# The Reduction of 1,2-Dinitrobenzene by the Cyanohydrin of *p*-Nitrobenzaldehyde

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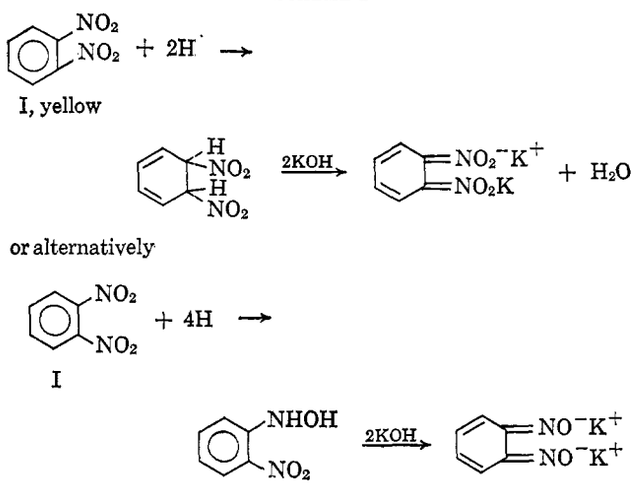
The reduction of *o*-dinitrobenzene by the cyanohydrin of *p*-nitrobenzaldehyde and a number of other substituted benzaldehydes has been studied. The rates of reduction were followed spectrophotometrically, monitoring the change in optical density at 560 mμ, ascribed to the di-*aci* form of *o*-nitrophenylhydroxylamine. Only *p*-nitro- and *p*-cyanobenzaldehyde reacted at an appreciable rate to form a compound capable of effecting the reduction of *o*-dinitrobenzene. A kinetic study of the reaction of *p*-dinitrobenzaldehyde, cyanide ion, and *o*-dinitrobenzene revealed a first-order dependence on *p*-nitrobenzaldehyde and cyanide ion, and a zero-order dependence on *o*-dinitrobenzene. The kinetics indicate that the rate-determining step is the reaction of *p*-nitrobenzaldehyde with cyanide ion to form the cyanohydrin anion, which then reacts rapidly with the aromatic nitro compound to yield the di-*aci*-*o*-nitrophenylhydroxylamine. The isolation of the products of this reaction is also reported.

Feigl[1] reported that a variety of reductants was capable of effecting the reduction of 1,2-dinitrobenzene (I) in the presence of alkali to *o*-nitrophenylhydroxylamine. This reaction served as the basis for qualitative spot tests for such compounds as hydroquinone, ascorbic acid, benzoic acid hydrazide, and reducing sugars. Feigl proposed the sequence shown in Scheme I.[2-4]

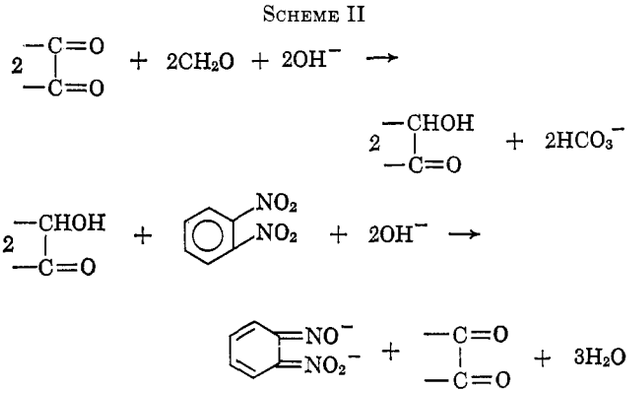
SCHEME I




Formaldehyde was also found to effect the reduction of *o*-dinitrobenzene, but at a slow rate. The addition of α-diketones enhanced the reaction. It was postulated[1] that formaldehyde reacted with α-diketones in the reaction sequence in Scheme II. The α-diketone is regenerated to react cyclically with another molecule of formaldehyde.

A similar reaction was proposed for *o*- and *p*-quinones.[5] It would follow that a catalytic reaction involving aromatic aldehydes and cyanide ions would result in a benzoin condensation whose products would reduce *o*-dinitrobenzene. The formation of the characteristic blue color of the *o*-nitrophenylhydroxylamine dianion[4] could be used to monitor the reaction. Aryl

SCHEME II




aldehydes with electron-withdrawing substituents (*p*-Br, *p*-$NO_2$) would not undergo the benzoin condensation and would not, therefore, be expected to effect the reduction of *o*-dinitrobenzene. Nevertheless, it was found that *p*-nitrobenzaldehyde, in the presence of cyanide ion, rapidly effected the reduction. It has been shown[6] that *p*-nitrobenzaldehyde readily forms a cyanohydrin. Ide and Buck[7] argued that *p*-nitrobenzaldehyde does not undergo the symmetrical benzoin condensation because the electron density in the *p*-nitrobenzaldehyde cyanohydrin anion is conjugatively removed from the carbon atom involved in the nucleophilic attack.

It was proffered,[7] in contrast, that *o*-nitrobenzaldehyde undergoes the symmetrical benzoin condensation because the nitro group and the cyanohydrin anionic group [$-^{\ominus}\ddot{C}(CN)OH$] are not conjugated owing to steric constraint to coplanarity, allowing localization of the electrons on the carbon atom of the anionic cyanohydrin moiety. However, neither *o*-nitrobenzaldehyde nor *p*-nitrobenzaldehyde has been reported to yield symmetrical benzoin condensations. Thus, Kekrantz and Alquist,[8] in refutation of earlier reports[9] showed that *o*-nitrobenzaldehyde, upon treatment with cyanide, yielded *o*-azoxybenzoic acid, *o*-nitrosobenzoic acid, and unchanged aldehyde. Heller,[10] moreover, demonstrated that the cyanohydrin of *p*-nitrobenzaldehyde treated with dilute alkali was converted to *p*-

(1) F. Feigl, "Spot Tests in Organic Analysis," Elsevier Publishing Co., New York, N. Y., 1956, pp 131–132.
(2) J. Meisenheimer, *Ber.*, **36**, 4174 (1906); **39**, 2528 (1909); **50**, 1161 (1911).
(3) R. D. Block and D. Boling, *J. Biol. Chem.*, **129**, 1 (1939).
(4) R. Kuhn and F. Weigand, *Ber.*, [2] **69**, 1969 (1936).
(5) Reference 1, pp 205–206.
(6) R. Baleer, *et al.*, *J. Chem. Soc.*, 191 (1942); 1089 (1949).
(7) W. S. Ide and J. S. Buck, *Org. Reactions*, **4**, 269 (1948).
(8) E. Kekrantz and A. Alquist, *Ber.*, **41**, 878 (1908); **43**, 2606 (1910).
(9) V. Popovici, *ibid.*, **40**, 2562 (1907); **41**, 1851 (1908).
(10) G. Heller, *ibid.*, **46**, 285 (1913).

nitrobenzoic acid, *p,p'*-dicarboxyazobenzene, and *p*-nitrosobenzoic acid.

This report deals with an examination of the reaction between the anions of the benzaldehyde cyanohydrins and 1,2-dinitrobenzene with a view toward clarification of the aforementioned discrepancies.

## Results and Discussion

A number of substituted benzaldehydes were screened for their ability to effect the reduction of *o*-dinitrobenzene in the presence of cyanide to *o*-nitrophenylhydroxylamine. The rates of reduction were followed spectrophotometrically by monitoring the change in the optical density at 560 mμ, ascribed to the di-*aci* form of *o*-nitrophenylhydroxylamine (II)[4] (Table I).

TABLE I

INITIAL RATES OF REDUCTION OF *o*-DINITROBENZENE BY SUBSTITUTED BENZALDEHYDES IN THE PRESENCE OF CYANIDE ION[a]

| Aldehyde substituent | ΔOD/min[b] |
|---|---|
| *p*-Nitro | 0.20 |
| *o*-Nitro | 0.010 |
| *p*-$Me_2N$ | 0 |
| *p*-$Et_2N$ | 0 |
| *m*-OH | 0 |
| 2,4,6-Trihydroxy | 0 |
| 2-Cl-4-$Me_2N$ | 0 |
| *p*-Isopropyl | 0 |
| *p*-H | 0 |
| *p*-Methoxy | 0 |
| *p*-Ethoxy | 0 |
| *p*-Benzyloxy | 0 |
| 3,4-Dimethoxy | 0 |
| 3,4,5-Trimethoxy | 0 |
| *p*-Acetamido | 0 |
| 2,4-Dimethoxy | 0 |
| *p*-Bromo | 0 |
| 2,4,6-Trinitro[c] | 0 |
| *p*-Cyano[d] | 0.14 |
| 2,6-Dichloro | 0 |
| *m*-Methoxy | 0 |
| 2,4,6-Trimethyl | 0 |
| 2-Ethoxy-3-methoxy | 0 |
| *m*-Fluoro | 0 |
| *p*-Fluoro | 0 |
| 4-Chloro-3-nitro[e] | 0 |
| *m*-Nitro[e] | 0 |
| *o*-Chloro | 0 |

[a] *o*-Dinitrobenzene = 0.1 *M*, aldehyde = 0.1 *M*, $CN^-$ = $5 \times 10^{-6}$ *M*. [b] Negative results are reported for runs containing 0.1 *N* cyanide ion, while positive results were obtained at indicated cyanide ion concentration. Initial rates are reported as the rate of change in optical density per minute. [c] Turns red due to a pH effect. [d] This compound displays a green fluorescence. [e] $2 \times 10^{-5}$ $CN^-$ needed to effect reaction.

It is to be noted that *p*-nitrobenzaldehyde reacted twenty times faster than *o*-nitrobenzaldehyde. The rate of reaction of the *m*-nitro derivative was immeasurably slow, but the rate is faster with higher concentrations of cyanide. The remaining aldehydes did not enter into the reaction, except for the *p*-cyanobenzaldehyde, which had a rate approximately $^2/_3$ that of the *p*-nitro derivative. The 4-chloro-*m*-nitro derivative reacted at about the same rate as the *m*-nitro. The *p*-bromo and *p*-fluoro benzaldehydes did not react with cyanide at an appreciable rate to effect the reduction of *o*-dinitrobenzene.

An attempt was made to isolate the products of the cyanide-catalyzed reduction of *o*-dinitrobenzene by *p*-nitrobenzaldehyde. *p*-Nitrobenzaldehyde was treated, under preparative conditions, with potassium cyanide and *o*-dinitrobenzene in aqueous methoxyethanol solvent. After acidification, successive ether and bicarbonate extractions quantitatively yielded on neutralization *p*-nitrobenzoic acid. Upon evaporation of the remaining ether solution, a complex brown-yellow solid resulted which displayed several spots on a thin layer silica gel chromatographic plate employing benzene–ethanol as the developing solvent. No attempt was made to identify the colored reduction products.

A kinetic study of the reaction revealed a first-order dependence on *p*-nitrobenzaldehyde and cyanide ion, and a zero-order dependence on *o*-dinitrobenzene (Table II). The rate was measured by following the change with time of the absorbance at 560 mμ. The reaction kinetics are in consonance with the reaction in Scheme III, where $k_2$, $k_1 >> k_{-1}$. The proposed rate-limiting step is (1) where $k_1 = 5 \times 10^3$ l. mole$^{-1}$ min$^{-1}$, approximating the rate of formation of the cyanohydrin anion of *p*-nitrobenzaldehyde. The reaction rate is also dependent on the pH of the solution (Table II). One possible intermediate, *p*-nitrobenzoyl cyanide,

TABLE II

KINETICS OF THE REACTION INVOLVING *o*-DINITROBENZENE, *p*-NITROBENZALDEHYDE, AND CYANIDE ION[a]

A. [*o*-Dinitrobenzene] = $5 \times 10^{-2}$ *M*, [$OH^-$] = $2.5 \times 10^{-2}$ *M*, [$CN^-$] = $5 \times 10^{-5}$ *M*

| [*p*-Nitrobenzaldehyde], *M* | Initial rate[b] × $10^5$ |
|---|---|
| $5 \times 10^{-5}$ | 1.1 |
| $1 \times 10^{-4}$ | 2.2 |
| $2.5 \times 10^{-4}$ | 5.1 |
| $5.0 \times 10^{-4}$ | 11.0 |
| $2.5 \times 10^{-3}$ | 51.0 |

B. [*p*-Nitrobenzaldehyde] = $5 \times 10^{-2}$ *M*, [$CN^-$] = $5 \times 10^{-5}$ *M*, [$OH^-$] = $2.5 \times 10^{-2}$ *M*

| [*o*-Dinitrobenzene], *M* | Initial rate[b] × $10^5$ |
|---|---|
| $5 \times 10^{-6}$ | 65.0 |
| $2.5 \times 10^{-5}$ | 65.0 |
| $5.0 \times 10^{-5}$ | 65.0 |
| $2.5 \times 10^{-4}$ | 65.0 |
| $5.0 \times 10^{-3}$ | 75.0 |

C. [*p*-Nitrobenzaldehyde] = $5 \times 10^{-2}$ *M*, [*o*-Dinitrobenzene] = $5 \times 10^{-2}$ *M*, [$OH^-$] = $2.5 \times 10^{-2}$ *M*

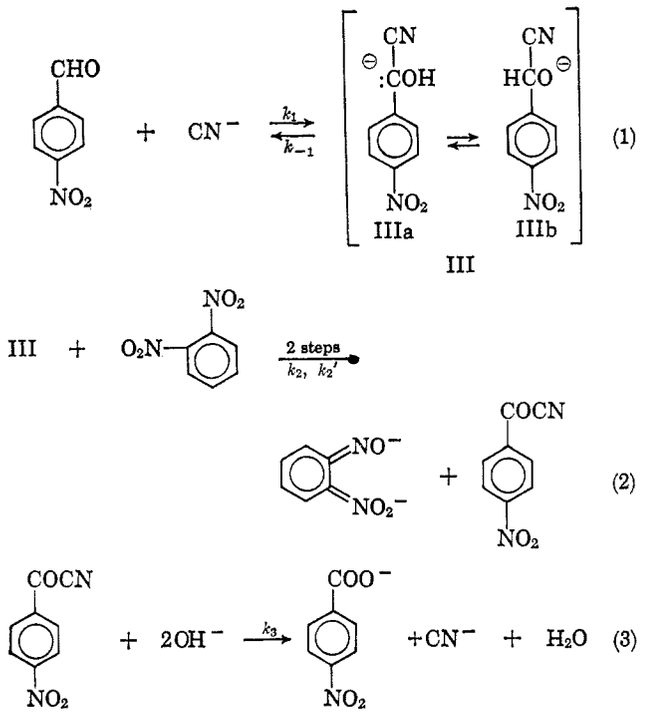
| [Cyanide ion], *M* | Initial rate[b] × $10^5$ |
|---|---|
| $2.5 \times 10^{-6}$ | 4.2 |
| $5.0 \times 10^{-6}$ | 8.5 |
| $1.0 \times 10^{-5}$ | 18.0 |
| $2.0 \times 10^{-5}$ | 40.0 |

D. [*p*-Nitrobenzaldehyde] = $5 \times 10^{-2}$ *M*, [*o*-Dinitrobenzene] = $5 \times 10^{-2}$ *M*, [$CN^-$] = $5 \times 10^{-5}$ *M*

| pH | Initial rate[b] × $10^5$ [c] |
|---|---|
| 6.0 | 0 |
| 7.0 | 18 |
| 8.0 | 37 |
| 9.0 | 75 |

[a] $T$ = 23°. [b] Initial rates expressed as moles per liter per minute. Rate = $k_1$[$CN^-$][*p*-nitrobenzaldehyde]; $k_1 = 5 \times 10^3$ l. mole$^{-1}$ min$^{-1}$. [c] Rate dependence due to differences in $k_a$ of the HCN and/or the molar absorptivity of the dye as a function of pH.

SCHEME III




is reported to be rapidly hydrolyzed by base.[11] In further support of the rapid alkaline hydrolysis of the aroylcyanides to yield the aroyl acid and cyanide ion, the model compound, benzoyl cyanide, was dissolved in dilute alkaline solutions and the rate of cyanide liberation was followed electrochemically (see Experimental Section for details). It was found that at all pH values greater than 7, the cyanide ion liberation was immeasurably fast. It is thus reasonable to expect the rapid hydrolysis of *p*-nitrobenzoyl cyanide to *p*-nitrobenzoic acid and cyanide ion ($k_3$ is very fast and is nonrate limiting). Further work is in progress to determine whether electron or hydride transfer is involved in step 2 of Scheme III.

Qualitative esr studies of undeaerated solutions of *p*-nitrobenzaldehyde, *o*-dinitrobenzene, and cyanide ion in aqueous methoxyethanol solvent revealed the absence of free radicals throughout the course of the reaction, even after the solution had attained a deep blue coloration. In view of the rapid rate of reaction between the carbanion (III) and *o*-dinitrobenzene, the nondetectability of free-radical species in this reaction is not unexpected. In contrast, as will be reported elsewhere,[12] the reaction between benzoin anion and *o*-dinitrobenzene yields free radicals, having appreciable half-lives.

The order of reactivity, as noted in Table I, of the *p*-nitro- > *p*-cyano- > *o*-nitro- > *m*-nitrobenzaldehyde, may then be correlated with relative rates of formation and stabilities of the corresponding nitrobenzaldehyde cyanohydrin anions. Here the generally accepted argument of Gould[13] appears to be applicable.[14] Interestingly, the *m*- or *p*-halogen-substituted benzaldehydes display a marked inhibition in the rate of benzoin condensation.[7] Moreover, they do not form appreciable concentrations of cyanohydrin anions capable of transfering electrons to the nitro aromatic molecule. This effect appears to be attributable to the inability of halogen substituents to assist in charge delocalization of the anion.

The inability of *o*-, *m*-, and *p*-nitro-substituted benzaldehydes to undergo the symmetrical benzoin condensations can be ascribed to an inter- or intramolecular electron transfer resulting in a simultaneous oxidation of the cyanohydrin group and reduction of the nitro group. Qualitative experiments indicate[15] that 1,3,5-triphenyltetrazolium chloride, resazurin, and indophenol serve as electron acceptors in this reaction.

## Experimental Section

**Molar Absorptivity of the Dye and Kinetic Studies.**—In order to measure the molar absorptivity of the blue dye produced from the reduction of the *o*-dinitrobenzene by III, a pure sample of *o*-nitrophenylhydroxylamine monoacetate was prepared as follows. Two grams of *o*-dinitrobenzene (Aldrich Chemical Co.) (0.012 mole) was dissolved in 50 ml of tetrahydrofuran with slight heat and stirring. Zinc dust (2.0 g) and ammonium chloride (3.0 g) were then added and the stirring was continued for 3 hr at room temperature. The initial pale yellow solution turned deep brown yellow. The suspension was filtered and 15 ml of acetic anhydride–pyridine (3:1) was added. The solution now became yellow. After 0.5-hr acetylation time, 10 vol of ice–water were added and 1.8 g (83% yield) of a yellow solid was obtained, which upon recrystallization from ether–petroleum ether (40–60° fraction), melted at 44–45° (uncor). The purity of the compound was checked by infrared (N–H, 3.01 $\mu$, ester carbonyl, 5.72 $\mu$), and elemental analysis (*Anal.* Calcd for $C_8H_8N_2O_4$: C, 48.9; H, 4.08. Found: C, 48.4; H, 3.8.). Repeated attempts to obtain stable preparations of *o*-nitrophenylhydroxylamine by the method given by Kuhn and Weigand[4] were unsuccessful. Known concentrations of the purified monoacetate were then hydrolyzed with excess base to form the blue compound, and the absorbance was determined at a pH of 9 at various time intervals until a stable, maximum value was obtained. From these experiments, an average molar absorptivity of $2.3 \times 10^3$ at pH 9.0 was obtained.

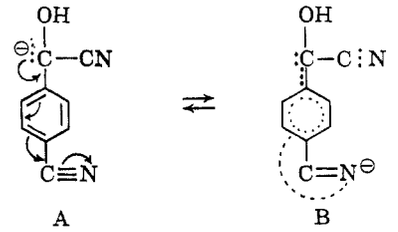
All rates were calculated by dividing the change in optical density at 560 m$\mu$/min ($\Delta$OD/min) by the molar absorptivity of the dye. Results are reported in moles per liter per minute (Table II).

The substituted benzaldehydes were screened for their ability to effect the reduction of *o*-dinitrobenzene in the presence of cyanide as follows: 1 ml of a 0.1 *M* solution of the aldehyde was added to 1 ml of 0.1 *M* *o*-dinitrobenzene and 0.1 ml of 0.5 *M* NaOH. The spectrophotometer was adjusted to read zero absorbance at 560 m$\mu$. At zero time, 0.1 ml of $CN^-$ was added (final *M* $5 \times 10^{-6}$), and the rate of change of optical density was recorded *vs.* time. The relative rates of reaction are reported in Table I as $\Delta$OD per minute. The order of dependence of the reaction of *o*-dinitrobenzene with *p*-nitrobenzaldehyde and cyanide ion upon each reactant was determined by varying the concentration of each reactant while holding the others constant.

**Isolation of the Products of the Reaction of *o*-Dinitrobenzene, *p*-Nitrobenzaldehyde, and Cyanide.**—The products of reactions 1 and 2 were prepared by reacting *p*-nitrobenzaldehyde (0.002 *M*), cyanide (0.002 *M*), and *o*-dinitrobenzene (0.01*M* ), dissolved in 75 ml of methoxyethanol, to which 1.0 g of sodium hydroxide

(11) H. V. Kolbe, *Ann. Chem.*, **90**, 62 (1854).
(12) D. N. Kramer, G. G. Guilbault, and F. M. Miller, in preparation.
(13) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, Inc., New York, N. Y., 1962, pp 396–397.

(14) Note: The *p*-cyanobenzaldehyde cyanohydrin anion may be stabilized *via* charge delocalization owing to contribution of canonical form B.




(15) G. G. Guilbault and D. N. Kramer, *Anal. Chem.*, in press.

in 50 ml of water was added. After stirring for 0.5 hr, the deep blue solution was diluted with 3 vol of water, neutralized with HCl, and extracted with ether. The ether solution was then extracted with 5% sodium bicarbonate, and the bicarbonate solution was then carefully neutralized. A light tan solid was obtained which, after recrystallization from aqueous ethanol, melted at 238–240° (lit., *p*-nitrobenzoic acid, mp 242°). The infrared spectrum (mull) coincided with the spectrum of an authentic sample of the acid. A nearly quantitative conversion of *p*-nitrobenzaldehyde to *p*-nitrobenzoic acid was effected.

**Esr Studies.**—All esr studies were performed with an Alpha esr spectrometer. A 0.01 *M* solution of *o*-dinitrobenzene was prepared in 75-ml of methoxyethanol containing 0.05 mole of sodium hydroxide, 0.05 mole of *p*-nitrobenzaldehyde, and 0.05 mole of potassium cyanide in the presence of air. No free-radical signals were found.

**Electrochemical Measurement of Benzoyl Cyanide Hydrolysis.**—The rate of hydrolysis of benzoyl cyanide was studied electrochemically at various pH values, using silver and platinum electrodes. The two electrodes were placed into a 0.1 *M* buffer solution of the pH to be studied (Tris or phosphate) and the open-cell voltage between the electrodes was measured using a Keithley electrometer and a Brown recorder. The initial voltage was approximately zero. Then 0.1 ml of a $10^{-2}$ *M* solution of benzoyl cyanide was added and the rate of change of the voltage with time was automatically recorded. The amount of cyanide liberated was calculated from standard calibration plots of voltage *vs.* log $CN^-$ concentration, and the rate of production of cyanide was indicated by $\Delta E/\Delta t$. At all pH values studied it was found that cyanide was liberated at very fast rates, the yields of cyanide being almost quantitative.

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# The Mechanism of the Disproportionation of Ethylbenzene[1,2]

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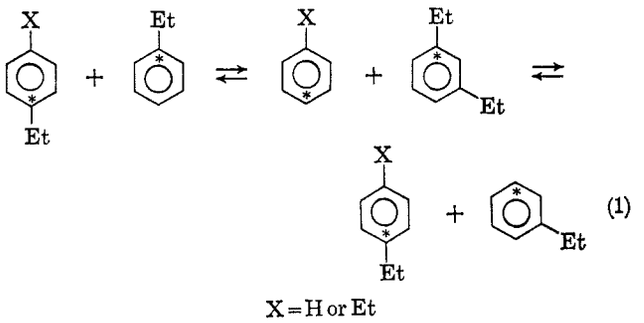
Ethylbenzene-1-$C^{14}$ was disproportionated with aluminum bromide and hydrogen bromide under the homogeneous conditions of Brown and Smoot to give benzene and di- and triethylbenzenes. A convenient method was developed for the degradation of the recovered ethylbenzene. The activity distribution in the ethylbenzene plus evidence from additional experiments demonstrate that *p*-diethylbenzene is an important intermediate in this disproportionation reaction. The essentially equal labeling in the *ortho* and *meta* positions of recovered ethylbenzene requires that the rate of the intramolecular migration of an ethyl group in ethylbenzene plus one-half of the rate of the reversal of *ortho* alkylation, if any, cannot be greater than one-half of the rate of reversal of any direct *meta* alkylation. All of the evidence and analogies are consistent with *para* alkylation followed by the intramolecular shift of an ethyl group as an important path in the formation of *m*-diethylbenzene, but other possibilities are not rigorously excluded.

The mechanism of the disproportionation (transalkylation) of alkylbenzenes has been widely studied.[5] Lien and McCauley[6] proposed that the reaction proceeded *via* a $\sigma$ complex, followed by displacement of the alkyl group by an alkylbenzene molecule. To explain the large rate difference between toluene and ethylbenzene, Brown and Smoot[7] suggested a preequilibrium of the $\sigma$ complex with a localized $\pi$ complex. The elegant study of Streitwieser and Reif[8] provided strong support for the proposal that the transalkylation proceeds *via* a Bartlett–Condon–Schneider hydride transfer.[9]




Results[5] on the disproportionation of ethylbenzene-1-$C^{14}$ exclude the localized $\pi$ complex as the major product-determining intermediate, in agreement with the conclusion of Streitwieser and Reif.[8] From the data given in Figure 1, it appeared that direct *meta* alkylation might be taking place, since an excess of radioactivity in the *meta* position compared with the *ortho* can only be reasonably explained by the reversal of *meta* alkylation (eq 1). However, the errors (due to the method of degradation and calculation) in the results[5] were large enough so that a decision on the equality or lack of equality of the activity in the *ortho* and *meta* position could not be made. The ratio of *ortho* to *meta* labeling from these earlier results was 0.6. A ratio of the *ortho* to *meta* activity near to 1 (*i.e.*, essentially equal labeling) might be the result expected if *m*-diethylbenzene were formed by *para* alkylation followed by intramolecular rearrangement (eq 2 and 3). *A priori* the rate of *ortho* alkylation might be expected to be slow owing to steric factors.[10] The intramolecular isomerization of ethylbenzene-1-$C^{14}$ to ethylbenzene-2-$C^{14}$ should take place somewhat more rapidly than the slow intramolecular isomerization of toluene-1-$C^{14}$,[11] and would also give *ortho* labeling. Therefore, equal activity in the *ortho* and *meta* positions would not exlude the possibility of *meta* alkylation, although an ex-

(1) Research was performed under the auspices of the U. S. Atomic Energy Commission.

(2) Presented at the Southwestern Regional Meeting of the American Chemical Society, Charleston, W. Va., 1964.

(3) Postdoctoral Research Associate, Brookhaven National Laboratory, 1960–1962.

(4) To whom inquiries should be sent.

(5) E. Ünseren and A. P. Wolf, *J. Org. Chem.*, **27**, 1509 (1962), and references therein.

(6) A. P. Lien and D. A. McCauley, *J. Am. Chem. Soc.*, **75**, 2407 (1953).

(7) H. C. Brown and C. R. Smoot, *ibid.*, **78**, 2176 (1960).

(8) A. Streitwieser, Jr., and L. Reif, *ibid.*, **82**, 5003 (1960); **86**, 1988 (1964).

(9) P. D. Bartlett, F. E. Condon, and A. Schneider, *ibid.*, **66**, 1531 (1944).

(10) D. A. McCauley, M. C. Hoff, N. Stein, A. S. Couper, and A. P. Lien, *ibid.*, **79**, 5808 (1957).

(11) H. Steinberg and F. L. J. Sixma, *Rec. Trav. Chim.*, **81**, 185 (1962).