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Part I: SYNTHESIS OF *o*-CYANOSTYRENE AND ITS
REACTIONS WITH AMINES.

Part II: CYCLOPROPANE CARBONITRILE: ATTEMPTS AT
ADDITION REACTIONS WITH NUCLEOPHILIC REAGENTS.

by

IRWIN L. KLUNDT

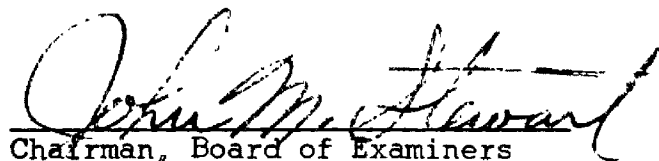
B. S. Washington State College, 1958

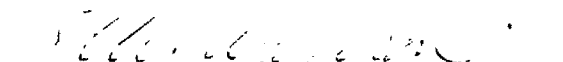
Presented in partial fulfillment
of the requirements for the degree of
Master of Science

MONTANA STATE UNIVERSITY

1959

Approved by:


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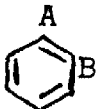

Part I
SYNTHESIS OF o-CYANOSTYRENE AND ITS
REACTIONS WITH AMINES

CHAPTER I

Introduction

o-cyanostyrene, , may be considered to be a vinylog of acrylonitrile, $\text{CH}_2=\text{CHCN}$. Vinylogs are compounds of the type

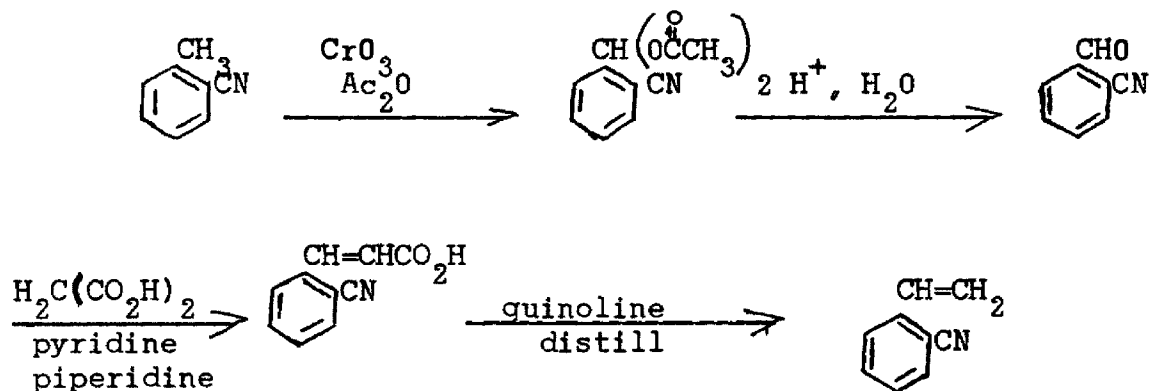
$\text{A}(\text{CH}=\text{CH})_n\text{B}$, in which groups A and B are linked through one or more conjugated vinylene groups. An empirical rule developed by Angeli¹ has been useful in correlating effects of this category. It states that substituents, situated ortho or para to each other on a benzene nucleus, behave qualitatively as though they were joined directly.

That is, groups A and B in  and  may be expected to

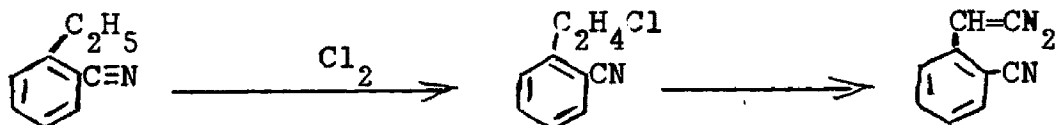
behave chemically much as they do in A-B. o-cyanostyrene would correspond to the vinylog, $\text{CH}_2=\text{CHCH}=\text{CHCN}$ (2,4 pentadienenitrile) of acrylonitrile, in which one conjugated vinylene group is part of the benzene ring. As is explained in Part II of this thesis (p. 16), compounds which contain an alkene linkage directly connected to a highly electron-withdrawing group or conjugated with it react by addition with nucleophilic reagents which contain labile hydrogen atoms such as amines, phenols, and mercaptans. Reactions of this type have been carried out on p-cyanostyrene², atropnitrile (α -cyanostyrene)³, and 2,4 pentadienenitrile⁴, and compared with the well known cyanoethylation reaction of acrylonitrile. It was found in the case of p-cyanostyrene that the electronegative effect of the cyano group

is diminished when passed through the benzene ring. This type of reaction has not been carried out on *o*-cyanostyrene and it is of interest to determine the effect of the cyano group in the ortho position conjugated with the alkene linkage and to compare the results of addition reactions with nucleophilic reagents with those of the open chain vinyllog, 2,4 pentadienenitrile, and with *p*-cyanostyrene.

o-cyanostyrene has been prepared by Marvel and Hein⁵ by the decarboxylation of *o*-cyanocinnamic acid after the following series of reactions:



It also has been prepared as outlined in a British patent to the Wingfoot Corp., Akron, Ohio⁶, according to the following route:

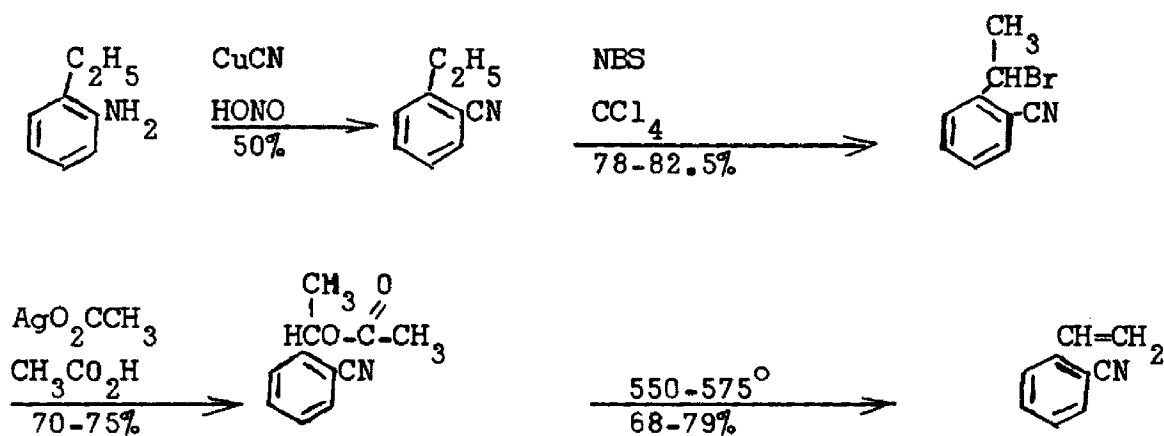


It was impossible to duplicate this latter procedure in this investigation. The reported overall yield of Marvel and Hein was extremely low (5.05%), the final pyrolysis step giving an especially poor yield. Therefore, new synthetic routes to this desired substance were investigated first.

CHAPTER 2

Discussion

Numerous routes to a new synthesis of o-cyanostyrene were investigated before a method was found that would produce the desired compound. The method finally used was the pyrolysis of o-cyano- α -phenethyl acetate, after the following sequence of reactions:



Several other methods that were tried but did not yield satisfactory results were: (1) the direct dehydrogenation of o-ethylbenzonitrile with chloranil (tetrachloroquinone), (2) pyrolysis of o-(α -bromoethyl) benzonitrile (the general method of the Wingfoot patent), (3) pyrolysis of the trimethyl quaternary ammonium hydroxide adduct of o-(α -bromoethyl) benzonitrile, (4) and the dehydrohalogenation of o-(α -bromoethyl) benzonitrile with quinoline, pyridine, and sodium amide. In the reaction of o-ethylbenzonitrile with chloranil, starting material was recovered. The reaction of the trimethyl ammonium bromide adduct with silver hydroxide apparently did not occur, as

starting material was recovered. The reaction of *o*-(α -bromoethyl) benzonitrile with pyridine produced the quaternary ammonium bromide salt instead of causing dehydrohalogenation. The reaction of *o*-(ζ -bromoethyl) benzonitrile with quinoline, in the presence of hydroquinone as a polymerization inhibitor, formed a tarry residue—apparently polymeric *o*-cyanostyrene. The dehydrohalogenation with quinoline was also attempted with *N*-phenyl-2-naphthylamine as an inhibitor, and a small amount (16%) of material was isolated which took up bromine and also reacted with potassium permanganate. This compound was identified as *o*-cyanostyrene by converting it to the dibromo derivative and determining its melting point. The attempted dehydrohalogenation of *o*-(α -bromoethyl) benzonitrile with sodium amide was carried out in liquid ammonia and refluxing benzene. Starting material was recovered from both attempts.

The *o*-cyanostyrene prepared by pyrolysis of the acetate ester had the same boiling point as that produced by Marvel and Hein but a different refractive index. It reacted with bromine to give the same dibromo derivative. Preparation of *o*-cyanostyrene by the method of Marvel and Hein showed that the index of refraction which they had reported was incorrect, as both methods of synthesis produced the same physical constants. This reported refractive index is believed to have been incorrectly read or copied by the investigator, since the use of their method gave a product with the same refractive index as that reported in this work. When hydroquinone was used as an inhibitor during the acetate pyrolysis, only 10% yield of the product was obtained. Polymerization had taken place to a large extent.

The yield was slightly improved (37%) when N-phenyl-2-naphthylamine was used as the inhibitor. It was found that with picric acid as an inhibitor 68-79% of the pure product could be isolated. Also, it was found that if the temperature of the pyrolysis column was above 600°, there was a considerable decrease in the yield of the product. The overall yield of o-cyanostyrene reported by Marvel and Hein was 5.05%, whereas, the method developed in this investigation produced an 18.5-24.4% overall yield.

Piperidine, benzylamine, cyclohexylamine, dimethylamine, morpholine, and n-butylamine were tried as addition reagents with the o-cyanostyrene. The secondary amines reacted much more readily than the primary amines. It appears that o-cyanostyrene is much less active toward addition of nucleophilic reagents across the ethylenic double bond than are some of its vinyllogs such as p-cyanostyrene, and 2,4 pentadienenitrile. Even under the most vigorous conditions the yields of the addition products were low. The catalyst used in all addition reactions was Triton B (benzyltrimethyl ammonium hydroxide). The yields of addition products ranged from 0 - 45% with the order of reactivity being as follows, the most reactive first: dimethylamine, piperidine, butylamine, morpholine, benzylamine, and cyclohexylamine. The physical constants of the addition products are given in Table I. The electron withdrawing effect of the cyano group is apparently not as strong when passed through the conjugated system of a benzene ring as when the cyano group is directly connected to the olefin group (α cyanostyrene), or when the effect is passed through an open chain conjugated system (2,4 pentadienitrile). Steric

hinderance may also play a part in lowering the yields. The reaction of piperidine with o-cyanostyrene and p-cyanostyrene did not produce very good yields of addition product. The yield with o-cyanostyrene being 34% and the yield with p-cyanostyrene being 21%, whereas with α -cyanostyrene the yield was 56%. In order to avoid any heat decomposition of the amine adducts (which takes place rather readily with amine adducts of other acrylonitriles) the products were isolated without distillation as the amine hydrochloride salts, and the yields are based upon these hydrochlorides.

CHAPTER III

Experimental (a) (b)

o-Ethylbenzonitrile⁷ In a 3 gal. crock was placed 447.8 g. (3.75 moles) of cuprous cyanide, 2.25 liters of water, and enough potassium cyanide to produce a clear solution (about 7.5 moles). Cracked ice then was added to cool the reaction to 0°. While the cuprous cyanide solution was cooling, 363 g. (3.0 moles) of o-ethylaniline was mixed in a 3 gal. crock with 750 ml. of 28% hydrochloric acid and cracked ice (about 3 kg.) to bring the reaction mixture to 0°. A solution of 211 g. (3.05 moles) of sodium nitrite in 600 ml. of water was added with stirring to the amine hydrochloride. The temperature was kept at 0 - 5° by the addition of cracked ice. At the completion of the addition of sodium nitrite the reaction mixture showed a distinct reaction for free nitrous acid on starch-iodine paper. This mixture was neutralized with dry sodium carbonate, using litmus paper to determine the end point.

The cuprous cyanide solution was cooled to 0° and 750 ml. of toluene was added. To this mixture was added the cold diazonium

(a) Carbon, hydrogen, nitrogen, and bromine analyses were done by Geller Microanalytical Laboratories, Bardonia, New York.

(b) Chlorine analyses were performed by the author according to the procedure described in Blib., ref. 8.

solution. During the addition, which takes about 20 minutes, such vigorous stirring was maintained that the toluene on the surface was constantly drawn down to the stirrer, and the temperature was maintained at 0 - 5° by the addition of cracked ice. At the completion of the addition of the diazonium solution, the mixture was stirred and maintained at 0° for an additional 30 minutes, and then allowed to rise to room temperature, which required about 3 hrs. The stirring was continued for 2 hrs. at room temperature, following which the reaction mixture was heated to 50° without stirring. The reaction was then allowed to cool to room temperature and the aqueous layer was drawn off by a siphon and extracted with benzene. The combined organic layers were steam distilled and the organic material which steam distilled was fractionally distilled, after removal of the solvent under reduced pressure, yielding 200 g. (50%) of the desired product, b.p. 91-93° (12 mm.), n_D^{24} 1.5218.

o-(α -Bromoethyl) benzonitrile In a 1-liter flask fitted with a reflux condenser (protected by a calcium chloride drying tube) was placed 60 g. (0.46 mole) of o-ethylbenzonitrile, 82 g. (0.46 mole) of N-bromosuccinimide, 5.5 g. (5 mole per cent based on NBS) of benzoyl peroxide, and 350 ml. of carbon tetrachloride. The reaction was illuminated with a 235 watt sun lamp and heated under reflux for 2½ hours, cooled, and filtered to remove the succinimide. The solvent was then removed under reduced pressure and the residual material was fractionally distilled to yield 79.4 g. (82.5%) of a pale yellow liquid, b.p. 99° (2-3 mm.), n_D^{20} 1.5759.

Anal. Calcd. for C_9H_8BrN : Br, 38.04.
Found: Br, 38.04.

Trimethyl ammonium bromide adduct of o-(α -bromoethyl) benzonitrile. In a 500 ml. flask was placed 350 ml. of cold benzene, 75 ml. (49 g., 1.0 mole) of trimethyl amine, and 21 g. (0.1 mole) of o-(α -bromoethyl) benzonitrile. This was allowed to stand at room temperature for 8 days. It then was filtered and the solid was recrystallized from an absolute ethanol-ether mixture. The product, 14.75 g. (55%), crystallized as flat white plates, m.p. 166.5-167.2.

Anal. Calcd. for $C_{12}H_{17}BrN_2$: N, 10.41.
Found: N, 10.36.

o-Cyano- α -phenethyl acetate In a 1-liter flask fitted with a reflux condenser (protected with a calcium chloride drying tube), stirrer, and dropping funnel was placed 83 g. (0.50 mole) of silver acetate and 400 ml. of glacial acetic acid. To this was added dropwise over 2 hrs. 79 g. (0.38 mole) of o-(α -bromoethyl) benzonitrile. The addition was carried out with the acetic acid just starting to reflux and with rapid stirring. After the addition was complete, the reaction was stirred for an additional 9 hrs., cooled, and the silver bromide was filtered off. The solution was then diluted with 4 liters of water and extracted with ether six times. The ether was stripped and the crude product was distilled at reduced pressure to yield 53 g. (75%) of colorless liquid, b.p. 95-97° (0.5 mm.), n_D^{20} 1.5120.

Anal. Calcd. for $C_{11}H_{11}NO_2$: C, 69.84; H, 5.82; N, 7.43.
Found: C, 68.94; H, 5.88; N, 8.15.

o-Cyanostyrene A Vicor pyrolysis tube filled with pieces of Vicor tubing was heated to a temperature of 550-575° in a vertical electrical heater and 26 g. (0.14 mole) of o-cyano- α -phenethyl acetate

containing a small amount of picric acid was dropped through it over a period of 35 minutes. The receiver contained some picric acid and was cooled in an ice bath. Distillation of the pyrolysis mixture in an Argon atmosphere gave 14.28 g. (78%) of a colorless liquid, b.p. 70-72° (3 mm.), n_D^{20} 1.5650. (see p. 4).

Anal. Calcd. for C_9H_7N : C, 83.69; H, 5.46.
Found: C, H,

o-(α,β dibromoethyl) benzonitrile A sample of o-cyanostyrene was dissolved in glacial acetic acid and an excess of bromine added. The reaction mixture was allowed to stand for 15 minutes, diluted with water, cooled and extracted with ether. The ether was dried over anhydrous magnesium sulfate. The ether was removed under reduced pressure and the crude material was recrystallized from an ethanol-water mixture to yield a white solid, m.p. 85-86°; Lit.⁵ 86-86.5°.

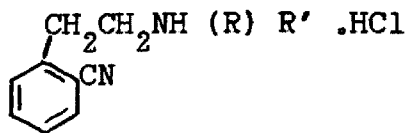
Dehydrohalogenation of o-(α bromoethyl) benzonitrile with quinoline Quinoline (10 g.) containing some N-phenyl-2-naphthylamine, was placed in a 300 ml. 3-necked flask and heated under reduced pressure such that its boiling point was about 170°. To it was added slowly 10 g. (0.047 mole) of o-(α bromoethyl) benzonitrile containing N-phenyl-2-naphthylamine. The heat was increased to about 190° to give equal rates of distillation and addition. The distillate was taken up in ether and extracted with 3 N hydrochloric acid. The ether solution was dried over anhydrous calcium chloride. Removal of the ether and fractional distillation of the crude product yielded 1 g. (16%) of a colorless liquid, b.p. 103-105° (15 mm.); n_D^{25} 1.5610. Lit.⁵ b.p. 53° (0.15 mm.), n_D^{20} 1.5756. (see p. 4).

Attempted dehydrohalogenation of o-(α -bromoethyl) benzonitrile. In a pressure bottle was placed 10 g. (0.05 mole) of o-(α -bromoethyl) benzonitrile and 8 g. (0.10 mole) of pyridine. The bottle was sealed and allowed to stand 18 hrs. and heated at 130-145° for 6 hrs. The reaction mixture was filtered and 11 g. of solid was recovered (m.p. 176.5-178). Based on the quaternary ammonium bromide salt this is a 77% yield. The liquid was distilled and was found to be pyridine.

Reaction of o-cyanostyrene with amines. In a pressure bottle was placed a two-fold excess of the desired amine, 4 drops of Triton B, and the desired amount of o-cyanostyrene. The bottle was sealed and heated on a steam bath for 4 hrs, and then allowed to stand for 24 hrs. at room temperature. The reaction mixture was taken up in benzene and washed several times with water. The benzene layer was dried over anhydrous magnesium sulfate, filtered, and dry hydrogen chloride was passed through it. The hydrochloride salt was then filtered and recrystallized from acetone.

TABLE I

Hydrochloride Salts of N-substituted β -(o-cyanophenethyl) amines



Amine used	Crude Yield %	Hydrochloride M.P. °C	Pure Hydrochloride M.P. °C	per cent Calcd.	Chlorine Found
piperidine	34	187-200	209-212	14.14	14.19
butylamine	14	oil			
cyclohexylamine	0				
benzylamine	0				
dimethylamine	46	151-154	153-155	16.83	16.66
morpholine	14	190-200	237-240	14.03	

CHAPTER IV

Summary

(a) Various routes to a new synthesis of o-cyanostyrene were investigated.

(b) o-cyanostyrene was prepared according to the following route: o-ethylaniline \longrightarrow o-ethylbenzotrile \longrightarrow o-(α -bromo-ethyl) benzotrile \longrightarrow o-cyano- α -phenethyl acetate \longrightarrow o-cyanostyrene.

(c) The addition reactions of o-cyanostyrene with n-butylamine, piperdine, benzylamine, dimethylamine, morpholine, and cyclohexylamine were studied.

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Part II

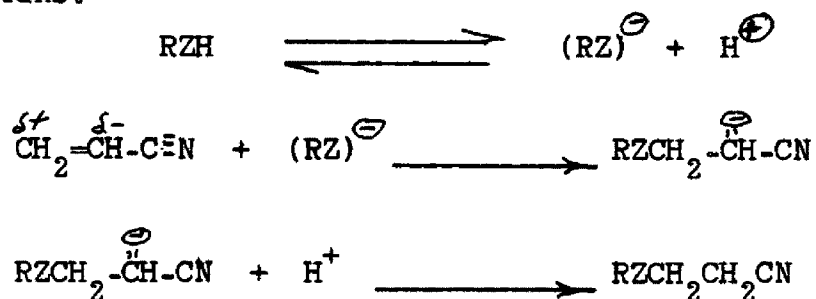
CYCLOPROPANE CARBONITRILE: ATTEMPTS AT ADDITION

REACTIONS WITH NUCLEOPHILIC REAGENTS

CHAPTER I

Introduction

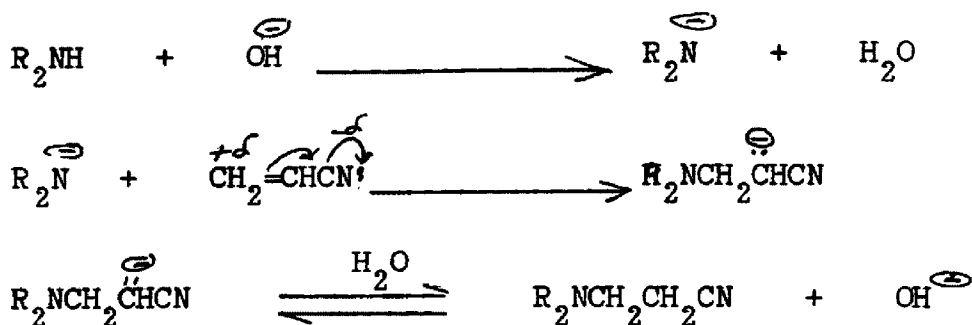
Simple olefins react as nucleophilic substances in their addition reactions, but the addition of a strong electron withdrawing group, such as cyano, to one of the carbon atoms connected by the double bond causes this double bond to now react as an electrophilic group, adding such nucleophilic reagents as amines, alcohols, and mercaptans.



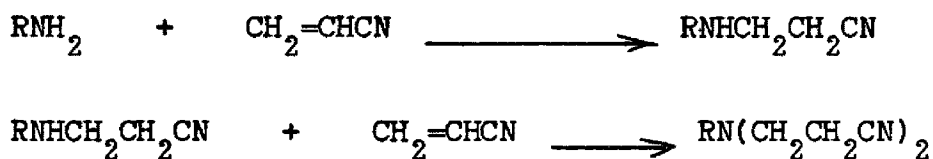
(Here, R is alkyl or aryl group; Z is S, N, or O atom)

The addition reactions of acrylonitrile ($\text{CH}_2=\text{CH}-\text{CN}$) and some of its homologs have been studied in great detail. Acrylonitrile reacts readily with amines, alcohols, and mercaptans to form the corresponding 2-cyanoethylamines, 2-cyanoethylethers, and 2-cyanoethylsulfides.

In general, amines add very readily to acrylonitrile, but the ease of addition varies considerably. With those amines which react slowly, an acidic or basic catalyst is desirable; with some amines a catalyst is essential.¹ Presumably the stepwise mechanism for the reaction in these cases may take place as follows:



Primary amines, in which there are two labile hydrogen atoms attached to the nitrogen atom, may react with one or two moles of acrylonitrile. Low temperatures favor the addition of one mole of acrylonitrile whereas high temperatures result in the addition of the initial secondary amine to a second molecule of acrylonitrile, especially if there is an excess of the nitrile.



Since the first preparation of cyclopropane and the presentation of the famous Strain Theory² of Baeyer's it has been postulated that the reactivity of cyclopropane should be quite high because of the large deviation in the bond angle from the normal bond angle of the carbon atom. In cyclopropane the three carbon atoms must form an angle of 60° with each other.

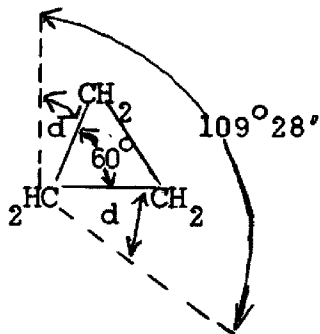


Figure 1

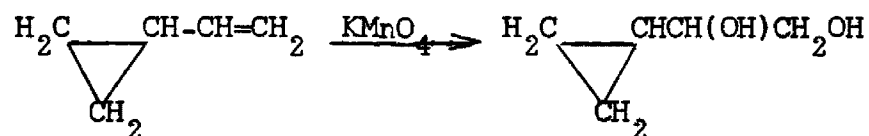
Baeyer considered the preferred angle between any two valences of a single carbon atom to be $109^{\circ}28'$. It is possible, however, for this angle to be allowed; such an alteration in the preferred angle leads to a condition of strain, the magnitude of which is proportional to the valence deviation, d , defined in terms of the equation

$$d = \frac{1}{2}(109^{\circ}28' - \text{bond angle})$$

The factor, $\frac{1}{2}$, was introduced by Baeyer because the total deviation from the preferred bond angle may be considered as divided equally between two bonds. Thus in the cyclopropane ring, the internal C-C bond angle must be 60° ; this differs by $49^{\circ}28'$ from the normal bond angle of $109^{\circ}28'$. This deviation would then cause the valence electrons to be brought toward each other causing strain in the ring. The valence electrons would tend to repel each other due to like charges and this would make the ring less stable. The valence electrons in a cyclopropane ring are not bound as tightly as electrons in a normal covalent bond and therefore they may act more like the π electrons of an alkene linkage.

It is well known that the cyclopropane ring exhibits marked resemblances to the alkene linkage in its tendency to act as a site of "unsaturation" and also that it undergoes addition reactions with the same reagents. The unsubstituted cyclopropane ring, therefore, acts as a nucleophilic center and reacts readily with electrophilic reagents such as halogens, hydrogen halides, sulfuric acid, and other compounds of this type. The ring may be hydrogenated to yield propane derivatives. Iodine and bromine also react fairly readily to

form 1:3 dihalogenopropanes. Halogen acids cause fission of the ring giving substituted propyl halides; the manner in which addition takes place is governed by the number and disposition of the substituent alkyl groups. The ring always opens between the carbon atoms which hold the smallest and largest number of alkyl groups, i.e. the Markownikoff rule of alkene addition is obeyed. The discriminating factor between the two classes of compounds is provided by the action of potassium permanganate; cyclopropyl compounds are untouched by this reagent in the cold whereas olefins react readily. The difference is well illustrated by the following reaction:



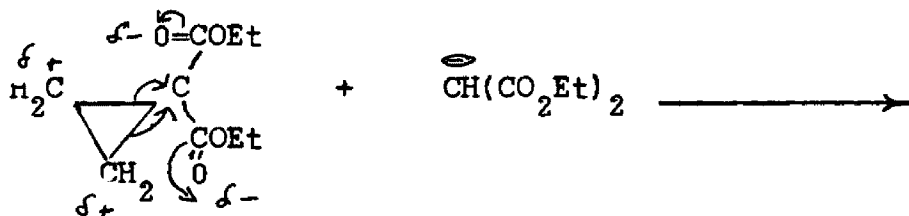
Ozone also has little effect on the three-membered ring³. Substituent electronegative groups diminish the additive reactivities of both alkenes and cyclopropanes to these reagents⁴.

It has been shown by Eastman⁵ that a cyclopropane ring cannot transmit conjugation if it is placed in the center of a carbon chain containing unsaturated groups on either side of it, but the ring can extend a chain of conjugation if it is placed at one end of the chain.

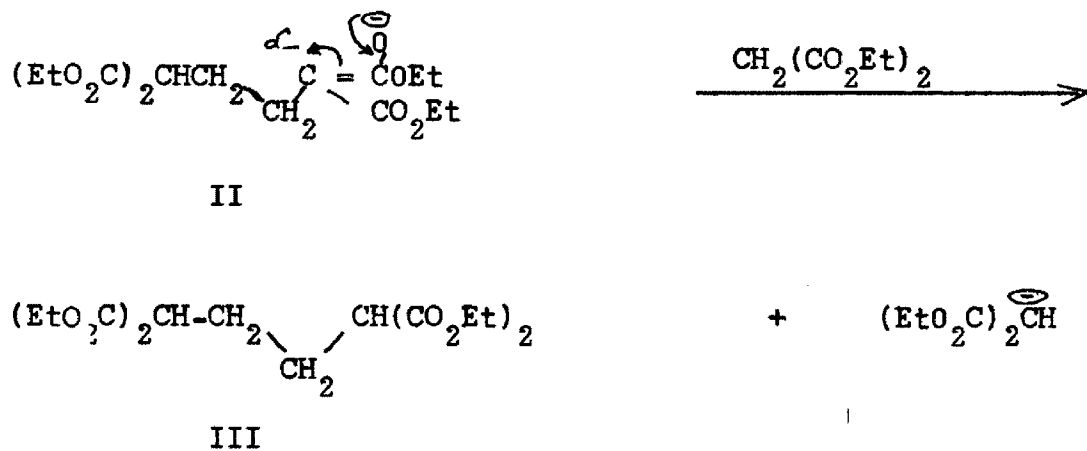
CHAPTER II

Discussion

Since there is no well-defined nucleophilic center in a cyclopropane ring conjugated with an unsaturated electronegative group, it is not unreasonable to expect that the ring might exhibit electrophilic reactivity toward a suitable reagent. This would be a mode of reaction similar to those which alkene linkages conjugated with an unsaturated electronegative group undergo. There are numerous examples in which the alkene linkage in such compounds acts as an electrophilic center and adds nucleophilic reagents such as amines, mercaptans, alcohols, weak acids, etc. Such a reaction for an electronegatively di-substituted cyclopropane has been observed in a reaction of di-ethyl 1, 1-cyclopropane dicarboxylate with diethyl malonate in the presence of sodium ethoxide to give tetra-ethyl 1, 1, 4, 4-butane tetracarboxylate⁶. The malonate ion is here apparently attacking an electrophilic carbon atom of the ring in the initial step of the reaction. This then causes the ring to open to produce the anion II.



Hydrogen exchange then occurs between the anion II and a molecule of malonic ester to give III and generates a malonate anion which may repeat the reaction cycle ⁷.

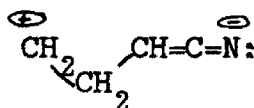


Studies of the ultraviolet absorption spectra⁸ offer convincing evidence that the cyclopropane ring is unsaturated in the sense that electrons of sufficient polarizability to conjugate with an adjacent unsaturated group are present. Quantum mechanical considerations indicate that intense absorption in the ultraviolet region is due to electronic transitions from a neutral ground state to ionic excited states⁹.

Rogers and Roberts¹⁰ indicate that the C-C bond electrons in the three-membered rings are more weakly bound than the usual electrons and tend to exhibit the characteristics associated with mobile electrons. This concept receives confirmation from the nature of the far ultra-violet spectrum of cyclopropane¹¹ and from the high value of the quenching cross-section of cyclopropane for cadmium resonance radiation¹². This cross-section increases if mobile electrons are present; the value for cyclopropane is intermediate between

those for olefins and paraffine respectively.

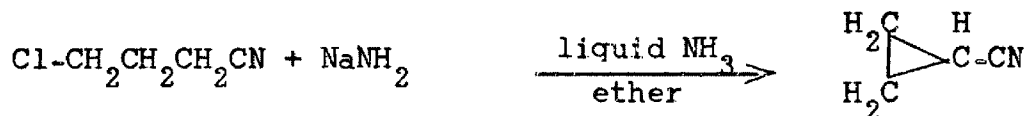
Dipole moment studies have been carried out on cyclopropane carbonitrile and the dipole moment has been found to be 3.75 D, which is 0.04 D higher than isopropyl cyanide. This may indicate a small contribution in the rest state from structures such as



tending to increase the moment. However, it must be observed that no great confidence can be placed in the interpretation of these moments since vinyl cyanide shows a decrease of about 0.1 to 0.2 D below aliphatic cyanides both in vapor and solution. The increase might be due entirely, or in part, to effects of induction¹³. The approach of a nucleophilic reagent or of a basic catalyst might be expected to enhance the shift of electrons to produce the above resonance form.

Since no investigation has been reported in the literature of attempts to carry out simple addition reactions between nucleophilic reagents and cyclopropane having one unsaturated electro-negative group substituted on the ring, the principal purpose of the research reported in this paper was to (a) determine the reactivity of the cyclopropane ring in cyclopropane carbonitrile toward nucleophilic reagents and (b) compare the results with those obtained from analogous open chain unsaturated nitriles. The experimental work was done with reagents which undergo familiar "cyanoethylation" reactions with acrylonitrile.

Cyclopropane carbonitrile was prepared by the reaction of γ -chlorobutyronitrile with sodium amide in a mixture of ether and liquid ammonia, which is the preparation described by Cloke¹⁴.



Preparation of this compound at different times produced clear liquids which had the same boiling point but did not have the same refractive indices; they did agree with several different reports in the literature, where similar variance was noted. As a check to see if the liquid isolation was actually cyclopropane carbonitrile, cyclopropylmethyl ketone was prepared by the reaction of methyl magnesium iodide with the suspected nitrile. The desired ketone was isolated in a 40% yield. It is interesting to note that 1,4 addition of the Grignard reagent (a strong base) did not occur. A 2, 4-dinitrophenylhydrazone derivative was prepared and a bright red solid was isolated which was identified by melting point. According to a generalization formulated by Dr. C. E. Redemann (based on unpublished observations at The California Institute of Technology), when the parent carbonyl compound has a double bond conjugated with the carbonyl group, the 2, 4 dinitrophenylhydrazone is colored red instead of being the usual yellow color. A few exceptions are known¹⁵.

Attempted addition reactions of cyclopropane carbonitrile were carried out with piperidine under varying conditions. The reactants were heated in a pressure bottle in different experiments with catalytic amounts of Triton B (benzyltrimethylammonium hydroxide), cupric acetate, aluminum chloride, sodium amide, sodium methoxide,

sodium ethoxide, and sodium. Reactions were also carried out under heat and pressure with equivalent amounts (to the nitrile) of aluminum chloride, sodium amide, and sodium ethoxide. No identifiable addition products were isolated from any of the reactions. A reaction was also carried out under heat and pressure in the presence of a catalytic amount of Triton B between cyclopropane carbonitrile and β -mercapto ethanol. A mercapto ethanol polymer was isolated from this reaction, but no addition compound.

CHAPTER III

Experimental

γ -Chlorobutyronitrile¹⁶. In a one liter three-necked flask fitted with a dropping funnel, stirrer, and a reflux condenser were placed 41 g. (0.60 mole) of potassium cyanide and 50 ml. of water. After the potassium cyanide dissolved, 175 ml. of 95% ethanol was added. To this was added 79 g. (0.50 mole) of 1-bromo-3-chloropropane over a period of 1 hr. The reaction mixture was then heated under reflux on a steam bath for 2 hrs., diluted with an equal volume of water and extracted with chloroform (2x40 ml.). The chloroform solution was washed with a 50% calcium chloride solution (2x30 ml.), once with 75 ml. of water, and dried over anhydrous calcium chloride. The chloroform was removed at reduced pressure, and the residual material was fractionally distilled to yield 26.5 g. (51%) of the desired product, b.p. 70-73° (10 mm.); n_D^{20} 1.4444.

(Lit.¹⁷ b.p. 77-78° (13 mm.); n_D^{20} 1.4446.)

Cyclopropane carbonitrile (cyclopropyl cyanide)¹³.

In a 500 ml. three-necked flask fitted with a stirrer and a reflux condenser was placed about 350 ml. of liquid ammonia. To this was added slowly 18 g. (0.785 mole) of sodium. A small amount of cobalt nitrate was placed in the flask to act as a catalyst. The sodium was added in small amounts and the reaction could be followed by the blue color of the mixture. When the blue color disappeared, more sodium was added. When the addition was complete, ether was

added at such a rate as to maintain the volume at about 300 ml. as the ammonia evaporated.

In a four liter Dewar flask equipped with a stirrer was placed 500 ml. of liquid ammonia and 60 g. (0.51 mole) of γ -chlorobutyronitrile. The ether solution of sodium amide was then added slowly over a period of 45 min. with stirring. The reaction mixture was stirred for 1 hr., a small amount of solid phenolphthalein was added and the excess sodium amide was neutralized with dry ammonium chloride. The reaction mixture was filtered and the ammonia was allowed to evaporate. Distillation at atmospheric pressure yielded 27 g. (79%) of the desired product, b.p. 129-131°, n_D^{25} 1.4207; b.p. 130°, n_D^{25} 1.4188. (Lit.¹⁸ b.p. 133-135, n_D^{25} 1.4208; Lit.¹² b.p. 65° (75 mm.), n_D^{25} 1.4188.)

Attempted Addition of Piperidine to Cyclopropane Carbonitrile. (A)

In a 125 ml. flask equipped with a reflux condenser protected by a soda lime trap was placed 15 g. (0.28 mole) of piperidine. Depending on the catalyst to be used either 1.06 g. (0.01 mole) of aluminum chloride, 1.0 g. (0.005 mole) of cupric acetate, 3.9 g. (0.1 mole) or 0.39 g. (0.01 mole) of sodium amide was added, the flask was heated on a steam bath and 6.7 g. (0.1 mole) of cyclopropane carbonitrile was then added. The reaction mixture was heated for 8-16 hrs., cooled, diluted with 100 ml. of a saturated salt solution, and the mixture was extracted with ether. The ether solution was dried over anhydrous magnesium sulfate. On distillation only starting material and a small amount of unidentifiable liquid were isolated.

Attempted Addition of Piperidine to Cyclopropane Carbonitrile (B)

In a pressure bottle was placed 25 ml. (0.25 mole) of piperidine and 0.01 mole of sodium methoxide, 0.1 mole of sodium ethoxide, 0.1 g. (0.001 mole) of aluminum chloride, or a drop of Triton B, depending on which catalyst was to be used. To this was added 6.7 g. (0.1 mole) of cyclopropane carbonitrile and the bottle was sealed. The reaction mixture was heated at 100-160° for 3-6 hrs. If a solid catalyst was used it was removed by filtration and the reaction mixture was fractionally distilled. No identifiable addition product was isolated.

Cyclopropyl-methyl ketone. A 250 ml. three-necked flask equipped with a reflux condenser (protected by a calcium chloride drying tube), stirrer, and dropping funnel was flame dried. In the flask was placed 2.7 g. (0.11 mole) of magnesium turnings and 10 ml. of anhydrous ether. To this was added, dropwise and with stirring, 15.6 g. (0.11 mole) of methyl iodide in 10 ml. of anhydrous ether. After the addition was complete, the Grignard reagent was stirred at room temperature for 30 min. To this Grignard reagent was added 6.7 g. (0.1 mole) of cyclopropane carbonitrile in 15 ml. of anhydrous ether. On completion of the addition the reaction mixture was stirred at room temperature for 1 hr. and then hydrolyzed with 100 ml. of 10% hydrochloric acid. After hydrolysis, the reaction mixture was stirred for 1½ hrs., the ether layer was separated and the aqueous layer was extracted with ether (2x25 ml.). The combined ether layers were dried over anhydrous magnesium sulfate, the ether was removed by distillation, and the residual material was fractionally distilled to yield 3.4 g. (40%) of a colorless liquid b.p. 101-108°, n_D^{25} 1.4210, Lit.³ b.p. 111°, n_D^{20} 1.4250.

Cyclopropyl-methyl ketone 2,4-dinitrophenylhydrazone.

A 2,4-dinitrophenylhydrazine solution was prepared by dissolving 2 g. (0.01) of 2,4-dinitrophenylhydrazine in 10 ml. of concentrated sulfuric acid and adding 15 ml. of water and 10 ml. of ethanol. This hot solution was added to 0.84 g. (0.01 mole) of cyclopropyl-methyl ketone in 20 ml. of ethanol. The solid product was recrystallized from an ethanol-ethyl acetate mixture. M.p. 147-149°. Lit.³ M.p. 149-150°.

Attempted Addition of β -Mercapto ethanol to Cyclopropane.

carbonitrile. In a pressure bottle were placed 7.8 g. (0.1 mole) of β -mercapto ethanol and 6.7 g. (0.1 mole) of cyclopropane carbonitrile. The bottle was sealed and heated for 3 hrs. at 120-170°. The it was cooled and allowed to stand 24 hrs., 1 ml. of Triton B was added, and the reaction mixture allowed to stand an additional 12 hrs. It was then heated at 120° for 13 hrs. On cooling the reaction mixture solidified. It was extracted with ether, the solid being ether insoluble. The solid which was isolated, 4 g., was found to be a β -mercapto ethanol polymer (m.p. 90-115°). A sodium fusion indicated sulfur to be present but no nitrogen.

The ether was removed on the steam bath, and an attempt was made to fractionally distill the residue. On heating the distilling flask a solid separated. The liquid continued to polymerize on standing.

CHAPTER IV

Summary

a. Cyclopropane carbonitrile was prepared by the action of sodium amide on γ -chlorobutyronitrile.

b. Cyclopropyl-methyl ketone was prepared by the action of methyl magnesium iodide on cyclopropane carbonitrile.

c. Reaction of cyclopropane carbonitrile with piperidine and β -mercapto ethanol were attempted under varying conditions using sodium amide, sodium methoxide, sodium ethoxide, Triton B, cupric acetate, and aluminum chloride as catalysts, and all attempts were unsuccessful.