

ELECTROPHILIC AROMATIC SUBSTITUTION OF SOME ANILINIUM OXIDES

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ABSTRACT

Three isomeric N,N,N-trimethylanilinium oxides were subjected to nitration, bromination and diazocoupling. The purpose was to investigate the activating effects of the oxide function on ring electrophilic substitution. This was performed in the presence of the deactivating trimethylammonium function in the three isomers. The directive influence of these isomers on the newly entering groups was also investigated.

INTRODUCTION AND DISCUSSION

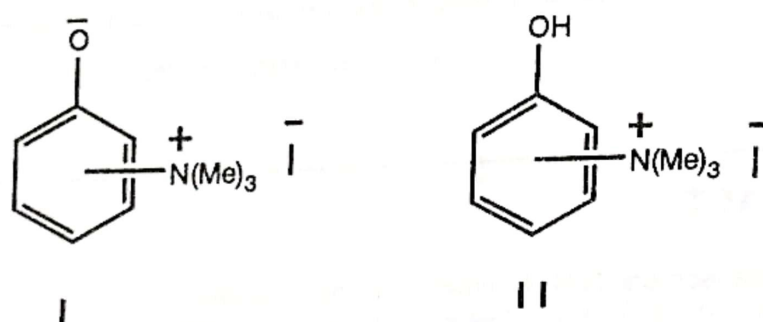
Bromination, nitration and diazocoupling reactions were chosen as examples of aromatic electrophilic substitution reactions in this investigation.

The three isomeric 2, 3- and 4-hydroxy-N,N,N-trimethylanilinium iodides (II) were prepared by reacting methyl iodide with the three isomeric aminophenols^(1,2).

The iodides were transformed to the corresponding oxides by ion-exchange on Amberlite resin IRA 400, and were obtained in fairly good yields. The pH of the eluted solution was strongly alkaline during the ion-exchange process⁽¹⁾.

The oxides (I) were nitrated by nitric acid (d 1.52) in acetone/acetic acid⁽⁶⁾ while diazocoupling was done by the use of p-nitrophenyl-diazonium fluoborate and p-bromophenyl-diazonium fluoborate, in deionized water, as electrophilic reagents^(3,4).

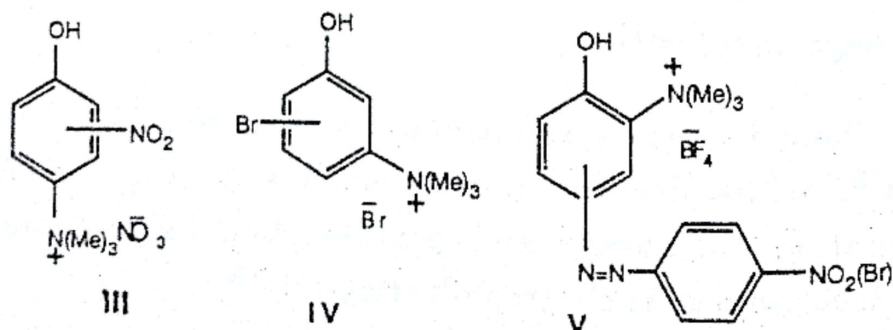
The diazonium fluoborates were prepared by the reaction of the corresponding diazonium chlorides with ammonium fluoborate. The product was isolated and dried when stable solids (for a least two weeks) were obtained^(3,4). Exact equivalents of the diazonium salts have been used for the coupling reactions.



Electrophilic substitution took place almost exclusively in the 5,4- and 3-positions of the 2-,3-, and 4-oxides, respectively with the production of the corresponding hydroxyanilinium salts e.g.: nitrates, hydrobromides and fluoborates.

On the other hand, monosubstitution was the only product found to take place which can be attributed to the deactivating effect of the newly entering electronegative groups as well as the subsequent formation of the hydroxyanilinium species. This was less activating for electrophilic substitution in acid medium than the corresponding oxides.

Monosubstitution has been confirmed by the use of NMR, and mass spectroscopy. Mononitronitrates (III), monobromobromides (IV), and mono - 4 - bromophenyl - diazofluoborate or mono - 4 - nitrophenyldiazofluoborates (V), were obtained in good yields from the three isomers.



Electrophilic aromatic substitution taking place in the three isomeric anilinium oxides under such mild conditions can be imply attributed to the strong activating effect of the oxide function. This easily outweighs the strong negative inductive (-I) effect of the trimethylammonium function and activates, as well the ring towards nitration, bromination and diazocoupling.

Compared to the trimethylammonium function, the oxide function is capable of localizing a negative charge at the ortho-and para-positions of the aromatic ring system by applying its strong mesomeric (+M) effect of the negative charge on the oxide oxygen (VI).

On the same grounds, the trimethylammonium function did not display neagive mesomeric effect (-M) to oppose the (+M) effect of the oxide function. If this takes place, it will lead to the formation of a pentacovalent nitrogen, a case which is absolutely impossible in the light of the electronic theory.

The effects of the trimethylammonium function can, therefore, be summed out as inductive (-I) and steric effects. In the presence of the oxide function they will be expected to affect the orientation of the entering groups only, a proposal which has been verified in the present investigation.

EXPERIMENTAL

Meting points are uncorrected and micronalyses were carried out at Alfred Bernhardt Micronalytical Laboratories W. Germany.

(I) 2-, 3-, and 4-Hydroxy-N,N,N-trimethylanilinium iodides (II):

To a solution of 2-, 3-, or 4-aminophenol (0.01 mole) in absolute ethanol (25 ml); anhydrous sodium carbonate (0.04 mole) and methyl iodide (0.04 mole) were added. The reaction mixture was heated under reflux for 2-3 hours the mixture was filtered while hot then couled to room temperature, and the separated solid was washed with acetone or absolute ethanol, dried and recrystallized from ethanol.

(2) N,N,N-trimethylanilinium-2-, 3-, and 4-oxides (I):

The solution of the iodide II (0.01 mole) in deionized water (300 mL) was eluted in a dropwise fashion over a column (12 mm wide and 40 cm length) of activated ion exchange resin (Amberlite resin I.R. 120). The pH of the dropping solution was approximately 9.5-10 during elution.

The first 5-10 mL of the eluent were excluded and after complete elution the column was washed with (20 mL) volumes of deionized water until the dropping solution was no more alkaline to universal indicator and the washings were added to the original.

The combined solution was evaporated under reduced pressure to give the oxides as fairly crystalline white solids.

Melting points of these derivatives were reported as follows:

<u>The oxide</u>	<u>Melting points</u>
2- oxide	178°C.
3-oxide	110°C.
4-oxide	202-203°C.

(3) 2-, 3-, and 4-hydroxy nitro-N,N,N-trimethylanilinium nitrates (III):

To a solution of the oxide (0.05 mole) in acetone/acetic acid mixture (4:1.4 mL) cooled at 0°C, nitric acid (d 1.52, 3.5 mL) was added dropwise. The rate of addition was controlled so that the temperature of the mixture was kept between 0-5°C. The reaction mixture was set a side for further half an hour at room temperature and then diluted with water.

The solid was collected, recrystallized from the appropriate solvent to obtain the mononitronitrates as fairly crystalline yellow solids (Table 1).

Table (1): Hydroxy-nitro-N,N,N-trimethylanilinium nitrates (III).

Compound	M.P.°C	Solvent	%C	%H	%N
2-Hydroxy-5-nitro	260	Benzene: acetone	*C: 41.7 *F: 42.0	5.02 5.12	16.21 16.32
3-Hydroxy-4-nitro	182-183	Acetone	C: 41.7 F: 41.92	5.02 5.18	16.21 16.25
4-Hydroxy-3-nitro	230-231	Methanol	C: 41.7 F: 42.04	5.02 5.28	16.21 16.10

*C = calculated. *F = found

NMR of compounds III:

- 1- Phenyl protons Ab system centered at δ 8.2, singlet at δ 8.5; methyl protons singlet centered at δ 3.3 and hydroxyl proton as a singlet at δ 7.6.
- 2- Phenyl protons AB system centered at δ 8.7, singlet at δ 8.4, methyl protons singlet at δ 3.6 and hydroxyl proton as a singlet at δ 7.3.
- 3- Phenyl protons AB system centered at δ 7.9, singlete at 8.8 methyl protons singlet centered at δ 3.5 and hydroxyl protons as a singlet at δ 7.9.

(4) 2-, 3, and 4-Hydroxy-bromo-N,N,N-triemthylanilinium bromides (IV):

To a solution of the oxide (0.007 mole) in absolute ethanol (30 mL), bromine, solution (0.013 mole) was added dropwise with stirring while heating under reflux. After complete addition, the reaction mixture was heated for additional hour and left to cool. The seperated solid was washed with absolute ethanol and recrystallised from the appropriate solvent (Table 2).

Table (2): Hydroxy-bromo-N,N,N-trimethylanilinium bromides (IV).

Compound	M.P. °C	Solvent	%C	%H	%N
2-Hydroxy-5-bromo	209-100	Acetone	C 34.72	4.14	4.50
			F 34.84	4.09	4.61
3-Hydroxy-4-bromo	182-183	Ethanol	C 34.72	4.14	4.50
			F 34.94	4.06	4.49
4-Hydroxy-3-bromo	230-231	Ethanol	C 34.72	4.14	4.50
			F 34.52	4.23	4.58

NMR of compound IV:

- 1- Phenyl protons AB system at δ 8.0, singlet at δ 8.3 methyl protons; singlet at δ 3.2 and hydroxyl protons singlet at δ 7.5.
- 2- Phenyl protons AB system centered at δ 8.3, singlet at δ 8.1 methyl protons; singlet at δ 3.3 and hydroxyl protons singlet at δ 7.1
- 3- Phenyl protons AB system at δ 7.6, singlet at δ 8.3 methyl protons; singlet at δ 3.2 and hydroxyl proton singlet at δ 7.3.

(5) 2-, 3-, and 4-Hydroxy-(4-bromophenyldiazo or 4-nitrophenyldiazo)-N,N,N-trimethylanilinium fluoborates (V):

To a solution of the oxide (0.042 mole) in deionized water (30 mL) 4-nitrophenyldiazonium fluoborate or 4-bromophenyldiazonium fluoborate (0.084 mole) in deionized water (40 mL) was added slowly with stirring and the mixture was set a side for half an hour. The separated solid was thoroughly washed with cold deionized water and then recrystallized from the appropriate solvent (Table 3 & 4).

Table (3): Hydroxy-(4-bromophenyldiazo)-N,N,N-trimethylanilinium fluorborates (V).

Compound	M.P.°C	Solvent	%C	%H	%N
2-Hydroxy-5-(4-bromophenyldiazo).	209-100	Acetone	C 42.65	4.03	9.95
			F 42.66	4.11	9.86
3-Hydroxy-4-(4-bromophenyl diazo).	211-212 dec	Methanol	C 42.65	4.03	9.95
			F 42,78	4.10	9.79
4-Hydroxy-3-bromo bromophenyldiazo).	223-5 dec	Acetone	C 42.65	4.03	9.95
			F 42.95	4.06	9.91

Table (4): Hydroxy-(4-nitrophenyldiazo)-N,N,N-trimethylanilinium fluoborates (V) B..

Compound	M.P.°C	Solvent	%C	%H	%N
2-Hydroxy-5(4-nitrophenyldiazo).	214-5	Acetone	C 46.40	4.36	14.43
			F 46.25	4.28	14.32
3-Hydroxy-4(4-bromophenyldiazo).	210-11	Methanol	C 46.40	4.36	14.30
			F 46.34	4.32	14.38
4-Hydroxy-3-bromo bromophenyldiazo).	229-30	Acetone	C 46.40	4.36	14.43
			F 46.64	4.18	14.49

NMR of compound (V) A & B:

- 1- Phenyl protons AB system centered at δ 7.9 (2 protons), AB system centered at δ 7.5 A and δ 8.2 B (4 protons), and a singlet at δ 8.1 (1 proton), methyl protons singlet at δ 3.4 and hydroxyl proton as a singlet at δ 7.2.

- 2- Phenyl protons AB system centered at δ 8.0 (2 protons), AB system centered at δ 7.5 A and δ 8.3 B (4 protons), and a singlet at δ 7.9 (1 protons), methyl protons singlet at δ 3.4 and hydroxyl proton as singlet at δ 6.9.

REFERENCES

- 1- H.M.R. El-Mouafi, Georgae Hvistendahl and Kjell Mndheim; Mass Spectrometry of Onium Compounds; J. Org. Mass, Spectrom., (19), 9, PP. 450-358.
- 2- R. Pflieger and K. Waldmann, Chem. Ber., 90, 2471 (1975).
- 3- D.T. Flood, Org. Syntheses, Coll. 11, 295 (1943).
- 4- A. Rose, Ogr. Reactions, 5, 193 (1949).
- 5- H.M.R. El-Mouafi; Egypt. J. Pharm. Sci., 32 (3-4) 901-909 (1991).

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عرضت أكاسيد الأنيلينيم الثلاثة المتناظرة للنترته والهجنة (بروم) والديازوكبلنج فى محاولة للتعرف على الأثر التنشيطى للأكسيد على الاستبدال فى الحلقة وذلك فى وجود مجموعة ثلاثى مثيل أمونيوم المشبطة للأستبدال ومحاولة لمعرفة الأثر التوجيهى على المجموعات الجديدة المستبدلة .