A STUDY OF THE PARTIAL OXIDATION OF
MONOSUBSTITUTED-p-XYLENES

BY

FREDERICK J. HONOLD

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STATEMENT OF PROBLEM

To study the partial oxidation of asymetrically monosubstituted derivatives of p-xylenes. The substituted group was to be inert to oxidation.

To determine the distribution of isomers and to discover if there was any directive influence due to the substituted groups already present in the benzene ring.

In most aromatic substitution reactions the attack on a benzene ring is led by an electron-seeking species and hence it is expected to occur at a point where the electron density is the greatest. Electron-releasing groups attached to the benzene ring will facilitate the reaction while electron-attracting groups will hinder the reaction. The ortho-para directing groups increase the electron density of these positions and thereby activate them. The meta directing groups attract electrons, decrease the electron density of the ortho-para positions and thereby deactivate them.

In general, oxidation is a loss of electrons by a substance. Hence, substituted benzenes with two oxidizable groups should be preferentially oxidized at that group which is attached at the point of greatest electron density.

The purpose of this work is to determine if there is any analogy between the directive influences which govern aromatic substitution and the side chain oxidation of aromatic compounds.

ABSTRACT

In the oxidation of 2-nitro-p-xylene (I) using alkaline potassium permanganate, the only product isolated was 2-nitro-terephthalic acid (II). Approximately half of the starting material was oxidized. The other half remained as unreacted starting material.

The chromium trioxide oxidation of 2-nitro-p-xylene (I) in glacial acetic acid, using sulfuric acid as a catalyst, yielded only 3-nitro-p-toluic acid (III).

The chromium trioxide oxidations, of 2-N-acetylamino-p-xylene (IV) with and without sulfuric acid catalyst, yielded no oxidation products which could be identified. About half of the starting material was recovered in each case.

In a low temperature alkaline potassium permanganate oxidation of 2-N-acetylamino-p-xylene a small amount of 2-N-acetylamino-p-toluic acid (V) and unreacted 2-N-acetylamino-p-xylene were isolated.

In the alkaline potassium permanganate oxidation of 2-N-acetylamino-p-xylene (IV) carried out at reflux small amounts of 2-N-acetylamino-p-toluic acid (V) and 3-N-acetylamino-p-toluic acid (VI) were isolated. The greatest amount of material recovered from the reaction was unreacted 2-N-acetylamino-p-xylene (IV).

The expected products from the partial oxidation of monosubstituted p-xylenes are found in the literature, but none of them have been previously prepared by partial oxidation of the substituted p-xylene. Instead they were prepared by the hydrolysis of the corresponding nitrile.

The sigma values of the Hammett Equation (I), which have been used successfully in predicting aromatic substitution reactions of polysubstituted aromatic compounds, were used and found to correlate the experimental results of this work.

The partial oxidation of 2-nitro-p-xylene yielded 3-nitro-p-toluic acid. This agreed with the correlation.

In the partial oxidation of 2-N-acetylamino-p-xylene, the results were poor. This result could also be explained in terms of the correlation.

LITERATURE SEARCH

In searching the literature for examples of the partial oxidations of monosubstituted xylenes it was found that most of the work had been done on monosubstituted m-xylenes. And then only with halogenated compounds.

The preparation of 4-bromo-3-methyl benzoic acid (VII) was accomplished by Fittig, Ahrens and Matheides. (2), (3) Pure 4-bromo-m-xylene (VIII) was boiled for several days in a dilute sulfuric acid-potassium dichromate solution.

(VIII) $\longrightarrow$ + 3[O](K2CR2O7 + H2SO4) $\longrightarrow$ (VII) + H2O (1)
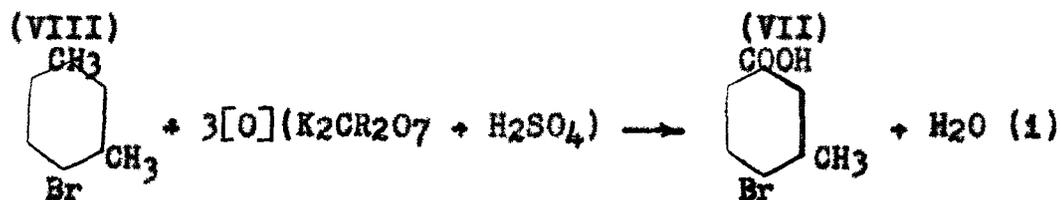
The same oxidation was accomplished by Jannisch and Diechmann (4), who used chromic acid and obtained the same product (VII).

Similar work on 4-chloro-m-xylene was done by Vollrath (5), in which 4-chloro-3-methyl benzoic acid (IX) was made. Here 4-chloro-m-xylene (X), potassium dichromate and diluted sulfuric acid were refluxed together for two days.

$$\text{(X)}\quad \underset{\underset{Cl}{|}}{\overset{\overset{CH_3}{|}}{\bigcirc}}CH_3 + 3[O](K_2Cr_2O_2+H_2SO_4) \longrightarrow \text{(IX)}\quad \underset{\underset{Cl}{|}}{\overset{\overset{COOH}{|}}{\bigcirc}}CH_3 + H_2O \quad (11)$$
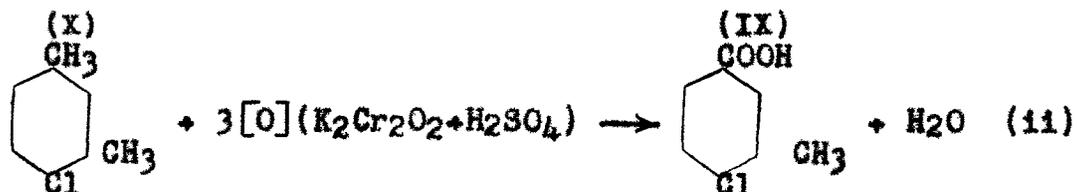
In the literature, there was no material to be found describing the partial oxidation of monosubstituted p-xylenes.

The monosubstituted p-xylenes were chosen for study because of the purity with which they could be obtained--without contamination of isomers.

The starting material for this study was practical grade p-xylene, which was nitrated with a solution of sulfuric and nitric acids. The crude nitrated product was purified by fractional distillation at reduced pressure.

Purified 2-nitro-p-xylene was one of the monosubstituted p-xylenes to be studied. Here, there was the possibility of forming three different products by a partial oxidation. The possibilities were as follows:

  (a) 2-nitro-p-toluic acid

  (b) 3-nitro-p-toluic acid

  (c) 2-nitro-terephthalic acid

A portion of purified 2-nitro-p-xylene was reduced catalytically to the corresponding xylidine. The xylidine was acetylated to give 2-N-acetylamino-p-xylene.

This 2-N-acetylamino-p-xylene required no further
purification and was the other monosubstituted p-xylene to
be studied. Here again, there was the possibility of
forming three different oxidation products. The possi-
bilities were as follows:

    (a)   2-N-acetylamino-p-toluic acid

    (b)   3-N-acetylamino-p-toluic acid

    (c)   2-N-acetylamino terephthalic acid

All of the forementioned products are reported in
the literature, but none were reported as being made from
the oxidation of the corresponding substituted p-xylene.
Instead they were prepared from the corresponding nitrile.

EXPERIMENTAL PROCEDURES

I - Preparation of the Starting Materials

A. 2-nitro-p-xylene (6)

(XI)   (I)

CH_3 CH_3

+ HNO_3 $\longrightarrow$ NO_2 + H_2O (iii)

CH_3 CH_3
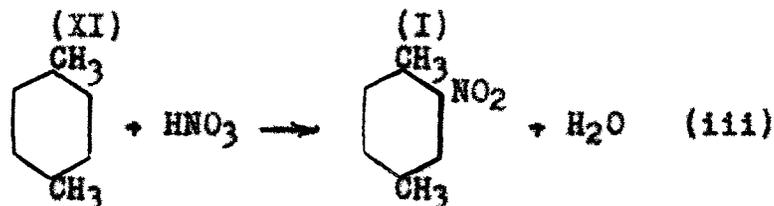
One kilogram of practical grade p-xylene (XI) (9.42 mols) and 24 gm of reagent grade urea (0.40 mols) were placed in a five liter, three-necked flask equipped with an agitator, thermometer, dropping funnel and cooling bath. The nitration mixed acid was prepared by adding 708 ml of concentrated nitric acid (specific gravity 1.42) to 708 ml of concentrated sulfuric acid (96%) with cooling. The mixed acid was added to the reaction flask at such a rate that temperature was held within a range of 45° to $55^{\circ}C$. After completion of the addition, the batch was agitated for 1½ hours at a temperature between 55° to $65^{\circ}C$. The reaction solution was cooled to $30^{\circ}C$ and transferred to a separatory funnel. The lower acid layer was drawn off and extracted with 1 liter of ethyl ether. This ether extract was then added, together with a second liter of ethyl ether to the upper layer. After washing the ether solution with 1-liter of water, it was washed with a liter of saturated sodium bicarbonate solution. This was followed

by another 1-liter water wash, leaving the ethereal solution neutral. The ethereal solution was concentrated on a steam bath until all the ether was driven off. The resulting crude 2-nitro-p-xylene was purified by steam distillation. After separating the purified 2-nitro-p-xylene from the water, the 2-nitro-p-xylene was dried with anhydrous magnesium sulfate. A further purification of 2-nitro-p-xylene was made by fractional distillation at reduced pressure (b.p. at 14 mm Hg - 114°C). The column used was glass and vacuum jacketed. It was 1 inch in diameter and 30 inches long. The packing used was Penn. State protruded 316 type stainless steel packing measuring 0.24 inches by 0.24 inches.

Yield 980 gm; 68.9% of theory

B.P. 240°C/760 mm reported 239.9°C/760 mm (7)

Density $1.129^{15°C}$ reported $1.132^{15°C}$ (7)

B. 2-N-acetylamino-p-xylene

1. Catalytic reduction of 2-nitro-p-xylene to 2,5-p-xylidine

(I) + $3H_2$ $\xrightarrow{\text{5% Pd on C}}$ (XII) + $2H_2O$ (1v)
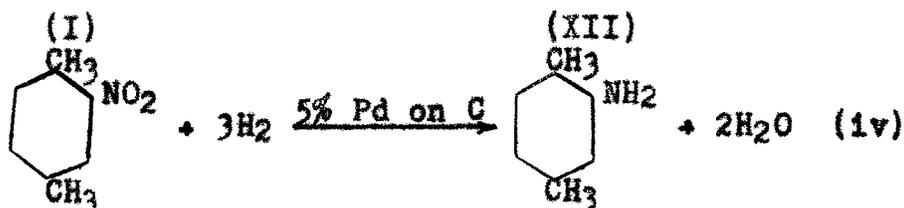
Seventy gm of purified 2-nitro-p-xylene (0.463 mols) and 75 ml of methanol were placed in a 350 ml glass hydrogenation bottle. Three gm of 5% palladium on carbon

catalyst was slurried in 75 ml of methanol, prechilled to -50°C, and added to the hydrogenation bottle. The bottle was put on a Parr Shaker. The bottle was evacuated and pressurized with hydrogen to 15 p.s.i.g. This was repeated two more times. Finally the pressure was brought up to 50 p.s.i.g. and the shaker started. The pressure was allowed to diminish to 30 p.s.i.g. The bottle was repressurized to 50 p.s.i.g. This procedure was continued until the reaction mixture stopped taking up hydrogen. This reduction was exothermic and proceeded between 42° to 47°C for 3 hours. The system was evacuated and the spent catalyst filtered off and washed with two 50 ml portions of methanol. The methanol solution was concentrated under vacuum until all the methanol had been driven off.

Yield 59.4 gm; 99% of theory

No attempt was made to purify the 2,5-p-xylidine (XII). It was used directly in the acetylation.

2. Acetylation of 2,5-p-xylidine (8)

$$(XII) + CH_3COCCH_3 \longrightarrow (IV) + CH_3COOH \quad (v)$$
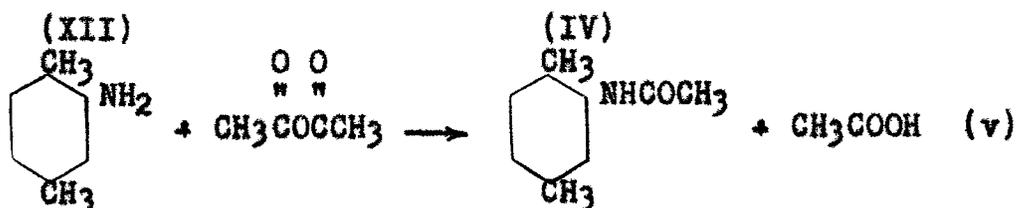
Forty gm (0.33 mols) of 2,5-p-xylidine (XII) was suspended in 827 ml of distilled water. Then 27.4 ml (0.33 mols) of concentrated hydrochloric acid was added

to the suspension with stirring. This solution was de-
colorized by agitating it with 3 gm of Darco G60 for 5
minutes at room temperature and filtering. A solution of
49.6 gm (0.60 mols) of anhydrous sodium acetate and 165
ml of distilled water was prepared and filtered clear.
With agitation, 386 ml (0.396 mols) of pure acetic an-
hydride, followed immediately by the sodium acetate
solution, were added to the 2,5-p-xylidine hydrochloride
solution. Agitation of the mixture was continued for 10
minutes at room temperature. The crystalline 2-N-acetyl-
amino-p-xylene (IV) was filtered by suction and washed
with two-50 ml portions of distilled water. The material
was dried at 70°C to constant weight.

Yield 47.3 gm; 87.8% of theory

M.P. 141.4°C; reported 141.2°C (9)

II - Oxidation of 2-nitro-p-xylene

Run II-A-1. Alkaline potassium permanganate in
aqueous media. Forty gm (0.264 mols) of 2-nitro-p-xylene
(I) was suspended in 700 ml of distilled water in a three-
necked five-liter flask, equipped with an agitator, reflux
condenser, dropping funnel and an electric heating mantle.
Then 21.6 gm (0.528 mols) of 97.9% sodium hydroxide was
added to the suspension. The suspension was brought to
reflux. A solution of 93.6 gm (0.582 mols) of reagent
grade potassium permanganate and 2,000 ml of distilled

water was added in 200 ml increments to the reaction
flask. Subsequent 200-ml increments of oxidizing solution
were not added until the purple color from the previous
addition had dissapated. The total addition time was 5½
hours. The reaction mixture was refluxed an additional
½ hour. The batch cooled naturally to room temperature
(22 hours). The manganese dioxide was filtered off and
the filtrate was concentrated at atmospheric pressure
until all of the unreacted 2-nitro-p-xylene had been dis-
tilled off. Five gm of unreacted 2-nitro-p-xylene was
collected as an immiscible oil from the distillate. After
cooling to room temperature, the residue was acidified
with 70 ml of concentrated hydrochloric acid to pH2 and
the solution was evaporated to dryness on a steam bath
under a forced draft of air, and then dried in a 70°C
oven. The dried material was broken up and refluxed with
3 li of methanol for 1½ hours, and the hot solution was
filtered from insoluble salt. Dry weight of a mixture of
potassium chloride and sodium chloride was 33.0 gm. The
filtrate was concentrated to 1200 ml, cooled and placed
in the refrigerator overnight. The crystalline material
(II-A-1-I) was filtered off the next day and washed with
two-50 ml portions of chilled methanol. Dry weight of
(II-A-1-I) was 5.8 gm. The filtrate was concentrated to
500 ml, and then cooled to -40°C with a dry ice-acetone
bath. The resulting crystals (II-A-1-II) were filtered

and washed with two-50 ml portions of chilled methanol.
Dry weight of (II-A-1-II) was 7.7 gm. The mother liquor
was taken to dryness on a steam bath. Five hundred ml of
acetone was added to the dry material and brought to re-
flux. An insoluble material (II-A-1-III) was filtered
from the hot solution. Dry weight of (III-A-1-III) was
12.3 gm. After concentrating the acetone filtrate to
100 ml, it was chilled for 3/4 hour at 5° to 10°C. The
resulting crystalline material (II-A-1-IV) was filtered
off and washed with two-20 ml portions of acetone. The
dry weight of (II-A-1-IV) was 7.0 gm. The filtrate was
taken to dryness yielding a solid (II-A-1-V) which weighed
11.2 gm.

Summary of Analytical Results

Fraction	Code	Weight	MP,°C	Equivalent Weight	Identification
II-A-1-I	–	5.8	over 300	not an acid	potassium and sodium chlorides
II-A-1-II	–	7.7	over 300	not an acid	potassium and sodium chlorides
II-A-1-III	–	12.3	over 300	435	mixture of potassium and sodium chlorides and 2-nitro terephthalic acid
II-A-1-IV	(II)	7.0	264-7	115.7	2-nitro terephthalic acid
II-A-1-V	(II)	11.2	245-8	121.5	crude 2-nitro terephthalic acid
Reported			262-3 (10)	105.5 (theory)	

(I)
CH₃ NO₂ ... CH₃ + 4KMnO₄ ⟶ (II) COOH NO₂ ... COOH + 4MnO₂ + 4KOH   (vi)
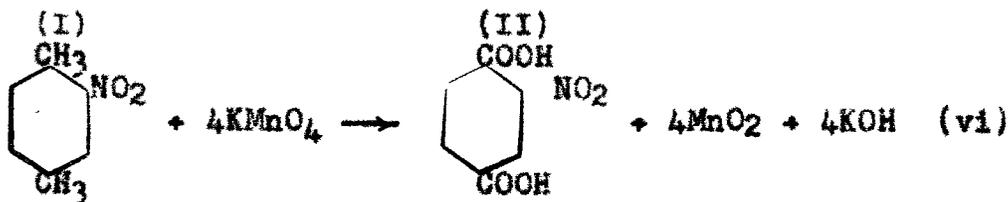
Run II-A-2. Alkaline potassium permanganate Oxidation
of 2-nitro-p-xylene in pyridine. Dissolved 27.9 gm (0.175
mols) of C.P. potassium permanganate and 7.2 gm (0.175
mols) of 97% C.P. sodium hydroxide in 700 ml of distilled
water. Dissolved 15 gm (0.1 mol) of 2-nitro-p-xylene in
3 li of pyridine which had been distilled over potassium
hydroxide between 114.5° and 116.0°C. The reaction solu-
tion was brought to reflux and the oxidizing solution was
added. The rate of adding the oxidizing solution was
adjusted so that the volume being added was approximately
equal to half the volume of the distillate being distilled
off. This was done to keep the amount of water in the
reaction down to a minimum. This addition required 3 hours.
After refluxing the reaction solution for an additional
hour, it was cooled slightly and 2 li of distilled water
was added. The batch was allowed to stand for 18 hours
until the color change was complete. Four li of distilled
water was added to the batch and it was distilled under
vacuum until the contents no longer gave an odor of pyri-
dine or unreacted 2-nitro-p-xylene. This final volume was
600 ml. The manganese dioxide was filtered off and washed
with 100 ml of methanol. The filtrate was light yellow in

color. Thirty ml of concentrated hydrochloric acid was added to the filtrate and it was placed in the refrigerator for 24 hours. Nothing developed, so the solution was taken to dryness on a steam bath under vacuum. One hundred ml of distilled water was added to the dried material and it was heated on the steam bath for 15 minutes, cooled to 10°C and the crystals (II-A-2-I) were filtered off. The dry weight of this material was 7.7 gms. It melted at 249° to 300°C and had an equivalent weight of 110.0. This material was identified as impure 2-nitro-terephthalic acid (II).

$$\text{(I)} \quad + 4KMnO_4 \longrightarrow \quad \text{(II)} \quad + 4MnO_2 + 4KOH \quad (vi)$$
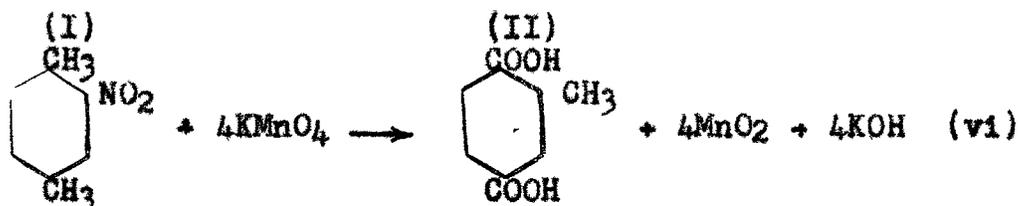
Run II-A-3. Alkaline potassium permanganate oxidation of 2-nitro-p-xylene in acetone.

Dissolved 27.9 gm (0.175 mols) of C.P. potassium permanganate and 7.2 gm (0.175 mols) of 97% sodium hydroxide in 670 ml of distilled water. Dissolved 15.1 gm (0.1 mols) of 2-nitro-p-xylene in 1,100 ml of acetone. At the boil, the oxidizing solution was added with good agitation over a period of 1 hour. The batch was refluxed for 45 minutes. The manganese dioxide was filtered off and washed with three-100 ml portions of warm acetone. The deep red filtrate was concentrated to 1-li at atmospheric pressure. It was then steam distilled

until no more unreacted 2-nitro-p-xylene came over in the distillate. The weight of unreacted 2-nitro-p-xylene, which was collected as an immiscible oil in the distillate, was 5.1 gm. The residue was cooled to $10^\circ C$ and acidified with 25 ml of concentrated hydrochloric acid to pH2. The solution was taken to dryness on the steam bath under a forced draft of air yielding oils and salt. The dried material was dissolved in 200 ml of methanol and refluxed for 15 minutes and then concentrated to 50 ml. The concentrate was cooled to $10^\circ C$ and the salt filtered off. The filtered methanol solution was taken to dryness yielding 3 gm of dark oils. Subsequent attempts at purifying this material were unsuccessful.

Run II-B-1. Chromium trioxide oxidation of 2-nitro-p-xylene. Dissolved 20.0 gm (0.196 mols) of 98% chromium trioxide in 20 ml of distilled water and 100 ml of pure glacial acetic acid. Dissolved 15.1 gm (0.10 mols) of 2-nitro-p-xylene (I) in 200 ml of pure glacial acetic acid. The oxidizing solution was added over a 1½ hour period at a temperature between 55° to $60^\circ C$. The batch was agitated an additional ½ hour; at which time the color change from orange to green had not taken place. The agitation was stopped and the batch was allowed to cool to room temperature and stand for 12 hours; at which time the oxidation was complete. The batch was concentrated on a steam bath,

using a forced air draft for 7 hours, to a low volume.
The batch was diluted to 300 ml with distilled water.
Twenty gm of sodium bicarbonate was added to the batch and
it was heated on a steam bath for ½ hour. After removal
from the steam bath, the undissolved sodium bicarbonate
was filtered off. After the batch had cooled overnight,
it had to be refiltered. The filtrate was acidified with
75 ml of concentrated hydrochloric acid to pH2. The entire
batch was taken to dryness under vacuum. It was then taken
up in 200 ml of methanol at room temperature. The undis-
solved salt was filtered off. The alcoholic filtrate was
taken to dryness yielding 5.9 gm of a crystalline material
(II-B-1-I) which had a greenish tint. The filtrate was
taken to dryness and yielded nothing. This material was
identified as impure 3-nitro-p-toluic acid. (III)

Yield 5.9 gm; 32.6% of theory

M.P. 186°-189°C; reported 190 (11)

Equivalent weight - 178.23; theory 181

$$\text{(I) } + 2CrO_3 \longrightarrow \text{(III) } + Cr_2O_3 + H_2O \quad \text{(vii)}$$
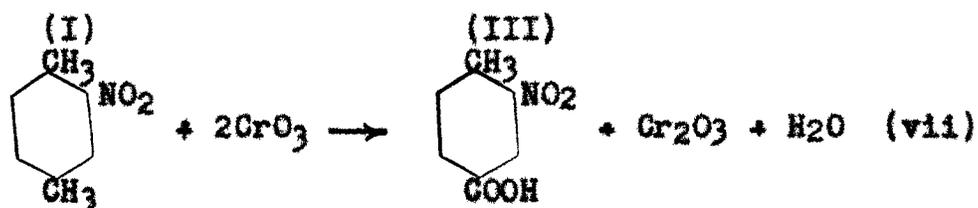
Run II-B-2. Chromium Trioxide oxidation of 2-nitro-p-
xylene using 0.79 mols of sulfuric acid as a catalyst. Dis-
solved 48 gm (0.47 mols) of 98% chromium trioxide in 47 ml
of distilled water and 200 ml of reagent grade glacial

acetic acid. Dissolved 30.2 gm (0.2 mols) 2-nitro-p-
xylene (I) in 300 ml of pure glacial acetic acid and added
44 ml (0.79 mols) of 96.5% reagent grade sulfuric acid.
The oxidizing solution was added over a period of $1\frac{1}{2}$ hours
at a temperature between 42° to $53^\circ C$. An additional 60 ml
of acetic acid was used to complete the transfer of the
oxidizing solution. Agitation was continued for an addi-
tional hour. The batch was diluted with 5 li of distilled
water and put in the refrigerator for 15 hours. The
material which had crystallized was filtered off and washed
with two-100 ml portions of distilled water.

(II-B-2-I) Yield 16.0 gm; 44% of theory

M.P. 186°-$189^\circ C$

Equivalent weight 177.6

The filtrate was extracted with four-1 li portions of
ethyl ether. The lower water layer was drawn off and
taken to dryness. No material was found. The ether
extracts were concentrated to 100 ml. The ether had been
driven off completely so that the 100 ml was an acetic
acid solution. This acetic acid solution was diluted with
300 ml of distilled water and chilled in an ice bath. A
second crystalline fraction formed which was filtered off.

(II-B-2-II) Yield - 2.0 gm

M.P. 141°-$185^\circ C$

Equivalent Weight 172.0

Further dilution of the filtrate from II with 800 ml of distilled water yielded a third fraction III.

(II-B-2-III) Yield 1.8 gm

M.P. 135°-269°C

Equivalent Weight 176.9

Further dilution with 500 ml of water yielded nothing, so the solution was concentrated to 100 ml.

A fourth fraction of material IV was filtered off and washed with three-30 ml portions of chilled distilled water.

(II-B-2-IV) Yield 1.3 gm

M.P. 164°-229°C

Equivalent weight 154.9

IV taken to dryness yielded nothing

Summary of Results

Fraction	Weight	M.P.	Equivalent Weight
II-B-2-I	16.0 gm	186°-189°C	177.6
II-B-2-II	2.0 gm	141°-185°C	172.0
II-B-2-III	1.8 gm	135°-269°C	176.9
II-B-2-IV	1.3 gm	164°-229°C	154.9

Total 21.1 gm; 57.8% of theory

All of this material was impure 3-nitro-p-toluic acid.

(III)

(I) (III)

$$CH_3\text{-}NO_2 \text{ (I)} + 2CrO_3 \longrightarrow CH_3\text{-}NO_2\text{-}COOH \text{ (III)} + Cr_2O_3 + H_2O \quad (vii)$$
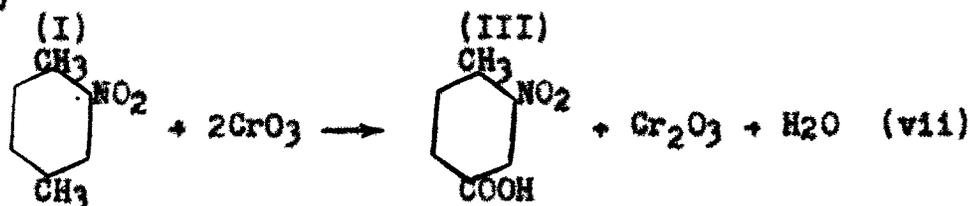
Run-II-B-3. Chromium trioxide oxidation of 2-nitro-
p-xylene using 1.193 mols of sulfuric acid as a catalyst.
Dissolved 48 gm (0.47 mols) of 98% chromium trioxide in 48
ml of distilled water and 200 ml of reagent grade glacial
acetic acid. Dissolved 30.2 gm (0.2 mols) 2 nitro-p-xylene
in 300 ml of glacial acetic acid and added 66 ml (1.193
mols) of 96.5% reagent grade sulfuric acid. The oxidizing
solution was added over a period of 50 minutes at a temp-
erature range of 64° to $66^{\circ}C$. An additional 100 ml of
reagent grade glacial acetic acid was used to complete the
transfer of the oxidizing solution. The batch was agitated
an additional hour while the temperature was maintained
between 60° to $70^{\circ}C$. The batch was diluted with 2 li of
distilled water and agitated for 15 minutes. The batch
was then extracted with four-1 li portions of benzene.
These benzene extracts were taken to dryness yielding
(II-B-3-I).

    II-B-3-I Yield 25.5 gm

        M.P. $139^{\circ}-177^{\circ}C$

        Equivalent weight 156.4

The water layer from I was extracted with two-2 li
portions of warm benzene. The benzene extracts were taken
to dryness, yielding oils. These oils were taken up in 50
ml of methanol and taken to dryness yielding a crystalline
material.

II-B-3-II Yield 1.8 gm

M.P. 160°-181°C d.

The water layer was then extracted with three-2 li portions of ethyl ether. These ethyl ether extracts were taken to dryness yielding 2.0 gm.

II-B-3-III Yield 2.0 gm

M.P. over 270°C

First purification of (II-B-3-I). 10.0 gm of the 25.5 gm of (II-B-3-I) was dissolved in 80 ml of ethanol (3A). The batch was then decolorized by refluxing with 1 gm of Darco G60 for 3/4 hour. After filtration, the charcoal filter cake was washed with two-10 ml portions of ethanol. The batch was concentrated to 50 ml and put in the refrigerator for one day. The crystalline material (II-B-3-IV) was filtered and dried.

Yield 5.2 gm

M.P. 183.6°-190.6°C

Equivalent weight 180.1

This material was identified as 3-nitro-p-toluic acid. (III)

Three gm of the 5.2 gm of (II-B-3-IV) was dissolved in 160 ml of 0.1N sodium hydroxide solution and precipitated with a solution of 2.1 ml of concentrated hydrochloric acid and 50 ml of distilled water. The crystalline material (II-B-3-V) was filtered off and dried in a 70°C oven.

Yield 1.3 gm

M.P. 187.4°-190.6°C

Equivalent weight 179.4

Appearance - pale yellow crystals

This material was 3-nitro-p-toluic acid. (III)

Second purification of (II-B-3-I). Dissolved 2.5 gm
(0.61 mols) of 97.5% sodium hydroxide pellets in 50 ml of
distilled water. Added 10.0 gm of (II-B-3-I) and diluted
with 100 ml of distilled water. Boiled on a hot plate
maintaining a constant volume by the addition of more dis-
tilled water. Boiled for 1 hour until solution was complete
and there wasn't any odor of unreacted 2-nitro-p-xylene.
The batch was cooled to room temperature and a solution of
5.4 ml (0.063 mols) of concentrated hydrochloric acid and
150 ml of distilled water was added. The batch stood for
two days at room temperature. The crystalline material (II-
B-3-VI) was filtered off by suction and washed with two-30
ml portions of distilled water.

Yield 7.7 gm

M.P. 179°-183°C

A further purification was affected by dissolving the
7.7 gm in a solution of 1.9 gm (0.463 mols) of 97.5% sodium
hydroxide pellets and 300 ml of water and refluxing for 1
hour. After cooling the batch to room temperature, a dilute

solution of 4.1 ml (0.477 mols) of concentrated hydrochloric acid and 200 ml of distilled water was slowly added over a period of 1 hour with good agitation. This solution was then allowed to stand for 24 hours. The crystals (II-B-3-VII) were filtered off and washed with three-20 ml portions of distilled water. It was dried in a 60°C dryer for 24 hours.

> Yield 5.0 gm
>
> M.P. 187°-189.5°C
>
> Equivalent weight 179.0

This 5.0 gm was then dissolved in 100 ml of ethanol at room temperature. It was then treated with 0.5 gm of activated carbon (KB Darco) for $\frac{1}{2}$ hour and filtered. After washing the carbon with two-10 ml portions of ethanol, the solution was taken to dryness by passing a stream of air over the evaporating dish containing the alcoholic solution. The dried crystalline material (II-B-3-VIII) was further dried in a 60°C dryer for 24 hours.

> Yield 4.8 gm
>
> M.P. 191°C; reported 190°C (11)
>
> Equivalent weight 180.1; theory - 181
>
> Appearance - yellow in color
>
> This material was pure 3-nitro-p-toluic acid. (III)

III - Oxidation of 2-N-acetylamino-p-xylene

Run III-A-1. Chromium trioxide oxidation in glacial acetic acid without a sulfuric acid catalyst at a moderately low temperature. Forty gm (0.392 mols) of 98% chromium trioxide was dissolved in 600 ml of warm reagent grade glacial acetic acid. Dissolved 32.6 gm (0.200 mols) of 2-N-acetylamino-p-xylene (IV) in 200 ml of glacial acetic acid. The oxidizing solution was cooled to 8°C and added with agitation, to the acetic acid solution of 2-N-acetyl-amino-p-xylene. The oxidizing solution was added over a 2½ hour period while the batch temperature was maintained between 13° to 16°C. After the completion of the addition of the oxidizing solution, the batch was agitated for 2 hours at a temperature range between 16° to 20°C. At this time there wasn't any evidence of a color change. The color of the solution was a dark brown. The reaction mixture was placed in the refrigerator for 13 hours. At this time it had a slight green color. It was agitated at 13°C for 2 hours and then poured into 1 kg of ice and agitated for 1 hour. The batch was placed in the refrigerator for 3½ hours. At this time 600 ml of distilled water was added. The reaction mixture was extracted with 6 li of benzene. The benzene extract was taken to dryness leaving a solid, off-white residue which weighed 24.6 gms. This material was not an acid and melted at 134°C. A mixed melting point with 2-N-acetylamino-p-xylene gave no depression indicating that

this material was unreacted 2-N-acetylamino-p-xylene (IV).
An infra-red analysis showed this material to be impure
2-N-acetylamino-p-xylene.

Run III-A-2. Chromium trioxide oxidation in glacial
acetic acid without sulfuric acid catalyst at a moderate
temperature. Ten gm (0.098 mols) of 98% chromium trioxide
was dissolved in 200 ml of warm reagent grade glacial acetic
acid. Dissolved 8.15 gm (0.050 mols) of 2-N-acetylamino-p-
xylene (IV) in 50 ml of pure glacial acetic acid. The ox-
idizing solution was cooled to 17°C and added to the solution
of 2-N-acetylamino-p-xylene. (IV) This reaction mixture was
allowed to stand at room temperature for 24 hours. At
first the temperature rose slightly from 17° to 31.5°C over
a period of 35 minutes and then started falling to the room
temperature of 28°C. After standing 24 hours, the color
change was complete and the reaction mixture was diluted with
1 li of water. The reaction mixture was then extracted
three times with 500 ml portions of benzene. The combined
benzene extracts were then washed three times with 250 ml
portions of distilled water. The benzene extracts were then
treated with 1 gm of activated charcoal (KB Darco) for 15
minutes. After filtering off the charcoal, the filtrate
was taken to dryness, under vacuum. The weight of the solid
off-white residue was 4.6 gm. This material was not an
acid and melted at 133°C. A mixed melting point with 2-N-

acetylamino-p-xylene gave no depression, indicating that this material was the same as the starting material. An infra-red analysis showed this material to be impure 2-N-acetylamino-p-xylene. (IV)

Run III-A-3. Chromium trioxide oxidation in glacial acetic acid with a sulfuric acid catalyst at a moderate temperature. Dissolved 8.15 gm (0.050 mols) of 2-N-acetylamino-p-xylene (IV) in 75 ml of glacial acetic acid. Ten gm (0.098 mols) of 98% chromium trioxide was dissolved in 6 ml of warm distilled water. Then 140 ml of reagent grade glacial acetic acid and 1.5 ml (0.027 mols) of 96.5% sulfuric acid were added. After cooling the oxidizing solution to 20°C, it was added to the solution of 2-N-acetylamino-p-xylene maintaining a temperature range of 20° to 25°C over a period of 1¼ hours. It was agitated for an additional 45 minutes at 20° to 25°C. The batch was then added to 1 kg of ice and allowed to stand 21 hours. It was extracted with five-500 ml portions of benzene. After water washing the benzene extracts with three-250 ml portions of distilled water, the benzene extracts were taken to dryness on the steam bath yielding 5.7 gm of material.

This material would not titrate as an acid. It melted at 137° to 139°C and gave no melting point depression when mixed with 2-N-acetylamino-p-xylene. An infra-red analysis showed this material to be impure 2-N-acetylamino-p-xylene. (IV)

Run III-B-1. Alkaline potassium permanganate oxida-
tion at 50° to 60°C. Dissolved 7.8 gm (0.0493 mols) of
reagent grade potassium permanganate in 250 ml of distilled
water. Four gm (0.0246 mols) of 2-N-acetylamino-p-xylene
(IV), 1.0 gm (0.0425 mols) of 97.9% sodium hydroxide pellets
and 1,900 ml of distilled water were added to a 3-necked,
3 li flask -- equipped with an agitator and thermometer.
The 2-N-acetylamino-p-xylene solution was warmed to 30°C.
Addition of the oxidizing solution was started. No increase
in temperature was noted so the solution was heated to 50°C
and addition of the oxidizing solution was continued. The
reaction was still very slow, so the temperature was in-
creased to 60°C and was maintained there until the comple-
tion of the addition of the oxidizing solution. This
addition time was 1 3/4 hours. The reaction mixture was
agitated for an additional ½ hour at 60°C. The manganese
dioxide was filtered off and washed with two-100 ml portions
of warm distilled water. The yellow filtrate was cooled and
acidified with 6 ml of concentrated hydrochloric acid to
pH2. The filtrate was then extracted with two-1 li portions
of ethyl ether. The ether extracts were taken to dryness
yielding 2.5 gm of material. This material melted at 102.5°
to 104.0°C and had an equivalent weight of 561. The water
layer was re-extracted with two-1 li portions of benzene
which yielded 0.5 gm of material (III-B-1-I) when taken to

dryness. This material melted at 135° to 138°C, was not an acid and gave no melting point depression when a mixed melt was run with 2-N-acetylamino-p-xylene.

The 2.1 gm of material obtained from the ether extracts was heated with 50 ml of 0.1N sodium hydroxide for ½ hour. An insoluble material (III-B-1-II) was filtered off, which when dried weighed 0.9 gm. This material melted at 139° to 141°C and would not titrate as an acid. The filtrate was acidified with 50 ml of 0.1N hydrochloric acid to pH2, heated on a steam bath for ½ hour and then allowed to cool overnight. The crystalline material (III-B-1-III) was filtered off and dried. It weighed 0.5 gm, melted at 179°C d. and had an equivalent weight of 189.1. An infrared analysis of this compound showed that there were absorption bands present which could be assigned to the acid group, amide group and phenyl group. This material was identified as 2-N-acetylamino-p-toluic acid.

    Yield 0.5 gm

    Melting point 179°C d.; reported 177°C d. (12)

    Equivalent weight - 189.1; theory 189.1

(IV) + 2KMnO₄ → (V) + 2MnO₂ + 2KOH (viii)
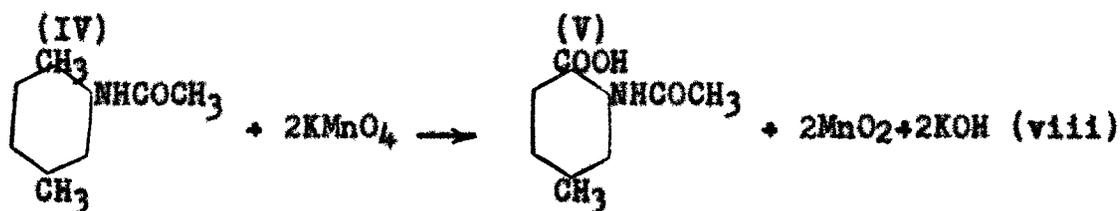
Run-III-B-2. Alkaline potassium permanganate oxidation at reflux. Dissolved 25 gm (.158 mols) of U.S.P. reagent grade potassium permanganate in 800 ml of warm distilled water. Dissolved 10 gm (.0612 mols) of 2-N-acetylamino-p-xylene (IV) and 2.5 gm (.0625 mols) of 97.9% C.P. sodium hydroxide pellets in 875 ml of distilled water at the boil. The oxidizing solution was added at reflux over a period of $1\frac{1}{4}$ hours. The rate was adjusted so that the oxidizing solution was used up as it was added. After completing the addition, 300 ml of water was distilled off. The distillate was a purplish brown and had a pH8. The manganese dioxide was filtered off and washed with two-100 ml portions of warm distilled water. The washes were combined with the filtrate and acidified to pH2 with 15 ml of concentrated hydrochloric acid. The acidified solution was extracted with four-1 li portions of ethyl ether. The extracts were washed with two-500 ml portions of distilled water. The ether extracts were taken to dryness yielding 7.3 gm of solid material which was designated as (III-B-2-I). It melted at 117° to 122°C and had an equivalent weight of 478. (III-B-2-I) was added to a solution of 1.5 gm (0.038 mols) of C.P. sodium hydroxide pellets dissolved in 200 ml of distilled water. Heated the mixture on a steam bath for $\frac{1}{2}$ hour, cooled to 20°C and filtered. After washing the residue with two-50 ml portions of warm water, it was dried in a 70°C oven to constant weight. Sublimation was noted

during drying. Weight of (III-B-2-II) was 3.2 gm. It
melted at 139°C and gave no depression with a mixed melt
with 2-N-acetylamino-p-xylene. In addition it would not
titrate as an acid. After acidifying the filtrate, it
was set aside for several days to crystallize. The crys-
talline material (III-B-2-III) was filtered off and washed
with two-10 ml portions of warm distilled water and dried
at 70°C to constant weight. (III-B-2-III) weighed 0.3
gm, melted at 213° to 247°C and had an equivalent weight
of 395. The (III-B-2-III) mother liquor was extracted with
six-100 ml portions of ethyl ether. After washing the ether
extracts with two-100 ml portions of distilled water, they
were taken to dryness on the steam bath. This material
(III-B-2-IV) weighed 1.9 gm. It melted at 102° to 108°C
and had an equivalent weight of 264. The water filtrate
was taken to dryness on a steam bath using a draft of forced
air. One hundred ml of acetone was added to the dry material
and refluxed together for 15 minutes. Insoluble salts were
filtered and dried. The weight of the salt was 2.3 gm. The
acetone solution was taken to dryness yielding 1.5 gm of an
oil. This oil was taken up in a solution of 0.4 gm of 97.9%
C.P. sodium hydroxide pellets dissolved in 40 ml of dis-
tilled water. After solution was complete, it was cooled
and acidified with a few ml of concentrated hydrochloric
acid. The solution was set aside for 3 days until crystals
came out of solution. The crystalline material was filtered

off and washed with two-20 ml portions of distilled water. It was dried and weighed 0.7 gm. It did not melt at 300°C and was water soluble. This material was salt. The water filtrate was taken to dryness yielding nothing.

The water solution from (III-B-2-I) was taken to dryness under vacuum. The dry solids were taken up in 300 ml of acetone at reflux. Insoluble salts were filtered off and dried. Dry weight of salt was 11.8 gm. The acetone filtrate was taken to dryness yielding 1.9 gm of an oil. This oil was taken up in a solution consisting of 0.4 gm of 97.9% sodium hydroxide pellets dissolved in 50 ml of distilled water and refluxed for ½ hour. Some material remained out of solution. The material (III-B-2-V) was filtered off hot and dried. It weighed 0.24 gm, melted at 272° to 274°C, had an equivalent weight of 189.1 and was light buff in color, and was identified as 3-N-acetylamino-p-toluic acid. (VI) The filtrate was acidified with a few ml of concentrated hydrochloric acid and taken to dryness. The dry material was taken up in 50 ml of acetone and the salt was filtered off. The acetone solution was taken to dryness yielding a buff colored crystalline material which weighed 1.51 gm. This material melted at 104° to 110°C. The 1.51 gm of material was dissolved in 100 ml of methanol and agitated with 3 gm of activated charcoal (KB Darco) for 15 minutes at room temperature. In spite of the charcoal,

the solution had a blue fluorescence. After filtering off
the charcoal, the yellow solution still had a blue fluores-
cence. The methanol solution was taken to dryness yielding
an oil which weighed 1.2 gm. This oil was heated with 50
ml of 0.1N sodium hydroxide solution for 3/4 hour on a steam
bath. The undissolved material (III-B-2-VI) was filtered
off warm and washed with two-20 ml portions of warm distilled
water and dried. Weight was 0.33 gm. It was not an acid
and melted at 139°C and was off-white in color. A mixed
melt with 2-N-acetylamino-p-xylene gave no depression in
melt. This material was unreacted 2-N-acetylamino-p-xylene
(IV). The caustic filtrate was decolorized with 0.5 gm of
activated charcoal (KB Darco) for 15 minutes. The filtered
solution was acidified with 55 ml of 0.1N hydrochloric acid
plus 3 ml of concentrated hydrochloric acid to pH2. The
acidified solution was extracted with two-250 ml portions
of ethyl ether. The blue fluorescence still remained. The
ethyl ether extracts were concentrated to dryness by a
forced air draft. Material was dried in a 70°C oven. Dur-
ing drying a white sublimate was noted. This material was
yellow in color and weighed 0.66 gm. It melted between
114° to 179°C with decomposition. This material was vacuum
dried at 50°C for 24 hours. At this time it weighed 0.50
gm. This material was designated as (III-B-2-VII). It
melted at 170° to 180°C d. and had an equivalent weight of
190.5; this was identified as 2-N-acetylamino-p-toluic
acid. (V)

In this Run both isomers were isolated.

Summary of Results

Fraction	Yield	M.P.	Equivalent Wgt.
(III-B-2-V) 3-N-acetylamino-p-toluic acid	0.24 gm	272°-274°C; reported 279°-281°(13)	189.1; theory 189.1
(III-B-2-VII) 2-N-acetylamino-p-toluic acid	0.50 gm	179°-180°C d.; reported 179°C d. (12)	190.5; theory 189.1

This reaction may be summed up as follows:

(IV)   (VI)   (V)

(III-B-2-V)   (III-B-2-VII)
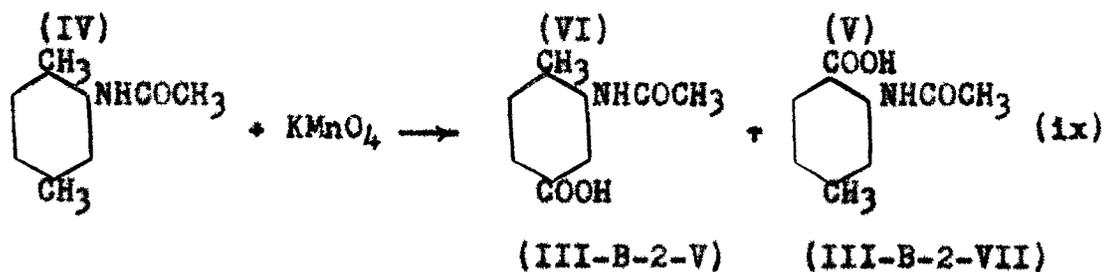
DISCUSSION

Run-II-A-1. Alkaline Potassium Permanganate Oxidation of 2-nitro-p-xylene in Aqueous Media

The alkaline potassium permanganate oxidation of 2-nitro-p-xylene in aqueous media yielded only 2-nitro-terephthalic acid and unreacted 2-nitro-p-xylene. This was probably caused by the heterogeneity of the reaction: that any partially oxidized material was rendered water soluble and consequently oxidized preferentially to the 2-nitro-p-xylene, which was immiscible.

Run II-A-2. Alkaline Potassium Permanganate Oxidation of 2-nitro-p-xylene in Pyridine

The same reaction carried out in pyridine also yielded only 2-nitro terephthalic acid and unreacted 2-nitro-p-xylene. However, this reaction was homogeneous. The only apparent explanation for the results would be that the partially oxidized material is more readily oxidized by this system than is the starting material.

Run II-B-1. Chromium Trioxide Oxidation of 2-nitro-p-xylene in Glacial Acetic Acid without Sulfuric Acid Catalyst

With chromium trioxide without a catalyst 3-nitro-p-toluic acid was isolated. The quality was fair and the yield was 32.6 percent of theory. No 2-nitro-p-toluic acid was isolated from this reaction.

Run II-B-2. Chromium Trioxide Oxidation of 2-nitro-p-xylene in Glacial Acetic Acid with 0.79 mols of Sulfuric Acid Catalyst

When oxidant was increased from 1.96 mols to 2.35 mols per mol of 2-nitro-p-xylene and 3.95 mols of sulfuric acid per mol of 2-nitro-p-xylene were used, a yield of fair 3-nitro-p-toluic acid was obtained -- 44 percent of theory. An additional 5.1 gm of crude 3-nitro-p-toluic acid was isolated. The total yield of 21.1 gm was equivalent to 57.8 percent of theory.

Run II-B-3. Chromium Trioxide Oxidation of 2-nitro-p-xylene in Glacial Acetic Acid with 1.193 mols of Sulfuric Acid Catalyst

Increasing the sulfuric acid from 3.95 to 5.97 mols per mol of 2-nitro-p-xylene and running the reaction at a slightly higher temperature yielded a total of 25.5 gms of crude 3-nitro-p-toluic acid. An additional 1.8 gm of poorer quality material was isolated from the mother liquor. A purification of a portion of the better quality material gave a yield equivalent to 26.3 percent of theory. The melting point and equivalent weight of this material agreed very well with the literature values. Neither 2-nitro-p-toluic acid nor 2-nitro-terephthalic acid were isolated from this oxidation.

Runs III-A-1, 2 and 3. Chromium Trioxide Oxidation of 2-N-acetylamino-p-xylene

When the chromium trioxide oxidation, with and without,
a sulfuric acid catalyst was tried on 2-N-acetylamino-p-
xylene no oxidation products were isolated. Only unreacted
2-N-acetylamino-p-xylene was recovered and identified. As
the reaction temperature was increased the recovery decreased.
In the recovery of the starting material it was noted in
each case that there was some sublimation. This indicates
the possibility of quinone formation which may have been
facilitated by the hydrolysis of the N-acetylamino group.

Run III-B-1. Alkaline Potassium Permanganate Oxidation of 2-N-acetylamino-p-xylene at 50° to 60°C

When alkaline potassium permanganate was used at 60°C
in oxidizing 2-N-acetylamino-p-xylene, 1.4 gm of unreacted
2-N-acetylamino-p-xylene and 0.5 gm of 2-N-acetylamino-p-
toluic acid were isolated. This yield of 2-N-acetylamino-
p-toluic acid was 10.6% of theory.

Run III-B-2. Alkaline Potassium Permanganate Oxidation of 2-N-acetylamino-p-xylene at Reflux

When the same reaction was carried out at the boil,
0.24 gm of 2-N-acetylamino-p-toluic acid and 0.66 gm of
3-N-acetylamino-p-toluic acid were isolated. The total
yield was 7.6 percent of theory. 3.55 gm of unreacted 2-
N-acetylamino-p-xylene was recovered from this reaction.
Here again there were indications of quinone formation --

the bluish fluorescence of solutions and the sublimation noted upon drying unreacted 2-N-acetylamino-p-xylene.

The oxidations of 2-N-acetylamino-p-xylene were not clean-cut. Isolation of the products was hampered by the occlusion of salts. If this work is to be pursued further, it is suggested that ion exchange resins could be a useful tool in isolating the oxidation products.

Another suggestion for future work would be the investigation of the effect of pH on the partial oxidations of monosubstituted xylenes. In the partial oxidation of 2-nitro-p-xylene with alkaline potassium permanganate no decent results could be obtained. However, when the oxidant was changed to the acid chromium trioxide system, the partial oxidation of 2-nitro-p-xylene was successful.

On the other hand, the opposite results were observed in the partial oxidation of 2-N-acetyl-p-xylene. Here partial oxidation, although to a very slight degree, was only realized when the oxidation system was switched from the acid chromium trioxide to the alkaline potassium permanganate.

The Application of the Hammett Sigma Values in Interpreting the Experimental Results

In interpreting the results, attention may be brought to the sigma values of the Hammett Equation (14), which have been used successfully in predicting aromatic substitution reactions of polysubstituted aromatic compounds.

The effects of substituents in many reaction series involving benzene derivatives can be correlated with the acid strength of the corresponding benzoic acid. (15) From these observations Hammett proposed the general quantitative relationship between the nature of the substituent and the reactivity of the side chain which is known as the Hammett Equation and may be expressed in the form:

$$(A) \quad \log (k/k^0) = \rho \, \sigma \qquad (16)$$

Where k and k^0 are the rate or equilibrium constants for reactions of the substituted and the unsubstituted compounds respectively, σ is the substituent constant which depends only on the nature and position of the substituent and ρ is the reaction constant which depends on the reaction, the conditions and the nature of the side chain. (17)

The sigma values, or substituent constants, were defined originally by the equation:

$$(B) \quad \log (K/K^0) = \sigma \qquad (18)$$

Where K^o and K are the dissociation constants of benzoic acid and its monosubstituted derivatives, respectively.

For all substituents for which there is an accurate value for the dissociation constant, of the correspondingly substituted benzoic acid, the sigma value is given directly by equation (B). Then for any reaction series for which there are data for a reasonable number of meta and para substituted derivatives, the value of the reaction constant ρ is the slope of the line obtained when log k is plotted against σ for a number of reactions. Since the reaction constant is constant for all substituents and depends only on the reaction series, then for a given reaction series, the sigma value (σ) may be calculated by substituting the corresponding k in equation (A). (19)

The substituent constant (σ) is a measure of the effect of the substituent on the activation energy of the unsubstituted compound. (20) However, this interpretation of substituents is of little value because not much is known about estimating such energies. A better interpretation to the problem can be visualized when σ is thought of as a measure of electron density of the substituent at the reaction site. A recent evaluation of the effects of substituents on the electron density in a side chain, which consisted of measurements of the nuclear magnetic resonance

absorption of F and Cl in substituted fluro- and chloro-
benzenes, confirms with some degree of validity, the
latter interpretation.

Although the Hammett equation is an empirical re-
lation which was suggested by the parallelism of the ef-
fects of substituents on equilibrium constants, if the
assumption that substituent constants are proportional to
changes in electron density, then σ values can be correla-
ted with electron densities calculated by molecular orbital
theory. (21)

According to H. H. Jaffee, in a reaction series the
effect of substituents on activation energies in polysub-
stituted compounds can be expressed as the sum of the in-
dividual effects of the substituent in the corresponding
monosubstituted compounds (22) and the effect of multiple
substitution on the reactivity of the side chain can be
expressed by the equation in the form:

$$ \text{(C)} \quad \log (k/k^{o}) = \rho \sum \sigma \qquad (23) $$

The sigma values were applied to the compounds used
in this work, to two compounds for which the partial
oxidation products are known and to four other compounds
in order to predict their partial oxidation products.
This was done to see if there is any correlation between
the sums of sigma values of a monosubstituted xylene and
its partial oxidation product.

<u>Application of the sigma values to 2-nitro-p-xylene</u>

where σ for pCH_3 = -0.170

σ for mCH_3 = -0.069

σ for pNO_2 = +0.778   (24)

σ for mNO_2 = +0.710

the following results were obtained:
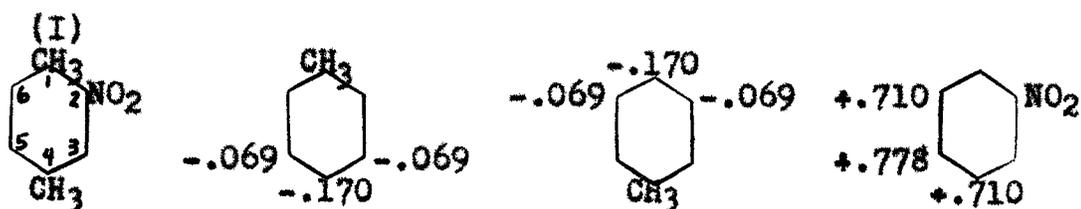
Summing up the sigma values for each position of the benzene nucleus, the following result was obtained:

Position	$\sum\sigma$
1	-.170
2	-.069
3	-.069
4	+.540
5	+.709
6	+.641

In examining the above results at positions 1 and 4, which are the centers for oxidation, it can be seen that position 1 is one of high electron density while position 4 is one of comparatively low electron density. From the results of the partial oxidation of 2 nitro-p-xylene, the only product isolated was 3-nitro-p-toluic acid.

(III)
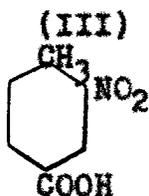
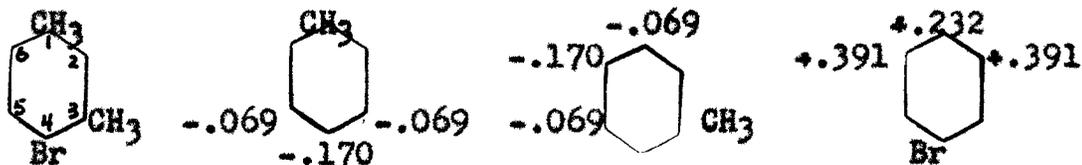Here oxidation was at position 4 -- a point of low electron density.

Application of the sigma values to 4-bromo-m-xylene (2), (3), (VIII)

To see if there was any value to this observation, the principle was applied to a known reaction -- the partial oxidation of 4-bromo-m-xylene to 4-bromo-3 methyl benzoic acid.

(VIII)   (VII)

$+ 3 \begin{bmatrix} 0 \end{bmatrix} (K_2Cr_2O_7 + H_2SO_4) \longrightarrow$ $+ H_2O$ (1)
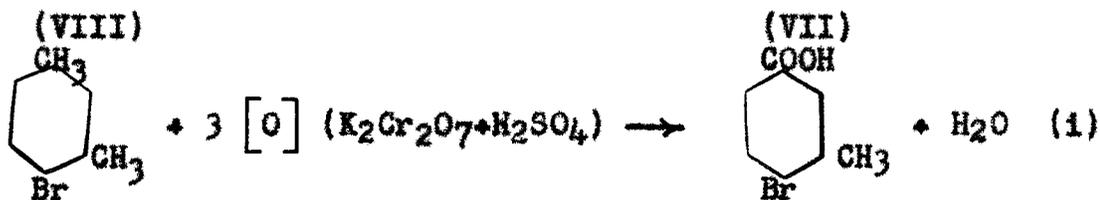
where σ for pBr $= + .232$

σ for mBr $= + .391$ (24)

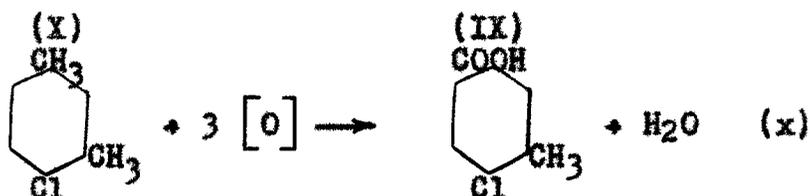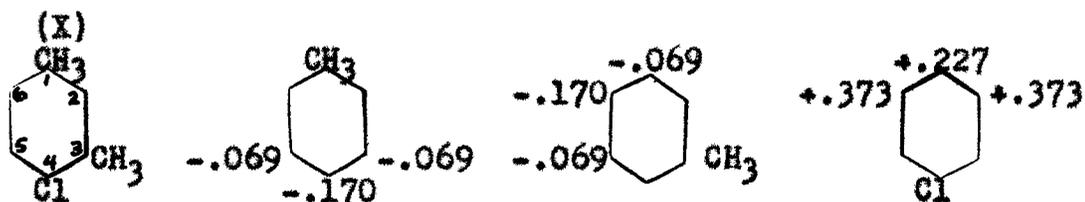| Position	$\sum \sigma$
1	+.163
2	+.391
3	-.069
4	-.170
5	-.138
6	+.221

Here again oxidation was at position 1, the point of lower electron density compared to position 3 -- a point of high electron density. This agrees with the reported result. (2), (3)

Application of the sigma values to 4-chloro-m-xylene (5), (X)

The partial oxidation of 4-chloro-m-xylene to 4-chloro-3-methyl benzoic acid (IX).

$$\text{(X)} + 3\,[O] \longrightarrow \text{(IX)} + H_2O \qquad (x)$$

where σ for pCl = + .227

σ for mCl = + .373   (24)

Position	$\sum \sigma$
1	+.158
2	+.373
3	-.069
4	-.170
5	-.138
6	+.203

Oxidation was at position 1 which was the point of lower electron density compared to the other possible oxidation site, position 3. This agrees with the reported result. (5)

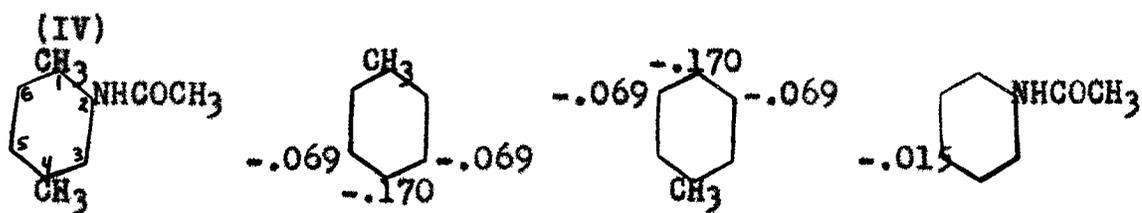### Application of the sigma values to 2-N-acetylamino-p-xylene (IV)

In applying the sigma values for 2-N-acetylamino-p-xylene

where σ for pCH_3 = -0.170

σ for mCH_3 = -0.069   (24)

σ for $pNHCOCH_3$ = -0.015

σ for $mNHCOCH_3$ while it is not given may be assumed to between 0 and -0.015 if compared with similar groups.

Position	$\sum \sigma$
1	-.170
2	-.069
3	-.069
4	-.170
5	-.084
6	-.069

Here the oxidation centers, positions 1 and 4, have about the same electron density which explains the fact that both isomers were formed.

At room temperature, the alkaline permanganate oxidation of 2-N-acetylamino-p-xylene yielded a small amount of 2-N-acetylamino-p-toluic acid (IV); Run III-B-1.

At reflux the same oxidation yielded a small amount of 3-N-acetylamino-p-toluic acid (V) and 2-N-acetylamino-p-toluic acid (IV); Run III-B-2.

This correlation of sigma values with the oxidation results of 2-N-acetylamino-p-xylene, where the reactive positions are of about the same magnitude, may account for the poor results obtained -- as compared with the study of the oxidation of 2-nitro-p-xylene.
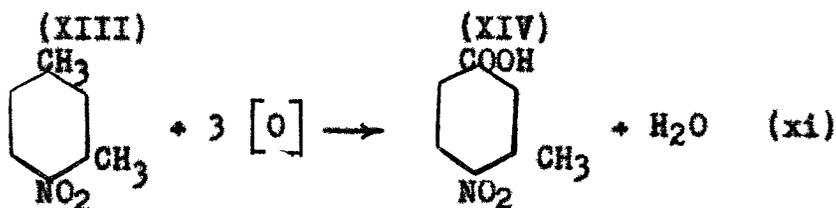
The Application of the Hammett Sigma Values in Predicting the Preferential Partial Oxidation of other Monosubstituted xylenes

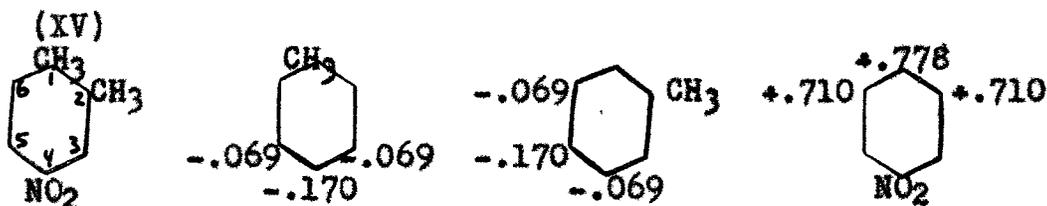### A. Application of the sigma values to 4-nitro-m-xylene (XIII)

(XIII)
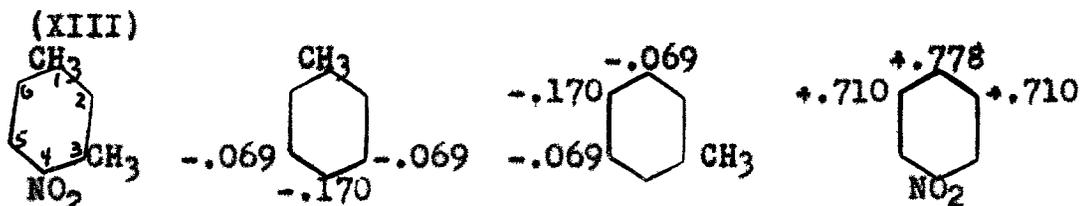
Position	$\sum \sigma$
1	+.709
2	+.710
3	-.069
4	-.170
5	-.069
6	+.540

Preferential oxidation would take place at position one to give 4-nitro-m-toluic acid.

(XIII)   (XIV)

$$+ \; 3 \; [O] \longrightarrow \qquad + \; H_2O \qquad (xi)$$

B. Application of the sigma values to 4-nitro-o-xylene (XV)

(XV)

Position	$\sum \sigma$
1	+.778
2	+.710
3	-.069
4	-.239
5	-.239
6	+.641

Here both oxidation centers, positions 1 and 2, have approximately the same low electron density and it may be expected that there would be almost an equal distribution of 4-nitro-o-toluic acid and 3-nitro-o-toluic acid.
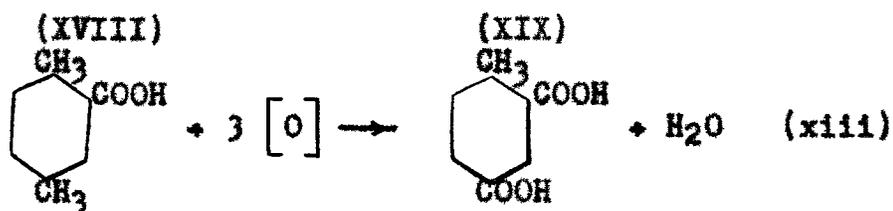

(XV) + 6 [O] → (XVI) + (XVII) + H₂O   (xii)
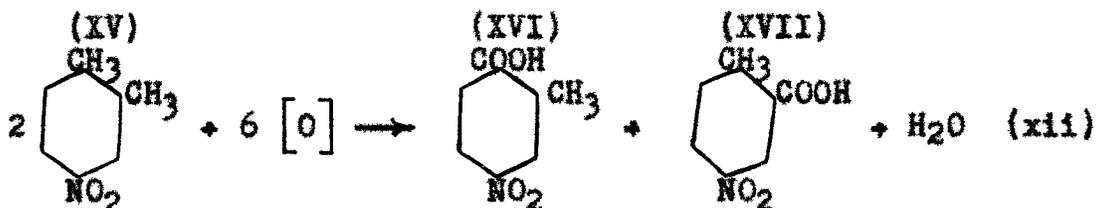
C. Application of the sigma values to 2, 5-dimethyl benzoic acid (XVIII)
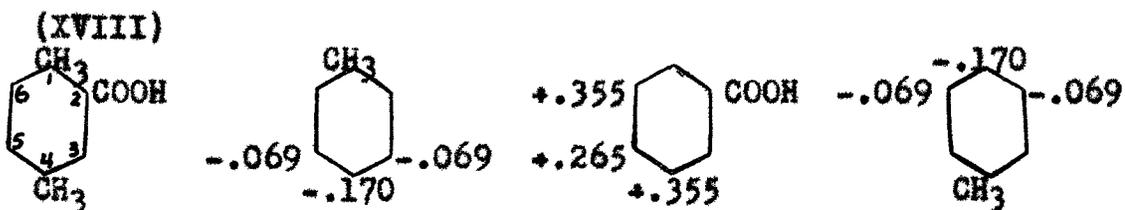
Position	$\sum \sigma$
1	-.170
2	-.069
3	-.069
4	+.185
5	+.196
6	+.286

Preferential oxidation would take place at position

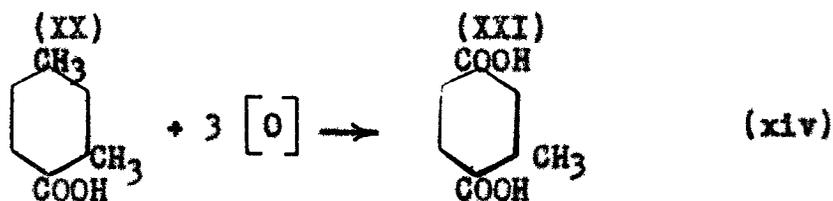4 rather than at 1 to give 4-methyl-m-terephthalic acid (XIX).

$$\text{(XVIII)} + 3\,[O] \rightarrow \text{(XIX)} + H_2O \qquad \text{(xiii)}$$

D. Application of the sigma values to 2, 4-dimethyl-benzoic acid (XX)
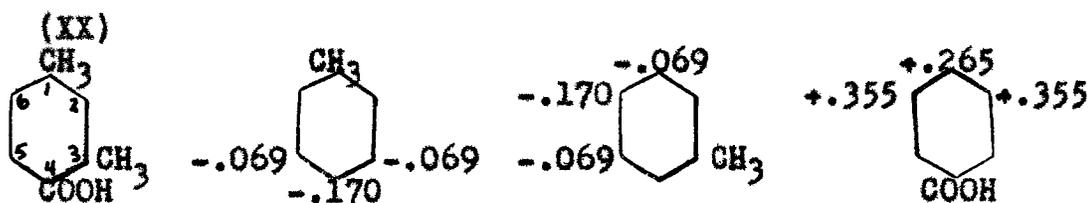
Position	$\sum \sigma$
1	+.196
2	+.355
3	-.069
4	-.170
5	-.138
6	+.185

Preferential oxidation would take place at position 1

rather than at 3 to give 2-methyl-terephthalic acid (XXI).

$$\text{(XX)} + 3\,[O] \rightarrow \text{(XXI)} \qquad \text{(xiv)}$$

Conclusion. In aromatic substitutions the negativity
of a position indicates a high electron density at that
carbon in the ring, which is susceptable to nucleophillic
attack. For oxidations, the concern is not that of the
ring carbon but rather that of the methyl group attached
to a ring carbon. Aromatic substitutions, as the name
implies, are substitution reactions whereas oxidations may
be thought of as elimination reactions involving the loss
of protons. In the former case a high electron density
is conducive to substitution and inhibits elimination.
Conversely, a low electron density (Positive o values)
would be conducive to eliminations.

The directive influence of aromatic substitutions is
directly opposite to the side chain oxidation of aromatic
compounds.

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