cyanide ion in the presence of oxidizing agent.

The nucleophilic reactions of cyanide ion and of anions from active methylene compounds with certain aryl-substituted unsaturated hydrocarbons,[2] aromatic nitriles,[3] aromatic nitro compounds,[4,5] and aromatic heterocycles[3b] in dipolar aprotic solvents appear to proceed *via* carbanionic addition products, usually formed reversibly, which by further reaction with added oxidizing agents or protonating agents or by electron exchange reactions, in which the original aromatic compound may participate, lead to a variety of products. Some of the reactions promise to be of unique value in synthesis. The initiation of the reactions of aromatic compounds results from electron withdrawal by an activating group, nitro or nitrile, which facilitates the addition of the cyanide ion to the aromatic system. It would be expected that a carbonyl group attached to a suitable aromatic system would be less effective than a nitro or nitrile group in facilitating attack by the cyanide ion. The present work was undertaken to test the reactivity of some aromatic carbonyl compounds toward cyanide ion.

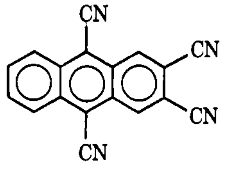
In the studies of the highly unsaturated hydrocarbons[2] and the nitriles[3] and nitro compounds[4] the development of color when the substance being tested was mixed with sodium cyanide in an aprotic solvent was taken as an indication of attack by cyanide ion with the formation of a carbanion. When simple aromatic carbonyl compounds, such as benzophenone, benzaldehyde, and ethyl benzoate, were tested in this way no significant color development was observed at ambient or slightly elevated temperatures, but, when the aromatic compound was one having a ketone, ester, acid chloride, or aldehyde function attached to the 9 position of the anthracene system, such a test solution developed a deep blue color, slowly at room temperature and rapidly at slightly elevated temperatures.

Examination of mixtures in which 9-benzoylanthracene **1a** and sodium cyanide were allowed to react in DMF revealed the presence of a number of products. By analogy with the reaction of the nitrile,[3] the carbanion **6** would be expected to form and to generate the keto nitrile **1d** even if no oxidizing agent were added. However, none of the keto nitrile was found, and a principal product isolated (23%, see Table I, expt A) was the unexpected one, 9-cyanoanthracene; benzoic acid (29%) was also isolated in this experiment, as well as 9,10-dicyanoanthracene (15%), 9,10-dihydroanthracene (20%), and a trace of anthracene. In an experiment (C) in which the oxidizing agent sodium anthraquinone-α-sulfonate[2b] (α-SAS) was employed, some (10%) of the originally expected keto nitrile **1d** was isolated, along with a somewhat larger amount (13%) of the 9,10-dinitrile. When the keto nitrile **1d**



1a, $X = C_6H_5CO$; $Y = H$
b, $X = CN$; $Y = H$
c, $X = Y = CN$
d, $X = C_6H_5CO$; $Y = CN$
e, $X = CH_3CO$; $Y = H$
f, $X = CHO$; $Y = H$
g, $X = ClCO$; $Y = H$
h, $X = CH_3OCO$; $Y = H$

2, 9,10-dihydroanthracene
3, anthracene
4, benzoic acid



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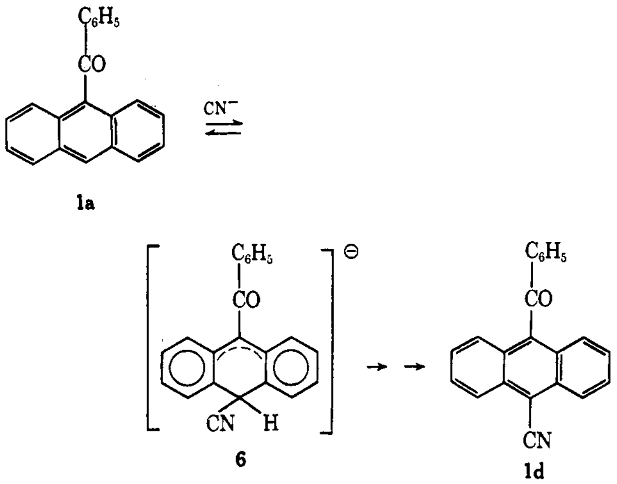
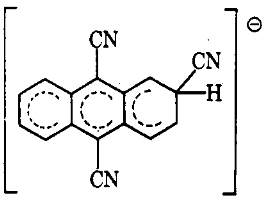


1a **6** **1d**



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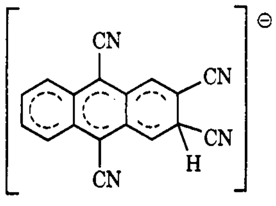

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[1] Grateful acknowledgment is made to the U. S. Army Research Office (Grant No. DA-ARO(D)-G679 and G857) for the partial support of this work.

[2] (a) B. E. Galbraith and H. R. Snyder, *J. Org. Chem.*, **32**, 380 (1967); (b) K. E. Whitaker, B. E. Galbraith, and H. R. Snyder, *ibid.*, **34**, 1411 (1969).

[3] (a) K. E. Whitaker and H. R. Snyder, *ibid.*, **35**, 30 (1970); (b) R. B. Chapas, R. F. Nystrom, and H. R. Snyder, *ibid.*, **37**, 314 (1972).

[4] (a) R. G. Landolt and H. R. Snyder, *ibid.*, **33**, 403 (1968); (b) R. F. Aycock, Ph.D. Thesis, University of Illinois, Urbana, 1969; (c) B. Vickery, *Chem. Ind.* (London), 1523 (1967).

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TABLE I

INTERACTION OF SODIUM CYANIDE WITH SUBSTITUTED ANTHRACENES IN DIMETHYLFORMAMIDE

Expt	Sub-strate	Mole ratio of reactants[a]	Reaction time, hr	% re-covered substrate	% **1b**	% **1c**	% **2**	% **3**	% **4**	% **5**	% other
A	**1a**	1:2.4:0	13.7	25	23	15	20	2	29	0	1 (**1a** + **3** complex)
B[b]	**1a**	1:2.5:0	8	30	9	12	6	0.7			5 (**1a** + **3** complex)
C	**1a**	1:2.4:3.1[c]	36	74	0	13	0	0	15	0.2	10 (**1d**)
D	**1a**	1:2.5:2.8[c]	11	87	0	6	0	0	Trace		
E[d]	**1a**	1:2:1.3[e]	8[f] + 11.5	21	0	27	0	0			
F	**1a**	1:2.5:1.3[e]	6[f] + 15	34	0	17	0	0	11	5	
G	**1d**	1:4.2:0	16	0	0	85	0	0	32	0	8 (impure 9-cyano-10-anthrone)
H	**1d**	1:3.2:1.5[c]	10.5	35	0	44	0	0	44	12	
I[b]	**1d**	1:3.3:1.4[c]	47	10	0	35	0	0	28	3	
J	**1c**	1:3.3:2.5[c]	27.7	82			0	0		18	
K	**1c**	1:9:5[c]	100	36			0	0		0	
L[g]	**1e**	1:2.5:1.6[e]	2.5[f] + 70			10					
M	**1f**	1:3.2:1.2[e]	4.5[f] + 16			28					
N[g]	**1g**	1:5:2[e]	0.1[f] + 35.5		0	10				2	17 (impure 9-cyano-10-anthroic acid)
O[d]	**1h**	1:2.4:1.3[c]	10.7	59		15					

[a] Substrate, NaCN, α-SAS. [b] Reaction mixture acidified with concentrated HCl. [c] Order of reagents added to reaction solvent: substrate, α-SAS, NaCN. [d] DMSO used as reaction solvent. [e] Order of reagents added to reaction solvent: substrate, NaCN, α-SAS. [f] Hours substrate and NaCN react before α-SAS addition. [g] Reaction product crystallized from hot DMF.

was separately prepared and submitted to the action of cyanide ion (expt G), it was converted in high yield (85%) into the 9,10-dinitrile. It is probable that **1d** occurs as an intermediate between the simple ketone and the dinitrile.

Another unexpected product from the reaction of 9-benzoylanthracene was a very slightly soluble substance having the composition of a tetracyanoanthracene. The similarity of the infrared spectrum of this substance to that of 2,3,9,10-tetramethylanthracene[6] suggests that it is the 2,3,9,10-tetracyano compound **5**. When the 9,10-dinitrile was treated with cyanide and the oxidizing agent (α-SAS) over a long period of time (expt J), substantially all of the dinitrile not recovered was converted into this same tetranitrile, obtained in about 18% yield.

Trisler and Frye[7] have found that the reaction of benzil with cyanide ion in DMSO proceeds by nucleophilic attack on the carbon atom of one of the active carbonyl groups, followed by a series of reactions which include isomerizations and addition to a second molecule of benzil, with the final ejection of cyanide ion and the formation of α,α′-stilbenediol dibenzoate in high yield; no substitution in the aromatic system was observed. It would not be surprising if 9-anthraldehyde (**1f**) would react preferentially at the carbonyl carbon atom, preventing attack of the aromatic system. However, when the reaction of the aldehyde (**1f**) was carried out in the presence of the oxidizing agent α-SAS, the dinitrile (**1c**) was isolated in a yield (28%) comparable to that obtained from the benzoyl compound (**1a**). Also, the methyl ketone (**1e**), the acid chloride (**1g**, which probably reacted as the acyl cyanide), and the methyl ester (**1h**) all produced some of the dinitrile (**1c**) in reactions in which the oxidizing agent α-SAS was present.

There seems little doubt that the reactions occurring when cyanide ion and 9-nitroanthracene,[4a] 9-cyanoanthracene,[3] or even acridine[3b] are brought together in DMF or DMSO proceed through an anionic intermediate, similar to a Jackson–Meisenheimer complex,[5] formed by attack of the cyanide ion upon the unsubstituted carbon of the central ring of the aromatic compound. The products obtained from 9-benzoylanthracene can be accounted for on the basis of a similar addition product **6**, but the addition proceeds less readily, because of the lesser electron withdrawal by the acyl group, and, at the higher temperatures required, further reactions, including oxidation–reductions, presumably proceeding *via* electron exchange reactions,[2b,8,9] and the participation of more active, newly introduced cyano groups lead to a greater variety of products. The isolation of some (10%) of the cyano ketone **1d** from a reaction conducted in the presence of the oxidizing agent α-SAS (expt C) and its further reaction to give 9,10-dicyanoanthracene **1c** in high (85%) yield are illustrative, and the latter process constitutes a new method of cleavage of activated aromatic ketones. The further reaction of 9,10-dicyanoanthracene to 2,3,9,10-tetracyanoanthracene **5** represents the first instance of attack by cyanide ion on a terminal ring of an activated anthracene compound. The tetracyano compound very probably is formed by way of the anion **7** which is oxidized to the tricyanoarene which reacts further *via* the addition product **8**.

Experimental Section[10]

Materials.—Unless otherwise specified, commercially available reagents were used without purification. Dimethylformamide, dimethyl sulfoxide, sodium cyanide, α-SAS, and laboratory nitrogen were dried as reported earlier.[3a] Brinkmann's No. 7734 silica gel was used for column chromatography. Thin layer chromatography analyses were carried out on sheets of Eastman chromagram 6060 silica gel with fluorescent indicator.

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[6] Sadtler Standard Spectra Catalogue, Sadtler Research Laboratory, 1517 Vine Street, Philadelphia, Pa. 19102, Spectrum 19885.

[7] (a) J. C. Trisler and J. F. Frye, *J. Org. Chem.*, **30**, 306 (1965). (b) J. C. Trisler, C. S. Aaron, J. L. Frye, and J. Y. Park, *ibid.*, **33**, 1077 (1968).

[8] E. H. Jansen and J. W. Happ, *ibid.*, **35**, 96 (1970).

[9] G. A. Russell and W. C. Danen, *J. Amer. Chem. Soc.*, **90**, 347 (1968).

[10] Melting points are not corrected. Microanalyses were performed by Mr. J. Nemeth and his associates, mass spectra were obtained by Mr. J. Wrona with an Atlas CH4 spectrometer, and Mr. R. Thrift and his associates used a Perkin-Elmer 521 infrared spectrophotometer to obtain infrared spectra in potassium bromide disks. Ultraviolet spectra were run in absolute ethanol on a Perkin-Elmer 202 spectrophotometer.

9-Benzoylanthracene (1a).—The preparation of 9-benzoylanthracene from anthracene and benzoyl chloride with aluminum chloride catalyst in ethylene chloride solvent at 0° was carried out according to the method of Gore and Hoskins.[11] The ketone was twice chromatographed on alumina and twice crystallized from acetic acid to ensure complete removal of anthracene from the ketone,[12a] mp 147.5–149° (lit.[11,12b] mp 148°).

9-Benzoyl-10-cyanoanthracene (1d).—The method of Whitaker and Snyder[3a] was used to convert 9-benzoyl-10-bromoanthracene into 9-benzoyl-10-cyanoanthracene with anhydrous cuprous cyanide in DMSO. The product was obtained in 81% yield after elution from silica gel with cyclohexane–benzene (9:1) and crystallization of the fluorescent yellow solid from acetic acid, mp 188–189° (lit.[13] mp 184–185 and 187–188°). The cyano ketone showed medium–strong infrared absorption bands at 2220, 1670, 1450, 1230, 875, 775, 765, 715, 710, and 635 cm^{-1}.

9-Anthroyl Chloride (1g).—To 50 ml of dry benzene were added Aldrich's 9-anthroic acid (2.22 g, 0.01 mol) and 2 ml of thionyl chloride distilled from trimethyl phosphite. The solution was refluxed for 1 hr and stirred 10 hr at room temperature. The volatile components were removed by distillation (steam bath), leaving a yellow-brown solid which was twice dissolved in a minimum volume of hot pentane–benzene, filtered, and concentrated in a nitrogen stream. A dull yellow solid, mp 93.5–94.5°, was obtained when the process was repeated with a mixture of cyclohexane–benzene. The acyl chloride was used without further purification.

Methyl 9-Anthroate (1h).—A solution of diazomethane in ether prepared from Aldrich's Diazald[14] was added to 9-anthroic acid (0.408 g, 0.0018 mol), giving yellow methyl 9-anthroate: 0.412 g, 95%; mp 110–111° (lit.[15] mp 111–112°); strong infrared absorption bands at 1722, 1210, 1024, 897, 743, and 730 cm^{-1}.

General Reaction Procedure.—The general reaction procedure used was similar to that reported earlier from this laboratory.[3a] The addition order of reactants and reaction times are listed in the table. Reactions were carried out at 80° using 1–3 mmol of organic substrate.

Isolation and Identification of Reaction Products.—Separation of the reaction products was advantageously carried out by column chromatography using silica gel.

Nitriles **1b** and **1c** have been identified during earlier investigations in this laboratory.[3,4a] Dihydroanthracene and anthracene were identified in expt A and B by comparison with gas chromatography retention times of known compounds on a 5 ft × $^1/_4$ in. column of 20% SE-30 on Chromosorb W at 235°.

The mixture of ketone **1a** and its anthracene complex was treated with a few milliliters of hot acetic acid; the complex was insoluble and collected by gravity filtration, mp 187–192° (lit.[12] mp 158°). The infrared spectrum showed the following absorptions which were new or shifted from those observed in anthracene or ketone **1a**: 2960, 1673, 1472, 1216, 1200, 1185, 822, 769, 695, 690, 670, 651, and 633 cm^{-1}. Strong absorptions of the parent hydrocarbon or ketone which no longer were apparent follow: anthracene, 1620, 1319, 958, 884, 739, 728, and 479 cm^{-1}; 9-benzoylanthracene, 898, 892, and 731 cm^{-1}. Mass spectrum (70 ev): *m/e* 460, 282, and 178.

In expt C, dinitrile **1c** and keto nitrile **1d** were not eluted cleanly by cyclohexane–benzene (1:1) from 10 g of silica gel. Fractional crystallization from chloroform ultimately yielded pure samples of each compound.

Benzoic acid was isolated from the filtrate in various experiments by addition of concentrated hydrochloric acid and extraction with methylene chloride. In turn, the methylene chloride solution was extracted with sodium hydroxide solution which was acidified to Congo Red paper and again extracted with methylene chloride, dried (Na_2SO_4), and evaporated to dryness, and the benzoic acid was crystallized from hot water.

Acidification of the aqueous filtrate in expt G caused precipitation of 15 mg of yellow solid. Its infrared spectrum indicated it was probably an impure sample of 9-cyano-10-anthrone.[4a]

9-Cyano-10-anthroic Acid.—In expt N, an additional fraction was eluted from the silica gel by absolute ethanol. The dark yellow solid was crystallized from aqueous acetic acid as a slightly impure sample of 9-cyano-10-anthroic acid, mp 224–226° with sublimation. Its infrared spectrum showed medium–strong absorptions at 3020, 2220, 1680, 1450, 1256, 770, and 725 cm^{-1}. Mass spectroscopy indicated that anthroic acid may be the contaminant.

Anal. Calcd for $C_{16}H_9NO_2$: C, 77.72; H, 3.67; N, 5.66; mol wt, 247.2. Found: C, 76.57; H, 4.02; N, 5.22; mol wt, 247 (mass spectrum).

Reaction of 9,10-Dicyanoanthracene. Preparation of 2,3,9,10-Tetracyanoanthracene (5).—A mixture of 9,10-dicyanoanthracene (0.295 g, 0.0013 mol) and α-SAS (1.035 g, 0.0033 mol) in 25 ml of DMF was degassed with nitrogen at 80° for 0.5 hr. Sodium cyanide (0.210 g, 0.0043 mol) was added and the solution turned dark blue in 10 min. After 4 hr the reaction mixture was quenched with a few milliliters of boiled water and poured into 300 ml of ice–water containing 12 g of ammonium chloride. The dark yellow precipitate (0.80 g) was collected and chromatographed on a short silica gel column. Elution with benzene gave 0.30 g of yellow-orange material, which was impregnated on a little silica gel which was added to the top of a silica gel column. Elution with benzene gave 0.24 g of unchanged 9,10-dicyanoanthracene (infrared spectrum) and 70 mg of an orange-brown solid which when dissolved in benzene gave a brilliant yellow-green fluorescent solution. The orange-brown solid was rechromatographed, yielding 67 mg (18%) of dark yellow solid to which was added 10 mg of the same material from another reaction. The combined solids were similarly chromatographed twice, yielding 67 mg of solid which was dissolved in 100 ml of hot ethyl acetate, filtered, and reduced in volume in a nitrogen stream. The amorphous dark yellow solid (35 mg, 9%) was essentially insoluble in the usual organic solvents. The infrared spectrum showed medium–strong absorptions at 3070, 2235, 2220, 1510, 1446, 1424, 1409, 1349, 1278, 1168, and 855 cm^{-1} and strong absorption at 772 cm^{-1}. The ultraviolet and visible spectra showed absorptions at λ_{max} 253 (sh), 272, 346, 364, 383, 414, and 442 nm; mass spectrum (70 ev) *m/e* (rel intensity) 278 (100), 251 (13), and 234 (9).

Anal. Calcd for $C_{18}H_6N_4$: C, 77.69; H, 2.17; N, 20.13; mol wt, 278. Found: C, 77.53; H, 2.12; N, 20.24; mol wt (mass spectrum), 278.

Registry No.—**1a**, 1564-53-0; **1c**, 1217-45-4; **1d**, 22970-75-8; **1e**, 784-04-3; **1f**, 642-31-9; **1g**, 16331-52-5; **1h**, 1504-39-8; **3**, 120-12-7; **5**, 37611-11-3; sodium cyanide, 143-33-9; benzoyl chloride, 98-88-4; 9-anthroic acid, 723-62-6; thionyl chloride, 7719-09-7; 9-cyano-10-anthroic acid, 37611-13-5.

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(14) L. F. Fieser and M. Fieser in "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 191.

(15) G. Behla, *Chem. Ber.*, **20**, 701 (1877).