



Homolytic substitution of substituted toluenes
by Alan O Rockswold

A THESIS Submitted to the Graduate Committee in partial fulfillment of the requirements for the degree of Master of Science in Chemistry
Montana State University
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Abstract:

Methods for synthesizing some substituted toluenes are briefly reviewed.

Possibilities for future work in the field of homolytic substitution are suggested.

Attempts at homolytic substitution of 2-amino-4-nitrotoluene resulted in the formation of an unknown compound.

Experiments to determine the identity of this unknown compound indicate that it was 4-nitroindazole.

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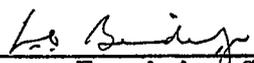
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A B S T R A C T

Methods for synthesizing some substituted toluenes are briefly reviewed.

Possibilities for future work in the field of homolytic substitution are suggested.

Attempts at homolytic substitution of 2-amino-4-nitrotoluene resulted in the formation of an unknown compound.

Experiments to determine the identity of this unknown compound indicate that it was 4-nitroindazole.

I N T R O D U C T I O N

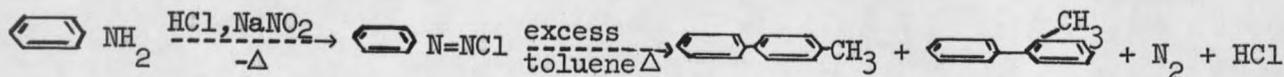
It has been long known that substituents in a benzene nucleus tend to orient any aryl group entering that benzene nucleus by homolytic substitution, (24) e.g. by a diazonium reaction, to a position ortho or para to the orienting group, regardless of the nature of the orienting group. Even those groups which are regarded as meta directing by the usual orientation rules of heterolytic reactions direct ortho and para in homolytic reactions.

The ultimate purpose of this research was to compare relative directing strengths of several groups, i.e. methyl, ethyl, isopropyl, tertiary butyl, methoxy and nitro, in homolytic substitution by observing yields of different isomers when benzenediazonium chloride reacted with various para-substituted toluenes.

The immediate objective of this thesis was to prepare some substituted toluenes for subsequent research and to prepare 2-methyl-5-nitrobiphenyl by homolytic substitution reactions.

L I T E R A T U R E H I S T O R Y

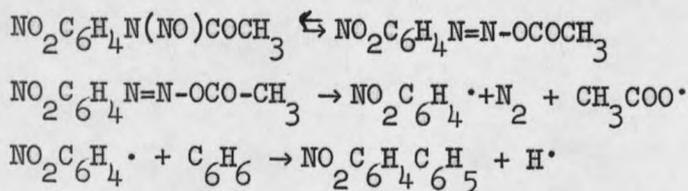
The Gomberg reaction has been established as a method of arylation since 1926. (16)



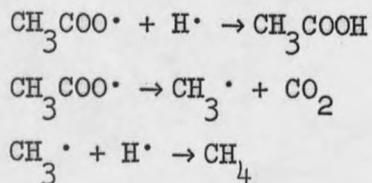
Later it was discovered that the usual rules of orientation did not apply to the free radical type reactions. (12 & 23) There should have been 40% ortho, 40% meta and 20% para isomers due to random coupling, but in homolytic reactions the entering groups were directed to the ortho and para positions, almost to the exclusion of the meta isomer.

Experimentation was begun to determine the nature and mechanism of these orienting forces. Almost all of the work up to the present time has been done using mono-substituted aromatics as starting materials. (12, 23, 18, 19 & 8) These starting materials have been treated with free radicals from various sources and the mixtures analyzed to determine percentage yields of the three possible isomers. (25)

Fuson (13) proposes a decomposition mechanism for this type of reaction using nitroso-m-nitroacetanilide as an example.



The terminating steps of the $\text{CH}_3\text{COO}\cdot$ group follow:



T H E O R E T I C A L

A homolytic reaction series was contemplated with disubstituted aromatics since previous work has been done mainly with mono-substituted aromatics.

Substituted toluenes were used since they would be liquid at the temperatures, 0-10°C., at which diazonium reactions are usually run.

The para position of toluene was blocked with a second substituent, because analysis of comparative directing strengths of the various substituents should be easier, since the entertaining free radical would be substituted ortho to one substituent or the other.

By running homolytic reactions with aniline on para substituted toluenes, analyzing each mixture for the two possible isomers, and assuming that the strongest orienting group will always direct primarily ortho, a series of relative orienting strengths could be established.

Physical constants of the possible biphenyls are needed so that one can determine the amounts of each biphenyl isomer in each homolytic reaction mixture.

There are several ways of synthesizing unsymmetrical biphenyls. Probably the most common method is the diazo method, (16) where an aromatic amine is diazotized by nitrous acid at low temperatures and then decomposed at a higher temperature in the aromatic solvent, which couples with the diazonium free radical.

Grignard reactions can also be used with certain limitations. (28) Cyclic ketones are treated with aryl magnesium halide, dehydrated and

then dehydrogenated to biaryls. This method cannot be used with compounds whose substituents react with the Grignard reagent or which cannot withstand dehydrogenation.

Unsymmetrical biphenyls can also be synthesized by the Ullman reaction (37) or by the Wurtz-Fittig reaction (9) by treating iodoaromatics with copper or sodium, respectively. The latter two methods are usually used for making symmetrical biphenyls. There is also produced a certain amount of the unsymmetrical compound as well as the two symmetrical ones.

The method that seemed to be most promising was the method by which the amino compound is acetylated, treated with nitrous oxide fumes or nitrosyl chloride, NOCl , and decomposed in the aryl solvent. (27) The nitrosyl chloride and the nitrous oxide modifications were both used.

MATERIALS AND APPARATUS

All materials used were laboratory reagents of C.P. or technical grade.

All apparatus was of pyrex glass with ground glass joints.

E X P E R I M E N T A L

1. p-TERTIARY BUTYLTOLUENE

t-BUTYLBENZENE was prepared by a Friedel-Crafts reaction (29) of benzene and t-butyl chloride in the presence of an amalgamated aluminum catalyst.

t-BUTYL-p-CHLOROMETHYLBENZENE was formed by heating a mixture of t-butyl benzene and polyoxymethylene, through which hydrogen chloride gas was passed. (5)

p-t-BUTYLTOLUENE was made by hydrolyzing the Grignard reagent (15) from t-butyl chloromethylbenzene with dilute sulfuric acid.

The yield by this method was about one percent and a more direct method was tried. The method below gave satisfactory yields.

p-t-BUTYLTOLUENE was prepared in 45% yield by heating toluene and isobutanol in the presence of fuming sulfuric acid. (3) This product was carefully fractionated and gave 13.7% yield of a product boiling at 184.0 - 184.5°C at 638 mm..

2. p-ETHYLTOLUENE

p-ETHYLBENZYLCHLORIDE was obtained by chloromethylating ethylbenzene by the use of polyoxymethylene and hydrogen chloride. (5)

NOTE! A marble chip placed in the still pot when distilling prevents the formation of tarry materials.

p-ETHYLTOLUENE was not synthesized since it was not needed at this time, but p-ethylbenzylchloride could probably be reduced by low pressure catalytic hydrogenation to p-ethyltoluene.

3. p-METHOXYTOLUENE

p-CRESOL was prepared by dissolving p-toluidine in dilute sulfuric acid, adding sodium nitrite and heating to decompose the diazonium salt. (17)

p-METHOXYTOLUENE was obtained by treating a cooled mixture of dilute sodium hydroxide and p-cresol with dimethyl sulfate. (20)

4. 2-AMINO-4-NITROTOLUENE

2-4-DINITROTOLUENE was obtained by nitrating p-nitrotoluene in the usual manner, (19) by means of concentrated nitric acid in concentrated sulfuric acid.

2-AMINO-4-NITROTOLUENE was sought by attempting to reduce 2-4-dinitrotoluene by passing hydrogen chloride through an alcoholic solution saturated with stannous chloride. This was a modification of the method reported by Burton. (7)

Due to the poor yield a different approach was tried.

2-AMINO-4-NITROTOLUENE was obtained by nitrating o-toluidine with concentrated nitric acid in concentrated sulfuric acid in the usual manner. (2) This method was modified by recrystallizing 2-amino-4-nitrotoluene from hot water.

ATTEMPTED SYNTHESIS OF 2-METHYL-5-NITROBIPHENYL

NITROSYL CHLORIDE was made by saturating fuming nitric acid with sulfur dioxide and treating with sodium chloride. (24)

ACETO-NITROSO-o-TOLUIDIDE was prepared by adding nitrosyl chloride to a solution of 2-amino-4-nitrotoluene in acetic acid and acetic anhydride. (22)

2-METHYL-5-NITROBIPHENYL

According to France, Heilbron, and Hey (11) 3-nitrobiphenyl can be obtained in 51% yield by treating m-nitroaniline with glacial acetic acid and acetic anhydride, followed by nitrogen oxides, N₂O₃, bubbled through the solution and decomposed in excess benzene.

When this method was tried in an attempt to make 2-methyl-5-nitrobiphenyl using 2-amino-4-nitrotoluene and benzene, an unexpected product resulted. The nitrogen content as determined by the Kjeldahl method (6) was 13.0% compared to a calculated nitrogen content of 6.5% for 2-methyl-5-nitrobiphenyl.

The same unknown compound was obtained by stirring aceto-nitroso-*o*-toluidine made with NOCl (22) in benzene 35 - 40°C. (27) and also by stirring in the presence of anhydrous sodium sulfate and anhydrous sodium carbonate. (26)

ATTEMPTS TO IDENTIFY UNKNOWN

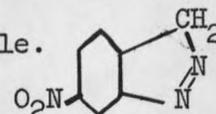
<u>TEST</u>	<u>RESULTS</u>	<u>INFERENCE</u>	<u>REFERENCE</u>
<u>Solubility</u>			
water	insoluble	} INERT ORGANIC COMPOUND	31
5% hydrochloric acid	insoluble		
5% sodium hydroxide	insoluble		
methyl alcohol	soluble		
ethyl alcohol	soluble		
isopropyl alcohol	soluble		
Melting point	188-9°C.		
Sodium hydroxide & acetone	negative	NEITHER DI-NOR TRI-NITRO COMPOUND	32
Tollens reagent	negative	COMPOUND NOT EASILY OXIDIZED	33
Reduced unknown & Tollens reagent	positive	NITRO COMPOUND	34

Ferric chloride in water	negative	NOT A PHENOL	35
Ferric chloride in alcohol	negative	NOT A PHENOL	35
Benzenesulfonylchloride	positive	SECONDARY AMINE	36

Molecular weight determinations using the ebullioscopic method with benzene and ethylene bromide as solvents were so erratic that no conclusions could be drawn from them.

The melting point values reported in the literature for aceto-o-toluidide (21) and nitroso-aceto-o-toluidide (25) were 151°C. and 90°C., respectively. These reported melting points do not agree with the melting point of the unknown compound.

A further literature search showed that Witt, Nölting and Grandmougin had attempted to make nitroso-aceto-o-toluidide by using sodium nitrite and hydrochloric acid and obtained 4-nitroindazole.



which they reported as having a melting point of 181°C. (38)

A low pressure catalytic hydrogenation showed that the compound took up 7.4 atoms hydrogen per mole. Eight atoms of hydrogen per mole are needed to saturate 4-nitroindazole.

The above results led us to conclude that the unknown compound is 4-nitroindazole.

Results of the quantitative analysis of the unknown compound are as follows:

Found	Calculated as 4-nitroindazole
N 23.42%	N 26.09%
C 48.28%	C 52.17%
H 3.95%	H 3.11%

FURTHER RESEARCH POSSIBILITIES

There are many unsymmetrical disubstituted biphenyls which have never been synthesized.

At the present time the following 2-5-disubstituted biphenyl compounds have been synthesized:

2-methoxy-5-methylbiphenyl (1)

2-isopropyl-5-methylbiphenyl (30)

2-methyl-5-isopropylbiphenyl (4)

2-nitro-5-methylbiphenyl (10)

The above compounds are possible isomers of homolytic substitution into the substituted toluene series of compounds mentioned in the introduction. Other 2-5-disubstituted biphenyls of interest in this series, which have not been synthesized are as follows:

2-methyl-5-nitrobiphenyl

2-methyl-5-methoxybiphenyl

2-methoxy-5-methylbiphenyl

2-methyl-5-ethylbiphenyl

2-ethyl-5-methylbiphenyl

2-methyl-5-t-butylbiphenyl

2-t-butyl-5-methylbiphenyl

Homolytic substitution reactions should be run on the various substituted toluenes and an analytical scheme should be developed to measure quantitatively the amounts of each geometric isomer formed.

Attempts should be made to correlate these findings and the relative strengths of the substituents with the final motive of being able to

predict qualitatively, at least, the position of the entering substituents.

An attempt should be made to formulate a reaction mechanism.

S U M M A R Y

1. Substituted toluenes have been synthesized for further research in the field of homolytic substitution.
2. A literature survey of the 2-5-disubstituted unsymmetrical biphenyls has been made and a list of 2-5-disubstituted unsymmetrical biphenyls which have been synthesized has been compiled.
3. The possibility of transforming 5-nitro-o-toluidine to 2-methyl-5-nitrobiphenyl by means of a homolytic reaction has been investigated. All the reactions tried gave good yields of a rearrangement product, 4-nitroindazole.

A C K N O W L E D G E M E N T S .

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L I T E R A T U R E C I T E D A N D C O N S U L T E D

1. Achel, J. Am. Chem. Soc., 63, 1948-52 (1941)
2. Anschütz, Ber., 19, 216 (1886)
3. Bielstein, System #470, 5 439
4. Bielstein, System #479, 619
5. Blanc, Bull. Soc. Chim., 33, 313 (1923)
6. Bradstreet, Chem. Rev., 27, 331 (1940)
7. Burton, J. Chem. Soc., 119, 1051 (1921)
8. DeTar and Scheifile, J. Am. Chem. Soc., 73, 1442 (1951)
9. Fittig, Ann. 121, 363 (1862) & 132, 201 (1864)
10. France, J. Chem. Soc., 1288-92 (1939)
11. France, J. Chem. Soc., 1288 (1939)
12. France, Heilbron & Hey, J. Chem. Soc., 1364 (1938) & 1283 (1939)
13. Fuson, "Advanced Organic Chemistry", John Wiley & Sons, New York (1950)
14. Gibson, J. Chem. Soc., 121, 278 (1922)
15. Gilman, J. Am. Chem. Soc., 51, 1576 (1929)
16. Gomberg and Pernert, J. Am. Chem. Soc., 48, 1372 (1926)
17. Griess, J. Chem. Soc., 20, 41-53 (1867)
18. Hey, Nechvatal & Robinson, J. Chem. Soc., 2892 (1951)
19. Hey, Stirling & Williams, J. Chem. Soc., 2747 (1954)
20. Hiers, Org. Syn., 9, 12 (1929)
21. Hillers, C.A., 9965a 48 (1954)
22. Huisgen, Ann., 573, 181-195 (1951)
23. Loibl, Stein & Weiss, J. Chem. Soc., 2074 (1949)
24. Nelson, J. Chem. Educ., 32, 606 (1955)

25. Nelson, J. Chem. Educ., 32, 609 (1955)
26. Organic Reactions, 2, 251 (1944)
27. Organic Reactions, 2, 252 (1944)
28. Organic Reactions, 2, 242 (1944)
29. Radziewanovsky, Ber., 28, 1137 (1895)
30. Sherwood, J. Chem. Soc., 1832-35 (1932)
31. Shriner & Fuson, "Identification of Organic Compounds", 58, John Wiley & Son, Inc., New York (1954)
32. Ibid, 138
33. Ibid, 145
34. Ibid, 149
35. Ibid, 98
36. Ibid, 91
37. Ullman, C.R., 38, 139 Ann. & 332, 40 (1904)
38. Witt, Ber., 23 3635 (1890)

