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Multinuclear Magnetic Resonance Spectroscopic and Semiempirical Molecular Orbital (AM1) Studies of Substituted Anisoles

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^{13}C, ^{15}N, and ^{17}O NMR spectra have been recorded for 4-nitroanisole (**1**), its 2-methyl-, 2-chloro-, 2-bromo-, 2-iodo-, 2,6-dimethyl-, 2,6-dichloro-, 2,6-dibromo-, and 2,6-diiodo-derivatives **2**—**9**, also nitrobenzene (**1a**), its 3-methyl-, 3-chloro-, 3-bromo-, and 3-iodo-derivatives **2a**—**5a** and 3,5-dichloro- and 3,5-dibromo-derivatives **7a** and **8a**. Analysis of the chemical shifts of carbon bearing nitro group and nitro oxygens in these compounds suggests that presence of one substituent *ortho-* to the methoxyl group enhances its resonance interaction with the benzene ring whereas presence of two *ortho*-substituents inhibits this resonance. However, in no case the resonance is completely inhibited. The extent of enhancement or inhibition is almost independent of the nature of the *ortho*-substituent. This conclusion has also been arrived by analyzing the reported chemical shifts of the *para*-carbons in anisoles **1b**—**9b** and the corresponding carbons in benzene derivatives **1c**—**9c**. Though evidence could not be obtained for steric enhancement of resonance using methoxyl oxygen chemical shifts, analysis of these chemical shifts in di-*ortho*-substituted anisoles **6**—**9** and **6a** furnishes evidence for steric inhibition of resonance. However, ^{15}N chemical shifts are of no use in studying these phenomena. Semiempirical molecular orbital calculations using AM1 Hamiltonian suggest that the methoxyl group is coplanar with the benzene ring in anisole, 4-nitroanisole and 2-substituted-4-nitroanisoles but is perpendicular to the benzene ring in 2,6-disubstituted-4-nitroanisoles. Moreover, in 2-substituted-4-nitroanisoles the *O*-methyl group is *anti* to the 2-substituent.

Several NMR spectroscopic studies[1—16] have been made on anisole and its derivatives with a view to getting information about mesomeric, inductive and steric effects caused by various substituents. This is understandable, because the methoxyphenyl group is a constituent of a variety of useful and interesting chemical moieties, such as lignin, and psychotomimetic entities as well as of mesogenic materials.[16] Many studies on substituted anisoles have emphasized that the presence of two substituents *ortho-* to the methoxyl group inhibits the resonance interaction between the methoxyl group and the π-system of the phenyl ring. On the other hand a recent NMR study[5] claims that the presence of one *ortho*-substituent enhances the resonance interaction between the methoxyl group and the phenyl ring. This subject of steric enhancement of resonance in mono-*ortho*-substituted anisoles was launched by Baliah and Uma[17] and has been studied extensively by them and their co-workers using various kinetic and spectroscopic methods.[18—20] From the ^{13}C and ^{17}O NMR studies of several di-*ortho*-substituted anisoles Schuster et al.[2] argue that in these compounds the resonance interaction of the methoxyl group with the aromatic ring increases with the nature of the *ortho*-substituent in the following order: isopropyl > ethyl < methyl ≪ methoxyl (in plane) < *t*-butyl. This has been explained in terms of repulsions between the lone pair electrons of the methoxyl oxygen and the bonding electrons of the proximate substituents.[2]

In addition of the experimental NMR studies, anisole and its derivatives have been a subject of several theoretical calculations.[13—16,21,22] The barrier to rotation about the C–O bond in anisole has been determined by several workers.[14,16] The preferred conformation of anisole also has been determined.[13,16] However, no such calculations have been made on *ortho*-substituted anisoles except *ortho*-di-methoxylbenzene[21,22] as well as on di-*ortho*-substituted anisoles.

Since steric effects in substituted anisoles and their conformational preferences are under continuous interest, we thought that multinuclear magnetic resonance spectroscopy combined with semiempirical MO(AM1) calculations can provide an useful scope to this important topic. In addition to ^{13}C NMR spectroscopy, especially interesting are ^{17}O NMR studies owing to few previous articles on substituted anisoles.[2,5,8—10,13] Further, introducing a new 'probing' substituent such as a nitro group at the *para*-carbon to the methoxyl group opens a new scope on investigating the resonance interactions between the subsutituent and the aromatic π-system in form of two additional NMR active nuclei included in the nitro group.

Therefore, in this work we have recorded the ^{13}C, ^{15}N, and ^{17}O NMR spectra of 4-nitroanisole (**1**), 2-methyl-4-nitroanisole (**2**), 2-chloro-4-nitroanisole (**3**), 2-bromo-4-nitroanisole (**4**), 2-iodo-4-nitroanisole (**5**), 2,6-dimethyl-4-nitroanisole (**6**), 2,6-dichloro-4-nitroanisole (**7**), 2,6-dibromo-4-nitroanisole (**8**), and 2,6-diiodo-4-nitroanisole (**9**). The NMR spectra have been also recorded for nitrobenzene (**1a**) and six *meta*-substituted nitrobenzenes **2a**—**5a**, **7a** and **8a** for the sake of comparison. In addition, semiempirical MO(AM1) calculations have been performed in order to relate the obtained NMR data with the conformational properties of the molecules.

Experimental

Materials. Nitrobenzene (**1a**) and *m*-nitrotoluene (**2a**) were commercial products of British Drug House (BDH). All the substituted anisoles were prepared by methylating the corresponding phenols except 2-iodo-4-nitroanisole (**5**).

General Method of Methylation of Phenols. The respective phenol (50 mmol) was dissolved in dry acetone (50 ml). Anhydrous potassium carbonate (10 g) was added to it. The mixture was kept under reflux on a water bath. Methyl iodide (10 ml) was added in portions during an hour. The reaction mixture was then refluxed for six hours. The solvent was removed in vacuo and the separated solid was recrystallized from aqueous ethanol.

4-Nitroanisole (**1**): Pale yellow crystals; mp 54 °C (lit[23] 54 °C).

2-Methyl-4-nitroanisole (**2**): Colorless needles; mp 64 °C (lit,[24] 63—64 °C).

2,6-Dimethyl-4-nitroanisole (**6**): Colorless needles; mp 91°C (lit,[25] 92 °C).

2-Chloro-4-nitroanisole (**3**): White needles; mp 97—98 °C (lit,[26] 97—98 °C).

2,6-Dichloro-4-nitroanisole (**7**): Colorless needles; mp 98 °C (lit,[27] 98 °C).

2-Bromo-4-nitroanisole (**4**): White needless; mp 107—108 °C (lit,[28] 108 °C).

2,6-Dibromo-4-nitroanisole (**8**): Colorless needles; mp 122 °C (lit,[29] 122 °C).

2,6-Diiodo-4-nitroanisole (**9**): White flakes; mp 134 °C (lit,[30] 134—135 °C).

2-Iodo-4-nitroanisole (**5**). *o*-Iodoanisole (12.7 g, 50 mmol) was dissolved in glacial acetic acid (10 ml). Cold concentrated nitric acid (5ml) was added dropwise with stirring. The mixture was heated on a water bath until brown fumes appeared. The product separated on cooling was recrystallized from aqueous ethanol. Light brown crystalline mass; mp 95 °C (lit,[30] 95 °C).

3-Chloronitrobenzene (**3a**). This was prepared by Sandmeyer's reaction from *m*-nitroaniline as described by Vogel.[31] Pale yellow solid; mp 44—45 °C (lit,[31] 44—45 °C).

3-Bromonitrobenzene (**4a**). This was prepared by brominating nitrobenzene in presence of iron as described by Vogel.[32] Yellow crystalline solid; mp 51—52 °C (lit,[32] 51—52 °C).

3-Iodonitrobenzene (**5a**). A mixture of *m*-nitroaniline (5 g, 36 mmol), concentrated sulphuric acid (4.1 ml) and water (30 ml) was stirred for 1 h. The mixture was cooled to 0—5 °C and diazotized with a solution of sodium nitrite (2.5 g, 36 mmol) in water (7.5 ml). The cold solution was added slowly with stirring into a solution of potassium iodide (10 g, 60 mmol) in water (30 ml). The mixture was then warmed on a water bath for about an hour, extracted with ether and washed with 1 percent sodium hydroxide solution. The resulting liquid after the removal of ether solvent, was distilled under vacuum. Pale yellow viscous liquid; bp 130—134 °C/9 mmHg (lit,[33] 133—134 °C/9 mmHg) (1 mmHg=133.322 Pa).

3,5-Dichloronitrobenzene (**7a**). This was prepared by the deamination of 2,6-dichloro-4-nitroaniline, obtained by chlorination of *p*-nitroaniline, following the procedure of Hodgson et al.[34] *p*-Nitroaniline (6.9 g, 50 mmol) was dissolved in concentrated hydrochloric acid (100 ml). Potassium chlorate (4.1 g) was added in small portions with stirring at constant temperature. After the addition was over, the mixture was diluted with water (100 ml). 2,6-Dichloro-4-nitroaniline was obtained as yellow flaky mass. It was recrystallized from aqueous ethanol. Yellow needles; mp 189 °C (lit,[30] 189 °C).

2,6-Dichloro-4-nitroaniline (5 g, 25 mmol) was dissolved in glacial acetic acid (30 ml). The solution was added dropwise to a solution of sodium nitrite (2 g) in concentrated sulphuric acid (10 ml) below 20 °C. After 30 min, the mixture was run into a vigorously stirred suspension of finely divided cuprous oxide (5 g). The mixture was heated under reflux on a water bath until the evolution of nitrogen gas ceased. The residue was steam distilled. The product was recrystallized from aqueous ethanol. Pale yellow needles; mp 64—65 °C (lit,[30] 65 °C).

3,5-Dibromonitrobenzene (**8a**). This was prepared by the deamination of 2,6-dibromo-4-nitroaniline which was obtained by bromination of *p*-nitroaniline. To a solution of *p*-nitroaniline (6.9 g, 50 mmol) in glacial acetic acid (100 ml) a solution of bromine (16 g, 5.3 ml, 100 mmol) in glacial acetic acid (20 ml) was added dropwise during four hours with vigorous stirring. The mixture was poured into a slurry of water (300 ml) and ice (100 g). The product that separated was recrystallized from aqueous ethanol. Yellow needles; mp 204 °C (lit,[35] 204 °C). The deamination of 2,6-dibromo-4-nitroaniline was done as in the case of 2,6-dichloro-4-nitroaniline. The product was recrystallized from aqueous ethanol. Pale yellow needles; mp 106—107 °C (lit,[35] 106 °C).

Method. All the spectra were recorded for 1 M $CDCl_3$-solutions (1 M=1 mol dm^{-3}) at 30 °C in 10 mm NMR tubes on a JEOL GSX 270 FT NMR spectrometer. All FID's were windowed by an exponential line broadening factor of the digital resolution prior to Fourier transformation to improve the signal/noise ratio in the frequency spectra.

The ^{13}C NMR spectra were recorded at 67.8 MHz with the following experimental parameters: spectral width 10000 Hz; number of data points 32 K; flip angle 90°; number of scans 100; acquisition time 1.4 s; pluse delay 5 s. The ^{17}O NMR spectra were recorded at 36.5 MHz with the following experimental parameters: spectral width 36000 Hz; number of data points 8 K; flip angle 90°; number of scans$>$300000; acquisition time 0.11 s; pulse delay 0.01 s. The ^{15}N NMR spectra were recorded at 27.3 MHz with the following experimental parameters: spectral width 7500 Hz; number of data points 32 K; flip angle 90°; number of scans$>$1200; acquisition time 2.2 s; pulse delay was 60 s to ascertain the full relaxation of the NO_2 group.

^{13}C chemical shifts are referenced to the signal of internal TMS. ^{17}O chemical shifts are referenced to the signal of an external D_2O capillary inserted coaxially inside the NMR tube. ^{15}N chemical shifts are referenced to the signal of neat nitromethane measured in a 10 mm NMR tube prior to the measurements for the samples.

Results and Discussion

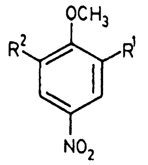
Assignment of Signals. In the ^{13}C NMR spectra, the weak signals could be assigned to the substituent-

Table 1. ^{13}C, ^{17}O, and ^{15}N Chemical Shifts for 4-Nitroanisoles **1**—**9**

Compound	^{13}C Chemical shifts, δ (ppm)								^{17}O Chemical shifts, δ (ppm)		^{15}N Chemical shifts, δ (ppm)
	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	OCH_3	CH_3	NO_2	OCH_3	NO_2
1	165.2	114.6	126.4	142.1	126.4	114.6	56.6	—	564.9	69.1	−12.0
2	163.4	128.4	126.4	141.5	124.1	109.8	56.6	16.8	564.2	66.4	−11.2
3	160.7	123.7	126.4	141.7	124.6	111.7	57.5	—	567.1	69.8	−14.6
4	161.5	112.3	129.5	142.1	125.3	111.4	57.5	—	566.6	75.6	−14.8
5	163.6	85.7	135.6	142.4	126.2	110.5	57.8	—	567.1	88.9	−14.9
6	163.0	132.8	124.6	144.0	124.6	132.8	60.4	16.8	571.2	27.5	−11.3
7	158.5	130.8	125.0	144.1	125.0	130.8	61.8	—	575.1	39.1	−17.9
8	160.4	119.1	128.7	144.8	128.7	119.1	61.7	—	577.5	47.9	−18.3
9	164.9	90.4	135.6	145.2	135.6	90.4	61.6	—	577.5	72.9	−18.5

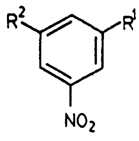
Table 2. ^{13}C, ^{17}O, and ^{15}N Chemical Shifts for Substituted Nitrobenzenes

Compound	^{13}C Chemical shifts, δ (ppm)							^{17}O Chemical shifts, δ (ppm)	^{15}N Chemical shifts, δ (ppm)
	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	CH_3	NO_2	NO_2
1a	148.8	124.1	129.9	135.2	129.9	124.1	—	574.3	−11.0
2a	148.8	124.3	140.4	135.9	129.6	121.1	21.7	573.6	−10.3
3a	149.3	124.4	136.0	135.3	131.0	122.3	—	577.2	−14.1
4a	149.3	127.3	123.4	138.2	131.2	123.7	—	577.0	−14.3
5a	149.1	132.9	94.1	144.0	131.3	123.3	—	578.1	−14.2
7a	149.6	122.9	136.7	135.1	136.9	122.9	—	579.2	−17.3
8a	149.6	126.1	124.0	140.5	124.0	126.1	—	581.6	−17.5



I

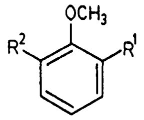
1. $R^1=R^2=H$
2. R^1=Me; R^2=H
3. R^1=Cl; R^2=H
4. R^1=Br; R^2=H
5. R^1=I; R^2=H
6. $R^1=R^2$=Me
7. $R^1=R^2$=Cl
8. $R^1=R^2$=Br
9. $R^1=R^2$=I



II

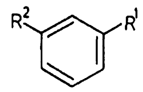
1a. $R^1=R^2=H$
2a. R^1=Me; R^2=H
3a. R^1=Cl; R^2=H
4a. R^1=Br; R^2=H
5a. R^1=I; R^2=H
6a. $R^1=R^2$=Me
7a. $R^1=R^2$=Cl
8a. $R^1=R^2$=Br
9a. $R^1=R^2$=I

Chart 1.



III

1b. $R^1=R^2=H$
2b. R^1=Me; R^2=H
3b. R^1=Et; R^2=H
4b. R^1=*i*-Pr; R^2=H
5b. R^1=*t*-Bu; R^2=H
6b. $R^1=R^2$=Me
7b. $R^1=R^2$=Et
8b. $R^1=R^2$=*i*-Pr
9b. $R^1=R^2$=*t*-Bu



IV

1c. $R^1=R^2=H$
2c. R^1=Me; R^2=H
3c. R^1=Et; R^2=H
4c. R^1=*i*-Pr; R^2=H
5c. R^1=*t*-Bu; R^2=H
6c. $R^1=R^2$=Me
7c. $R^1=R^2$=Et
8c. $R^1=R^2$=*i*-Pr
9c. $R^1=R^2$=*t*-Bu

Chart 2.

bearing carbons. These were further characterized by known substituent effects.[36)] Thus, the signal around 160 ppm should be due to the methoxyl-bearing carbon and that around 145 ppm should be due to the nitro-bearing carbon. The carbons bearing the other substituents (Me, Cl, Br, I) appear in the range 90—130 ppm. In 4-nitroanisoles **1**—**5**, the carbons *ortho*- to the methoxyl group appear at a considerably higher field than those *ortho*- to the nitro group. In **2**—**5**, C-3 and C-5 were distinguished based on known substituent effects. Thus, in **2** the signal at 124 ppm was assigned to C-5 since methyl group is known to shield a *para*-carbon but has only negligible effect on *ortho*- and *meta*-carbons. The signals in the nitro compounds **1a** to **5a**, **7a** and **8a** were assigned using known substituent effects of nitro group and the other substituents.

The ^{17}O signal of nitro group for the compounds **1**—**9**, **1a**—**5a**, **7a**, and **8a** appear in the range of 560 ppm to 585 ppm. The methoxyl oxygen signals of **1**—**9** appear in the range of 25 to 90 ppm. ^{15}N signal of the nitro group appears in the range of −10 to −19 ppm.

The various chemical shifts for 4-nitroanisoles **1**—**9** are given in Table 1. The chemical shifts of nitro compounds **1a**—**5a**, **7a**, and **8a** are given in Table 2.

^{13}C Chemical Shifts. In the previous study on 4-nitroanisoles[5)] the sum of the chemical shifts of *ortho*- and *para*-carbons has been used to study the variation in the resonance interaction of the methoxyl group. However, carbons *ortho*- to the methoxyl group

Table 3. Shielding Effects of Methoxyl Group on Various Nuclei in 4-Nitroanisoles **1**—**9**

Compound	Shielding effects on		
	para-Carbon	Nitro oxygen	Nitrogen
1	6.7	9.4	1.0
2	7.3	9.4	0.9
3	7.6	10.1	0.5
4	7.2	10.4	0.5
5	6.7	11.0	0.7
6[a)]	4.8	1.7	1.7
7	5.5	4.1	0.6
8	4.8	4.1	0.8
9[a)]	4.2	4.4	1.1

a) The chemical shifts for the corresponding nitro compounds have been calculated using additivity principle.

are subjected to steric effects, and are not good probes for studying the variations of its resonance effect by the *ortho*-substitution. Moreover, it has been shown that in saturated six-membered ring compounds a nearby substituent decreases the α-effect of another substituent.[37)] This is due to a steric effect. Such a steric interaction may occur in aromatic systems also. Indeed, in di-*ortho*-substituted systems the chemical shifts of the substituent bearing carbons are generally lower than those calculated using additivity principle. Furthermore, the *ortho*-carbons are also subjected to inductive effect of the methoxyl group which may also vary due to the introduction of *ortho*-substituents. However, the *para*-carbon in an anisole derivative is free from inductive and steric effects and this alone could be a satisfactory probe for srudying the variation in the resonance effect of the methoxyl group due to *ortho*-substitution.

The effect of the methoxyl group on the chemical shifts of the nitro-bearing carbons in **1**—**9** are obtained by comparing the shift values in the nitroanisoles **1**—**9** with those in the corresponding nitro compounds **1a**—**9a**. However, since the data could not be obtained for **6a** and **9a**, the relevant chemical shifts for these have been calculated using additivity principle. The effects of the methyl group and iodine were obtained by comparing the chemical shifts of *meta*-substituted compounds with that in nitrobenzene. The values obtained for the shielding effects of the methoxyl group in **1**—**9** are furnished in Table 3. In literature[2,36)] ^{13}C chemical shifts have been reported for mono- and di-*ortho*-substituted anisoles **1b**—**9b** (Chart 1). In such cases also the effects of the methoxyl group on the *para*-carbon have been determined in a similar manner by comparing with mono- and disubstituted derivatives **1c**—**9c** and these values are furnished in Table 4 (Chart 2).

Table 4. ^{13}C Chemical Shifts of C-4 in **III** and the Respective Carbon in **IV** and the Corresponding Differences

R^1	R^2	^{13}C Chemical shifts of		$\Delta\delta$ (ppm)
		C(4) in **III**,[a)] δ (ppm)	Respective carbon in **IV**,[b)] δ (ppm)	
H	H	120.7	128.5	7.8
Me	H	120.0	128.4	8.4
Et	H	120.1	128.6	8.5
i-Pr	H	120.3	128.6	8.3
t-Bu	H	120.3	128.3	8.0
Me	Me	123.4	128.3	4.9
Et	Et	123.5	128.7[c)]	5.2
i-Pr	*i*-Pr	123.9	128.7[c)]	4.8
t-Bu	*t*-Bu	122.9	127.6	4.7

a) Chemical shift values are taken from Ref. 2. b) Chemical shift values are taken from Ref. 36. c) The chemical shifts have been calculated using additivity principle.

Table 5. Calculated and Observed Chemical shifts for C-4 in 2,6-Disubstituted-4-nitroanisoles According to Ref. 5

Compound	Chemical shift of C-4	
	Calculated, δ (ppm)	Observed, δ (ppm)
6	140.6	143.2
7	143.4	143.3
8	144.2	144.0
9	146.0	144.5

It is seen that when there is one *ortho*-substituent, the shielding influence of the methoxyl group on the *para*-carbon is slightly higher than that in the corresponding compound without the *ortho*-substituent, an exception being **5** in which the shielding influence is the same as that in **1**. However, in all the di-*ortho*-substituted compounds the shielding effects of the methoxyl group on C-4 are lower than those on the corresponding compounds without *ortho*-substituents.

Thus, it seems that the presence of one *ortho*-substituent enhances the resonance interaction of the methoxyl group slightly but the presence of two *ortho*-substituents inhibits the resonance interaction. However, it is seen that even in di-*ortho*-substituted compounds the methoxyl group causes significant shielding on C-4. This shows that the resonance is not completely inhibited in the di-*ortho*-substituted compounds. Moreover, the shielding on C-4 in all the di-*ortho*-substituted compounds is in the range of 4.5 to 5.5 ppm. This shows that the extent of inhibition does not depend on the nature of *ortho*-substituent.

In the previous study on 4-nitroanisoles[5)] the chemical shift of C-4 (nitro-bearing carbon) has been calculated employing additivity principle using the substituent parameters for OMe, NO_2 and the *ortho*-substituents and these calculated values have been compared with the observed values. These values are given in Table 5. It is seen from Table 5 that only when the *ortho*-substituent is Me, the observed chemical shift of C-4 is considerably higher than that calculated, showing that presence of two methyl groups in the *ortho*-position inhibits the resonance. However, when the *ortho*-substituent is Cl or Br there is very little difference between the calculated and observed values and when *ortho*-substituent is I the observed chemical shift is lower than that calculated. This is rather misleading. This suggests that employing additivity principle to predict chemical shift in multisubstituted benzenoid compounds is invalid especially when two or more substituents are on adjacent carbons. In a previous study[11] it has been shown that a substituent X influences the SCS of a *para*-substituent Y on the carbon bearing X. In the present study the *para*-substituents are kept constant and the influence of the *ortho*-substituents on the effects of Y (OMe group) on the carbon bearing X (NO_2 group) has been studied.

^{17}O Chemical Shifts. Since the ^{17}O signal of the nitro group is shifted upfield by the introduction of a methoxyl group *para*- to it, in nitroanisole **1**—**9** the oxygens on the nitro group could also be used as a satisfactory probe for studying the variation in the resonance effect of the methoxyl group due to *ortho*-substitution.

In this case also the effect of the methoxyl group on the chemical shifts of nitro oxygens are obtained by comparing the chemical shift values in the nitroanisoles **1**—**9** with those in the corresponding nitro compounds **1a**—**9a**. For compounds **6a** and **9a** the ^{17}O chemical-shifts were calculated using additivity principle. The values obtained for the shielding effects of the methoxyl group in **1**—**9** are given in Table 3.

Examination of Table 3 shows that the shielding on the nitro oxygens also is slightly higher in derivatives with only one *ortho*-substituent than that in 4-nitroanisole an exception being **2**. However, in all the di-*ortho*-substituted compounds the shielding effects of the methoxyl group on nitro oxygens are lower than that in 4-nitroanisole.

Comparioson of ^{17}O NMR chemical shift of methoxyl oxygen in 4-nitroanisole and anisole reveals that the nitro group deshileds the methoxyl oxygen by 21.1 ppm. *ortho*-Substituents also have marked influence on the methoxyl oxygen chemical shift. An *o*-methyl substituent causes a slight shielding on the methoxyl oxygen whereas, an *o*-Cl, *o*-Br or *o*-I substituent deshields it. This deshielding increases in the order Cl<Br<I. This shows that in addition to electronic effects, steric and magnetic anisotropic factors may play a role in determining the methoxyl oxygen chemical shift. Hence, it is not possible to separate the influence of steric enhancement of resonance on the methoxyl oxygen chemical shift. Therefore, reliable evidence could not be obtained for steric enhancement of resonance using methoxyl oxygen chemical shift. Steric enhancement of resonance by an *ortho*-substituent should cause a deshielding on the methoxyl oxygen and this effect should be only small and almost constant for all the *ortho*-substituents. Hence, the effects of *ortho*-substituents in **2**—**5** may be taken as those due to steric and magnetic anisotropic effects especially in the case of Cl, Br and I.

If there is no inhibition of resonance in di-*ortho*-substituted compounds the methoxyl oxygen chemical shifts in these compounds should be almost equal to those calculated by adding twice the effect of the *ortho*-substituent in the corresponding mono-*ortho*-substituted compounds to the methoxyl oxygen chemical shifts of the corresponding compounds without *ortho*-substituents. The values calculated thus are compared with the observed values in Table 6. Examination of Table 6 shows that the observed values are considerably lower than the calculated values. This can be attributed to the decrease in the positive charge on the methoxyl oxygen due to inhibition of resonance by the *ortho*-substituents.

^{15}N Chemical Shifts. Nitrobenzene resonates at a higher field than nitromethane. This can be attributed to the fact that nitro group withdraws electrons from the benzene ring and as a consequence the electron density at the nitro group is greater in nitrobenzene than in nitromethane. The ^{15}N signal of the nitro group is shifted upfield only slightly by a *para*-methoxyl substituent. This suggests that the ^{15}N chemical shift of the nitro group is much less sensitive to the variation in the electron density of the nitro group. Considering this, it may be concluded that the electron density in the nitro group of nitrobenzene should be considerably higher than that in nitromethane.

However, *m*-Cl, *m*-Br, and *m*-I substituents cause a great upfield shift on the ^{15}N signal of the nitro group. These substituents cannot place a high negative charge on the nitro group. Perhaps these heavy atoms influence the ^{15}N chemical shift of the nitro group by a magnetic anisotropic effect operating through space. It is interesting to note from the data for *meta*-halo and 3,5-dihalo compounds that these effects are approximately additive.

AM1 Calculations. The barriers to rotation of the methoxyl group about the C–O bond have been determined based on AM1 calculations in 15° steps scaled to $E=0$ kJ mol^{-1} for the minimum energy conformation. Figure 1 shows the variation of the energy with

Table 6. Calculated and Observed ^{17}O Chemical Shifts of Methoxy Oxygen in Di-*ortho*-substituted Anisoles

Compound	Methoxy oxygen chemical shift	
	Calculated, δ (ppm)	Observed, δ (ppm)
6	63.7	27.5
6b	44.4	16.5[a)]
7	70.5	39.1
8	82.1	47.9
9	108.7	72.9

a) The chemical shifts value is taken from Ref. 2.

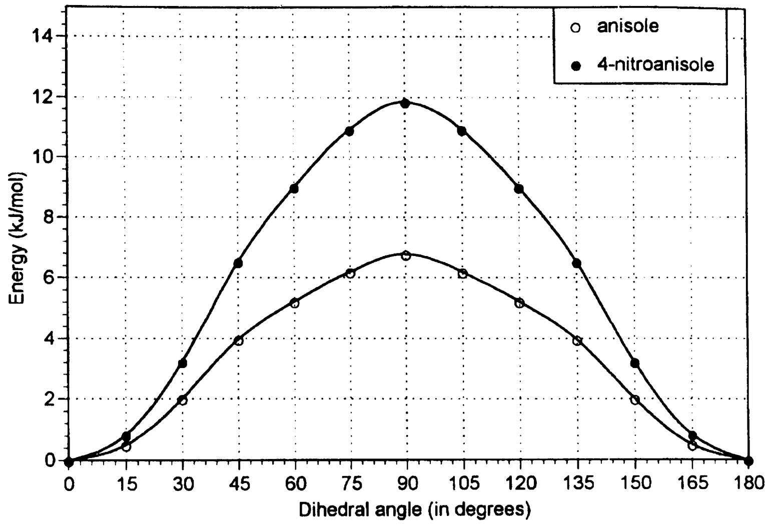


Fig. 1. Rotational barriers ($kJ\,mol^{-1}$) of anisole and 4-nitroanisole **1**.

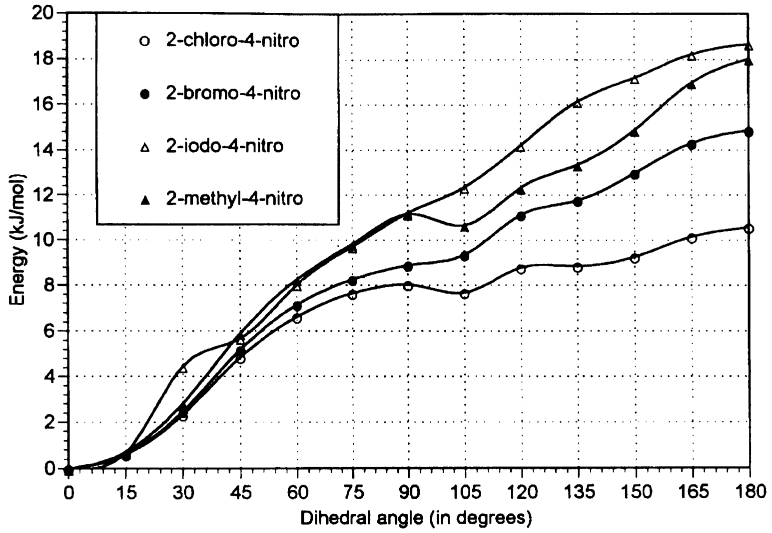


Fig. 2. Rotational barriers ($kJ\,mol^{-1}$) of 2-substituted anisoles **2**—**5**.

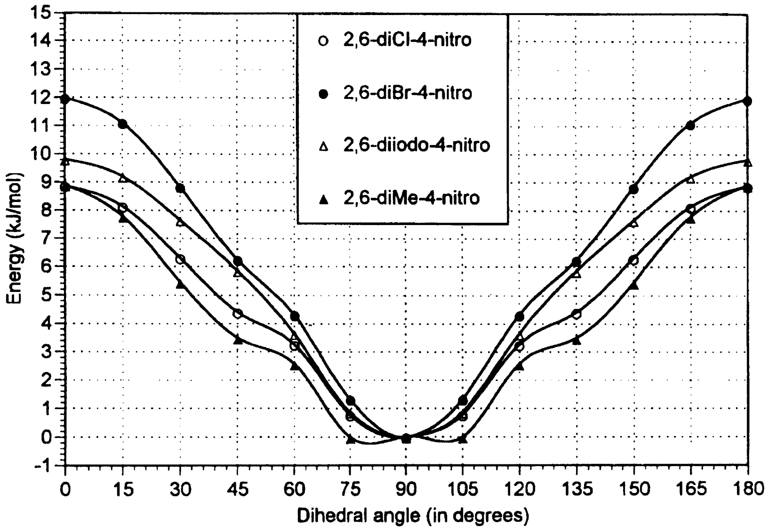
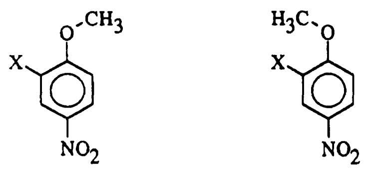


Fig. 3. Rotational barriers ($kJ\,mol^{-1}$) of 2,6-disubsutituted anisole **6**—**9**.



A **B**

Fig. 4.

the angle of rotation for anisole and 4-nitroanisole. The corresponding energy diagrams for 2-substituted and 2,6-disubstituted-4-nitroanisoles are shown in Figs. 2 and 3, respectively. In 2-substituted anisoles the angle has beeen taken as 0° for conformation **A** (Fig. 4) which has the methoxyl group coplanar with the benzene ring and the methyl group anti to the 2-substituent.

It is seen from Fig. 1 that in anisole and 4-nitroanisole the methoxyl group prefers to be coplanar with the phenyl group. For both these compounds the conformation in which the methoxyl group lies perpendicular to the phenyl ring has the maximum energy. However, in the case of 2-substituted-4-nitroanisoles the coplanar conformation **B** (Fig. 4) in which the *O*-methyl group is *syn* to the 2-substituent, has the highest energy. In the case if 2-halo-4-nitroanisoles the energy difference between conformations **A** and **B** increases in the order Cl<Br<I. Thus, the interaction between the halogen atom and the *O*-methyl group increases with increase in the size of the halogen atom and not with its electronegativity. Thus, it seems that conformation **B** is destabilized by steric interactions rather than by electrostatic interactions. The interaction due to a methyl group resembles that due to iodine.

From Fig. 3 it is seen that in all 2,6-disubstituted anisoles the perpendicular conformation is favored over the parallel conformation and the energy difference between perpendicular and parallel conformations increases in the order Cl≈Me&lt:I<Br. Except for chloro-substituent this trend is just oppsite to that found in 2-substituted-4-nitroanisoles. This can be explained as follows:

In conformation **A** of 2-substituted anisoles there is no interaction between the *O*-methyl group and the 2-substituent. Therefore, the energy difference between conformations **A** and **B** should reflect the interaction between the 2-substituent and the *O*-methyl group. However, in the case of 2,6-disubstituted-4-nitroanisoles the perpendicular conformation has the minimum energy. There will be some interaction between the *ortho*-substituents and the *O*-methyl group in the perpendicular conformation and this interaction will vary with the nature of the substituent. Thus in 2,6-disubstituted-4-nitroanisoles the energy difference between the perpendicular and parallel conformations is a measure of the difference in the interaction in the perpendicular and planar conformations.

Since the methoxyl group causes a considerable shielding on C-4 as well as on nitro oxygens in 2,6-disubstituted-4-nitroanisoles, it is obvious that even when the methoxyl group lies perpendicular to the benzene ring there is significant overlap of π-orbitals of the benzene ring with the non-bonded orbitals on oxygen.

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