The Nitration of Monoalkyl Benzene and the Separation of its Isomers by Gas Chromatography

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RINGKASAN

Di dalam tindakbalas penitration, ion nitronium, NO_2^+, dipercayai sebagai elektrofil penyerang. Bila tindakbalas ini dilakukan terhadap sebatian bergantian benzena monoalkil, kumpulan gantian ini memainkan peranan yang penting di dalam menentukan hasil yang akan didapati. Ini juga bergantung kepada cara bagaimana penitratan dilakukan. Lapuran ini ialah mengenai cara bagaimana peratusan isomer-isomer dapat ditentukan dengan menggunakan kromatografi gas.

SUMMARY

The nitronium ion, NO_2^+, is believed to be the attacking electrophile in the nitration reaction. When this reaction is carried out on monoalkyl substituted benzene, the substituents play a major role in determining the products obtained. The reaction also depends on the different methods of nitration employed. This report describes the method of determining the percentage of each isomer produced by gas chromatography.

INTRODUCTION

The mechanism of aromatic nitration has been described in great detail (Ingold, 1953; De La Mare *et al.*) (1959). Nitration is the most general process for the preparation of aromatic nitro compounds and it has played a great part in the development of theoretical organic chemistry. A wide variety of conditions are available for its preparation, but the mechanism is essentially the same. The attacking entity is believed to be the nitronium ion, NO_2^+, and this is the active electrophilic species (Gillespie *et al*, 1950). The evidence for the existence of the nitronium ion is mentioned by Westheimer and Kharasch (1946).

The rate of reaction is strongly dependent upon the nature of the substituent(s) in the aromatic nucleus. Further, the relative ease of substitution at different positions in an aromatic compound is also determined by the nature of the substitutions. Both these effects are of great importance in the synthetic applications of electrophilic aromatic substitutions.

This report describes the effect of monoalkyl substituents on aromatic rings. In the reaction with these compounds the intermediates for ortho —, meta — and para — substitution are 1,2,3 respectively, thus:
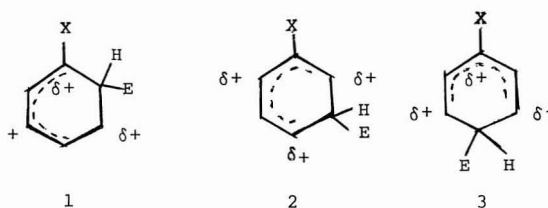

Since R is an electron releasing group, ions 1 and 3 will be stabilised when reacted with electrophile, E, such as NO_2^+. But when reaction occurs at meta positions (2), the substituent is further removed from a polarised carbon and its stabilizing influence is smaller. Hence, the ortho and para positions are more strongly activated than the meta position and the substituent is said to be ortho — para directing.

The similarity in the mode of operation of the polar effect on the artho and para positions leads to the expectation that the ratio of reactivities of these positions should be 2:1, there being two ortho positions and one para position. In practice, the ratio is normally different from this for two

main reasons. First, more subtle electronic effects than those apparent from the above discussion seem to be involved. Secondly steric hindrance between substituent and reagent can lead to ortho para ratios which are considerably less than 2:1.

It has been suggested that (Isaac, 1969) a mixture of ortho- (4), meta- (5) and para- nitrotoluene (6) could be separated satisfactorily in that order of elution using a six foot silicone column at 170°C. However using this column and several other silicone columns with variation of temperature and flow rate failed to give the expected chromatogram:
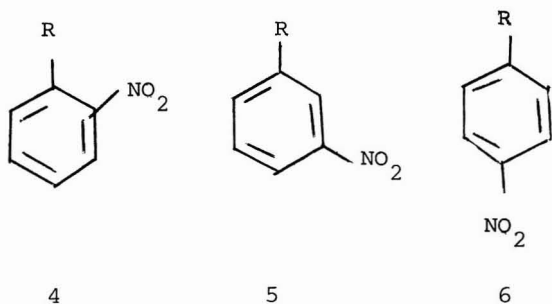
4, 5, 6 ; a, R = CH_3
b R = CH_2CH_3
c, R = $CH(CH_3)_2$
d, R = $C(CH_3)_3$

This difficulty was overcome by using a 2 metre carbowax 20M column at 170°C and a flow rate of 25 ml per minute. The composition of the chromatogram was worked out from the peak areas (using an integrator).

EXPERIMENTAL

Nitration by "mixed acid" method

Concentrated sulphuric acid (12 ml) was added slowly with ice-water cooling and stirring to nitric acid (68%, D = 1.41 ie. 0.15 mol). Alkylbenzene (0.1 mol) was placed in a three-necked flask fitted with stirrer, dropping funnel and thermometer. Then with vigorous stirring and cooling the nitrating acid previously cooled at 0° − 10°C was added slowly from the dropping funnel. The temperature of the mixture was kept at 5–10°C and after the addition was completed the mixture was stirred for a further 3 hours at room temperature. The reaction mixture was then carefully poured into about 300 ml of ice water and was vigorously stirred. The nitro compounds were extracted with ether in a separating funnel. The organic phases were washed with water, sodium bicarbonate and again with water. The ethereal extract was then dried over calcium chloride overnight. After filtration the ether was evaporated off to give a nitro compound. The product was then analysed using gas chromatography.

Nitration by cupric nitrate and acetic anhydride method

Cupric nitrate, $Cu(NO_3)_2.3H_2O$ (12.4 g, 0.05 mol) was added to acetic anhydride (80 ml) with magnetic stirring. A solution of the compound to be nitrated (alkylbenzene, 0.1 mol) in acetic anhydride (40 ml) was added dropwise with continuous stirring and cooling for 25 mins. at 15–20°C. After the addition was completed, the reaction mixture was stirred for another 3 hours at room temperature. Then the copper salts were filtered off and washed with a little ether. The filtrate was then poured into ice-water which was stirred continously until the acetic anhydride hydrolysed. The nitro compounds were extracted with ether and were washed with water twice and dried over magnesium sulphate overnight. The solution was then filtered and ether was evaporated off. The product was analysed by using gas chromatography. (The nitration was repeated to check the consistency of the results.)

Calibration curves for the nitrotoluene

Naphthalene was used as the internal standard and dissolved in toluene. The standard solution of naphthalene in toluene was made up to give a concentration of 130.102 g per litre. Five samples of the standard solution each of 5 ml were taken. To these were added samples of pure orthonitrotoluene, (2.445 g, 1.2475 g, 0.9355 g, 0.6235 g and 0.3122 g) and each were made up to 25 ml with toluene. These gave the weight/volume percentage of pure sample of 9.78, 4.99, 3.74, 2.49 and 1.25 respectively. Each solution was then chromatographed using the above conditions. The peak area of the orthonitrotoluene and the peak area of the naphthalene were measured using the integrator and the ratio was calculated. The ratio was then plotted against the weight/volume percentage of the pure component in each solution giving a calibration graph. The procedure was repeated for meta- and paranitrotoluene (Table 1).

Synthetic mixtures

0.6699 g ortho-nitrotoluene, 0.3849 g meta-nitro-toluene and 0.3277 g para-nitrotoluene were taken. 5 ml of standard naphthalene solution was added and the solution was made up to 25 ml

TABLE 1

Calibration Curves

Isomer	Wt. of Sample g	Weight/Volume %	Av. Peak Area Ratio
Ortho-nitro-toluene (4a)	2.4450	9.78	2.390
	1.2475	4.99	1.91
	0.9355	3.74	0.938
	0.6235	2.49	0.637
	0.3120	1.25	0.317
Meta-nitro-toluene (5a)	1.3106	5.24	1.242
	1.0151	4.06	0.947
	0.6755	2.70	0.632
	0.3375	1.35	0.326
Para-nitro-toluene (6a)	2.4192	9.68	2.203
	0.9095	4.84	1.108
	0.9071	3.63	0.815
	0.6045	2.42	0.524
	0.3025	1.21	0.226

with the solvent, toluene. The solution was then chromatographed three times and the average peak areas of ortho-, meta and para-nitrotoluene and naphthalene were used to calculate the ratios. Then using the calibration graphs, the weight/volume percentage of each was obtained.

From this the percentage composition was calculated and was compared with actual percentage used (Table 2). The above procedure was repeated using 1.7453 g of ortho-nitrotoluene 0.8177 g of meta-nitrotoluene and 1.4807 g of para-nitrotoluene.

Analysis of alkylnitrobenzene 4, 5 and 6

Two dilutions were prepared for each nitration. 5 ml of the standard naphthalene solution was

TABLE 2

Calibration Curves of Synthetic Mixtures

	0-nitrotoluene		m-nitrotoluene		p-nitrotoluene	
	(I)	(II)	(I)	(II)	(I)	(II)
Wt. of Sample (g)	0.6699	0.7453	0.3849	0.8177	0.3277	1.4807
Actual Wt./Vol.: %	2.680	6.981	1.539	3.271	1.311	5.923
Actual % Composition	48.46	43.16	27.83	20.22	23.71	36.67
Av. Peak Area Ratio	0.652	1.669	0.376	0.725	0.314	1.325
Wt./Vol. % from graph	2.700	6.950	1.600	3.280	1.400	5.950
Composition from graph	47.37	42.96	28.07	20.30	24.56	36.74

added to each dilution and the solution was made up to 25 ml with toluene. Each solution was then chromatographed at least three times to give average peak areas. The peak area ratio between

TABLE 3
Analyses of Alkylnitrobenzenes

	Nitration	Dilution	Isomer	Av. peak area of Isomer/Std	Wt./Vol. %	% Isomer[a]	% Isomer by 2nd method[b]
Nitrotoluene (4a, 5a, 6a)	1	1	o	1.371	5.70	49.89	59.00
			m	0.091	0.38	3.28	2.82
			p	1.204	5.35	46.83	38.18
	1	2	o	2.195	9.16	49.09	59.96
			m	0.166	0.67	3.75	2.95
			p	1.972	8.82	47.16	37.09
	2	1	o	1.361	5.66	49.53	60.69
			m	0.998	0.4	3.51	2.51
			p	1.277	5.37	46.96	36.79
	2	2	o	2.357	9.81	49.96	60.69
			m	0.147	0.62	9.21	2.38
			p	2.074	9.21	46.90	37.14
Ethylnitrobenzen (4b, 5b, 6b)	1	1	o	2.082	8.70	42.91	42.53
			m	0.208	0.88	11.32	5.30
			p	2.409	10.70	52.77	52.17
	1	2	o	2.035	8.51	43.30	42.2
			m	0.221	0.930	4.74	5.05
			p	2.290	10.20	51.96	52.71
	2	1	o	2.853	11.90	43.27	42.60
			m	0.306	1.30	4.73	5.24
			p	3.194	14.3	52.00	52.16
	2	2	o	2.816	11.78	42.85	42.54
			m	0.280	1.18	4.31	4.89
			p	3.254	14.53	52.84	52.57
Nitrocumene (4c, 5c, 6c)	1	1	o	0.763	3.17	22.70	22.99
			m	0.167	0.69	4.92	6.01
			p	2.243	10.10	72.38	71.00
	1	2	o	1.075	4.44	22.39	23.02
			m	0.234	0.99	4.98	6.04
			p	3.225	14.29	72.63	70.94
	2	1	o	0.881	3.65	22.12	23.32
			m	0.180	0.78	4.76	5.86
			p	2.700	12.05	73.12	70.82
	2	2	o	0.562	2.32	22.05	23.17
			m	0.120	0.51	4.81	6.07
			p	1.725	7.69	73.14	70.76
ter-butil nitrobenzen (4d, 5d, 6d)	1	1	o	0.198	0.80	3.95	9.72
			m	0.219	0.88	4.32	10.39
			p	4.700	18.60	91.73	79.89
	1	2	o	0.172	0.66	3.92	9.80
			m	0.186	0.78	4.63	10.53
			p	3.452	15.40	91.45	79.67
	2	1	o	0.206	0.79	4.18	9.13
			m	0.191	6.8	4.27	9.14
			p	3.825	17.04	91.55	81.73
	2	2	o	0.113	0.44	4.21	9.55
			m	0.113	0.46	4.35	9.98
			p	2.162	9.63	91.44	80.47

(a) Preparation by "mixed acid" method.
(b) Preparation by using Cupric Nitrate and acetic anhydride method.

the sample and naphthalene was calculated and the weight/volume percentage was obtained from the calibration graph. The percentage composition of ortho- meta- and para- products in the mixture was then calculated. (Table 3)

RESULTS AND DISCUSSION

The overall average percentage composition of isomers from the two different methods of preparations can be tabulated as in Table 4.

TABLE 4

Overall average percentage composition of isomers by two methods

Alkylnitro benzene	Mixed Acid Method			Cupric Nitrate & Acetic Anhydride		
	o	m	p	o	m	p
Nitrotoluene	49.67	3.42	46.96	60.08	2.66	37.3
Ethylnitrobenzene	43.08	6.27	52.39	42.47	5.12	52.27
Nitrocumene	22.31	4.86	72.82	23.12	5.99	70.88
Butylnitrobenzene	4.06	4.39	91.45	9.55	10.01	80.44

Some of the main features of the results are as follows: Each alkyl group activates all nuclear positions, the ortho· and para-positions being activated more than the meta-position. As the alkyl group changes from methyl to tert-butyl, the percentage composition of the para-isomer increases and the reverse is true for the ortho-isomer. This might due to the steric hindrance to ortho-substitution. The meta: para ratio does not change very much. The absolute values of the composition of the reaction products for a given compound depend on the reagents. Hence there is variation in the selectivity of the reagents used.

The influence of alkyl groups has been attributed to the electron releasing effect operating primarily at the ortho- and para-positions, and somewhat less strongly at the meta- position by relay. Alternatively the effect is such that it stabilises the transition states for ortho- and para-substitution more than it does for meta-substitution. The overall reactivity of the alkyl benzene decreases in the order $CH_3 \rightarrow CH_3 CH_2 \rightarrow (CH_3)_2 CH \rightarrow (CH_3)_3 C$ – (Norman et al., 1965), which might be seen as a hyperconjugation. However the sequence is the result of the decrease in partial rate factor for the ortho-isomer along the series. That decrease is convincingly attributed to a primary steric effect, for the overall polar effects of the substituents do not show much change (Cohn et al., 1952).

When para-positions are considered it is seen that they follow the sequence of inductive effects, and not of hyperconjugation.

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