A Convenient *ar*-S_E Laboratory Experiment Avoiding the Use of Sulfuric Acid: the Nitration of Diphenylmethane in CH_2Cl_2

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Abstract: The nitration of diphenylmethane to three main isomeric dinitro derivatives, performed with nitric acid in dichloromethane, is proposed as an organic laboratory experiment showing a number of advantages over typical aromatic nitrations in sulfuric acid.

Introduction

It is a widespread and justified practice in educational organic chemistry laboratory courses, as reflected in the contents of textbooks [1], to use nitration experiments as examples of aromatic electrophilic substitutions.

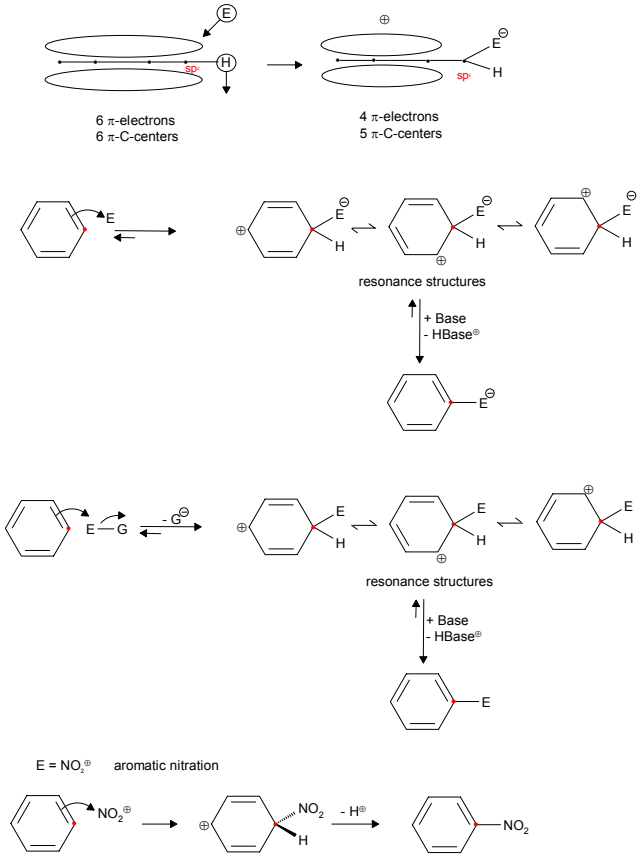
In the classical compact mechanism [6] for electrophilic aromatic substitution, the electrophile, E, approaches one of the aromatic carbons, either isolated or somehow associated (GE), from either side of the flat ring, eventually engaging two electrons of the π system and rehybridizing the attacked center from sp^2 to sp^3 (Scheme 1). Subsequently, a proton is lost from this position to yield the final substitution product.

The mechanism shown in Scheme 1 was the first one proposed. Not only are there variations, but other mechanisms, both ionic and radical, have been found and discussed in books devoted to electrophilic aromatic substitution.

In principle, the two mechanistic steps are reversible with the first step being rate determining, but, de facto, the reaction is irreversible in the case of nitration, most likely because of the fast equilibration to more stable Wheland-type isomers [12]. In the case of benzene as the substrate, there are five possible tautomers for its mononitration product (Scheme 2).

It would be desirable to limit the hazards presented by some chemicals and experimental procedures, as well as the toxicity of reagents and/or products and their disposal problems [13], in the presently common nitration experiments.

In fact, a cheap and frequent experiment involves the nitration of benzene, a very poisonous and flammable compound of relatively high volatility. Its nitration product, nitrobenzene, may be accompanied by variable amounts of 1,3-dinitrobenzene; the former is a very toxic substance, the latter is explosive. The nitration process has to be carefully performed with rather accurate temperature control. Work up of the reaction mixture involves an exothermic dilution with water and disposal of this spent aqueous and strongly acidic phase that is generated. Especially in experiments with limited amounts of substrate, a solvent (ethyl ether or hexane) is required for better phase separation. These flammable solvents must be evaporated in order to obtain the crude product, a high boiling liquid, which can be purified at reasonable temperatures only with a mechanical vacuum pump. This experiment is often followed by a reduction of the nitro group to yield aniline, another highly toxic compound. All of these products will eventually have to be disposed of safely [14].



Scheme 1. The compact mechanism for electrophilic aromatic substitution (benzene as the aromatic substrate).

Experimental

Safety Precautions. Some common chemicals, like HNO_3, which are used in our experiments, should be used in ventilated hoods. They present a number of hazards and are to be handled with well-known precautions. The toxicological properties of the widely used solvent, CH_2Cl_2, are found in a recent technical publication [15], which also contains other interesting information.

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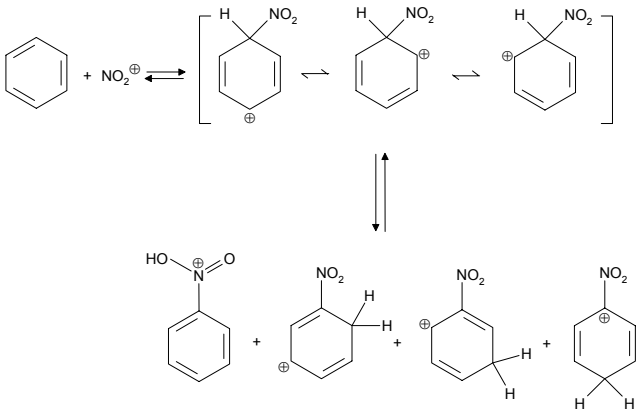
Table 1. Typical Quantitative Data (GC) for the Nitration of Diphenylmethane

		%					
	Ph_2CO	Dinitration products					
		o,*o*′-	*o*,*m*-′	*o*,*p*′-	*m*,*m*′-	*m*,*p*′-	*p*,*p*′-
At the end of the addition[a]	-	17.2	2.3	23.7	-	0.1	9.4
Intermediate (0.5 h) sampling	6.2	18.8	5.0	33.0	traces	6.0	30.6
Final (1 h) reaction mixture	4.7	19.2	4.2	34.0	traces	4.8	32.8
Final (1 h) reaction mixture[b]	[c]	13.5	4.4	33.3	traces	5.1	43.7

[a] There are some 47% mononitrodiphenylmethanes in the mixture.
[b] NMR data.
[c] Not detectable.



Scheme 2.

Dichlorometane from these experiments can be fully recovered by conventional distillation (bp 39.8 ºC at 760 torr; the azeotrope with water (98.5% dichloromethane) boils at 38.1 ºC at 760 torr [16]. It may be dried over Na_2SO_4, $CaCl_2$, or $MgSO_4$. It is interesting to compare also the low enthalpy of vaporization of dichloromethane, ΔH_v = 6.83 kcal mol^{-1} at 25 ºC, with that of water, ΔH_v = 10.51 kcal mol^{-1} at 25 ºC [17].

Not much published information is available about the stability of mixtures of technical absolute HNO_3 (d = 1.51 g mL^{-1}) in dichloromethane, although it is highly advisable [18] to cautiously pour the acid into the solvent with stirring [19]. The mixing of the two chemicals is endothermic. We have routinely prepared such solutions (up to ca. 15 mol L^{-1}) in our laboratory and found them to be stable for days at room temperature, but it may be advisable to store them at lower temperatures (≥ 2 ºC) in the dark.

Technical HNO_3 is usually reddish brown, owing to slow decomposition of HNO_3. It may be easily purified by passing it through a stream of dry air or nitrogen at room temperature to obtain a colorless liquid. This acid was found to be perfectly suitable for these experiments. It may be titrated before use.

Diphenylmethane presents no particular toxicological problems [20]. The toxicological properties of the products generated in these experiments are not known.

Procedure. We describe laboratory experiments using diphenylmethane that are performed under conditions that convert it completely to a mixture of dinitro derivatives.

Commercial fuming HNO_3 (212 mmol, 9 mL) was added over a period of ca. 35 min at an addition rate of one drop every 5 s, with vigorous stirring to a solution of diphenylmethane (5.0 g, 29.8 mmol) in dichloromethane (40 mL), which was cooled externally by means of a water bath.

After some HNO_3 was added, the solution became dark reddish brown, and towards the end of the addition the color turned to light red orange. At the end of the addition a sample was withdrawn, quenched with some water, dried over anhydrous Na_2SO_4, and analyzed by GC–MS. Analysis showed that the starting material was only partially dinitrated; complete dinitration was reached 30 min after the end of addition. The reaction was quenched by pouring the reaction mixture into cold water and adding dichloromethane (15 mL) to dilute the system. After separating the organic phase, the aqueous phase was extracted twice with 30 mL portions of CH_2Cl_2, which were combined with the original organic solution. The organic phase was washed with water (40 mL), dried over anhydrous Na_2SO_4 and the solvent was removed by distillation, obtaining 7.48 g of crude material (97.3% of the theoretical amount for complete dinitration). The conversion of the starting material was complete.

This sulfuric-acid-free method of aromatic nitration, under very mild and practically control-free conditions, has been recently introduced [21, 22]. Nitrations run smoothly and relatively slowly in this solvent although they are exothermic, little or no temperature control is needed, because they proceed to completion in 30 min to 3 hr.

GC–MS analysis (Table 1) revealed the presence of benzophenone (4.7%), *o*,*o*′- (19.2%), *o*,*m*′- (4.2%), *o*,*p*-′ (34.0%), *m*,*p*′- (4.8%) and *p*,*p*′- (32.8%) dinitro derivatives. A small quantity of the *m*,*m*′-isomer was also present (Figure 1, peak 6).

The solid was dissolved in a small amount (30 mL) of refluxing (bp 77 °C) ethyl acetate. Upon standing, the cooling solution released pale yellow crystals of *p*,*p*′-dinitrodiphenylmethane (mp 181.8 °C, lit. 183 °C [23, 24]), whose assay was established by GC analysis (Table 2). Concentration of the solution yielded more product of lesser purity. The ^{1}H-NMR spectrum of this isomer (Table 3) shows a singlet at 4.20 ppm (methylene hydrogens), a multiplet centered at 8.17 ppm (four aromatic hydrogens adjacent to the nitro groups), and a complex multiplet at 7.34 ppm (remaining aromatic hydrogens).

Full evaporation of the solvent on a water bath and redissolution of the residue into hot ethanol (bp 78 °C, 100 mL) followed by concentration (to 70 mL) and standing at room temperature yields *o*,*p*′-dinitrodiphenylmethane (mp 108.9 °C, lit. 118 °C [23]). GC analysis of that solid suggests that recrystallization may be useful to obtain a purer product (Table 2). The mother liquors from the isolation of the *o*,*p*′-isomer may be further concentrated and cooled to yield a mixture of mostly the *o*,*p*′- and *p*,*p*′-isomers. The new mother liquor was found to contain a substantial concentration of the bright yellow *o*,*o*′-isomer (ca. 70% of the total amount of dinitroderivatives) along with some benzophenone, a minor oxidation product of the original substrate. The presence of the *o*,*p*′- and *o*,*o*′-isomers can be established by inspection of the ^{1}H-NMR peaks for their aliphatic methylene groups, at 4.42 and 4.63 ppm, respectively.

Apparatus

A 100-mL three-neck round-bottomed flask is adequate to carry out the reaction. A thermometer should be inserted into one neck, in order to monitor the temperature during the addition. The central neck should carry a dropping funnel with pressure equalizer equipped with a granular Drierite valve for the addition of nitric acid. The remaining neck is used to withdraw samples. An Erlenmeyer flask equipped with a granular Drierite valve may also be used. An external water bath regulates any temperature hike of the reaction mixture

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Table 2. GC Quantitative Monitoring of Purification Attempts

	%						
	Ph_2CO	Dinitration products					
		o,*o*′	*o*,*m*′	*o*,*p*′	*m*,*m*′	*m*,*p*′	*p*,*p*′
Solid from 1st crystallization (EtOAc)	-	0.9	trace	3.5	-	4.8	90.7
Solid from 2nd crystallization (EtOH)	-	2.0	0.9	72.1	trace	4.0	20.6
Solid from 3rd crystallization (EtOH)	-	0.8	trace	58.6	-	8.1	32.1
Final mother liquor	18.7	55.6	12.0	8.5	trace	3.8	1.0

Table 3. ^{1}H- and ^{13}C-NMR Chemical Shifts for Diphenylmethane, the Three Mononitro Derivatives of Diphenylmethane, and the Main Isomers from Dinitration of Diphenylmethane ($CDCl_3$/TMS)

Compound	^{1}H NMR δ (ppm)	^{13}C NMR δ (ppm)
Diphenylmethane	3.92 (s, 2 H)	42.1
o-Nitrodiphenylmethane	4.25 (s, 2 H)	38.1
m-Nitrodiphenylmethane	4.06, (s, 2 H)	41.4
p-Nitrodiphenylmethane	4.06 (s, 2 H)	41.6
o,*o*′-Dinitrodiphenylmethane	4.63 (s, 2 H)	36.0
o,*m*′-Dinitrodiphenylmethane	4.42 (s, 2 H)	38.5
p,*p*′-Dinitrodiphenylmethane	4.20 (s, 2 H)	41.3

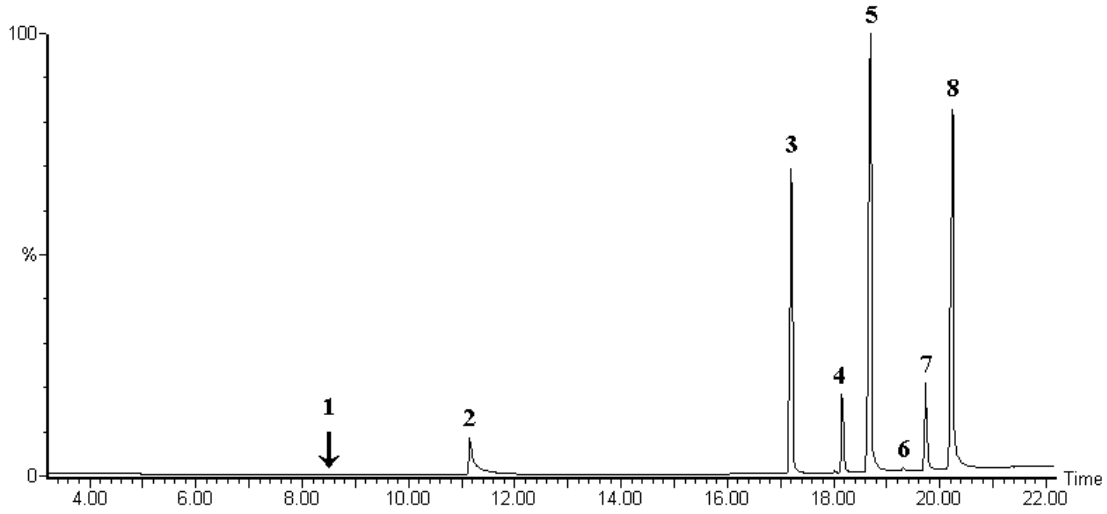

Figure 1. A total ion GC–MS profile of the mixture from the dinitration of diphenylmethane. **1**: diphenylmethane (RRT = 8.55 min); **2**: benzophenone (RRT = 11.15 min); **3**: *o*,*o*′-dinitrodiphenylmethane (RRT = 17.20 min); **4**: *o*,*m*′-dinitrodiphenylmethane (RRT = 18.15 min); **5**: *o*,*p*′-dinitrodiphenylmethane (RRT. = 18.70 min); **6**: *m*,*m*′-dinitrodiphenylmethane (RRT = 19.27 min); **7**: *m*,*p*′-dinitrodiphenylmethane (RRT = 19.73 min); **8**: *p*,*p*′-dinitrodiphenylmethane (RRT = 20.23 min). If a sample is withdrawn during the addition of nitric acid, quenched, and analyzed, it is possible to detect the three mononitro isomers *o*-nitrodiphenylmethane (RRT = 13.28 min), *m*-nitrodiphenylmethane (RRT. = 14.20 min), and *p*-nitrodiphenylmethane (RRT = 14.57 min).

(initially, the endothermic dissolution of nitric acid in dichloromethane counters the exothermicity of the reaction, but the latter effect eventually prevails). A magnetic stirrer should be used to ensure efficient agitation during the addition.

Additional Comments

The reaction may be accelerated by using more concentrated solutions, but adequate cooling upon mixing or slow addition near room temperature must be performed in order to avoid overheating. For example, complete dinitration may be achieved by the end of addition with the same quantities of diphenylmethane and nitric acid but with only 15 mL of dichloromethane provided that the mixture is cooled with a NaCl/ice bath (–10 °C).

The reaction is easily amenable to GC (GC–MS) monitoring by quenching tiny aliquots at set times.

Early monitoring, say minutes after mixing of the reagents, when the formation of dinitro derivatives is still minimal, allows a good estimate of the ortho-meta-para ratio.

Sequential observations of the quantitative composition of the reacting system will reveal a very surprising aspect of the process. Contrary to expectation, the ortho derivative is the more reactive, a fact countering (weak) steric and electronic effects.

GC (GC–MS) analysis of the reaction mixture at the onset of the process, when the production of the mononitro derivatives is largely prevalent, provides an opportunity to compare the observed regioselectivity with that of toluene in the classical experiment using sulfuric acid reported in standard textbooks [25]. The bulkier benzyl group hinders the ortho center (early transition state), but exhibits ortho-para orientation. The steric effect is strong causing the quantitative reversal of the ortho/para ratio found in toluene.

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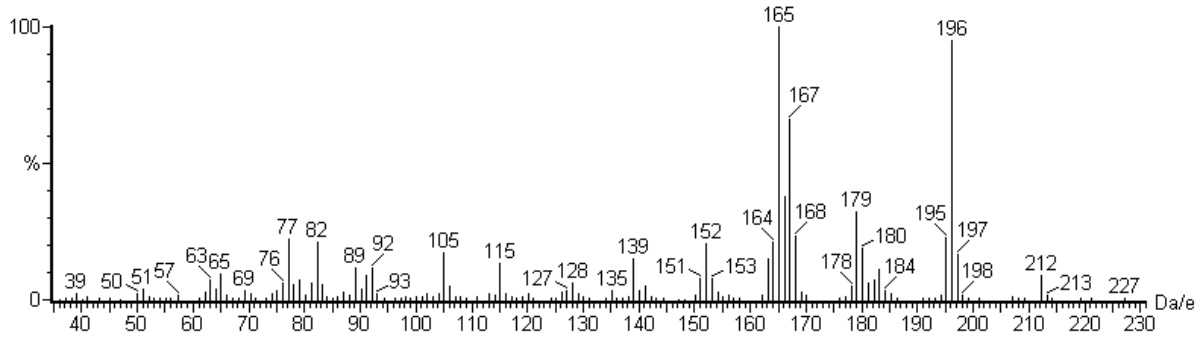

Figure 2. The positive EI mass spectrum of *o*-nitrodiphenylmethane.

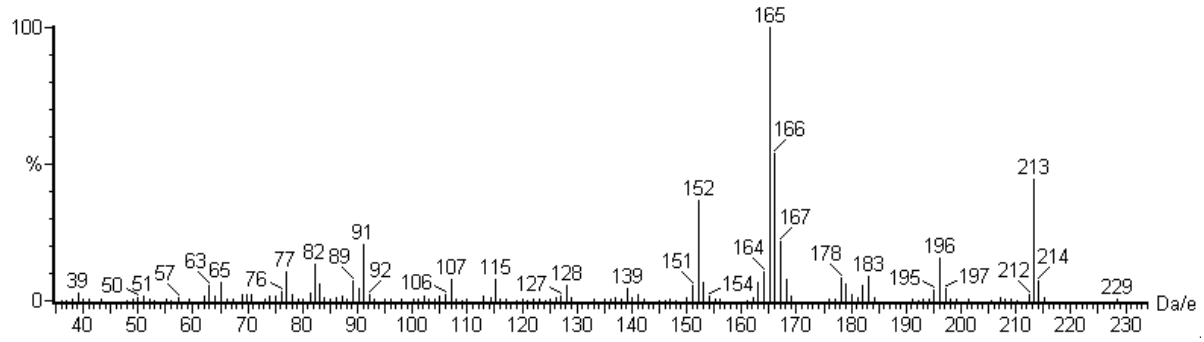

Figure 3. The positive EI mass spectrum of *m*-nitrodiphenylmethane.

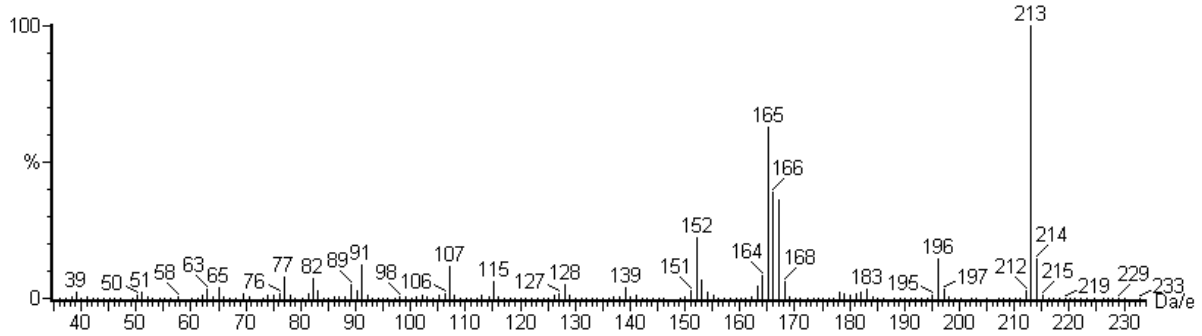

Figure 4. The positive EI mass spectrum of *p*-nitrodiphenylmethane.

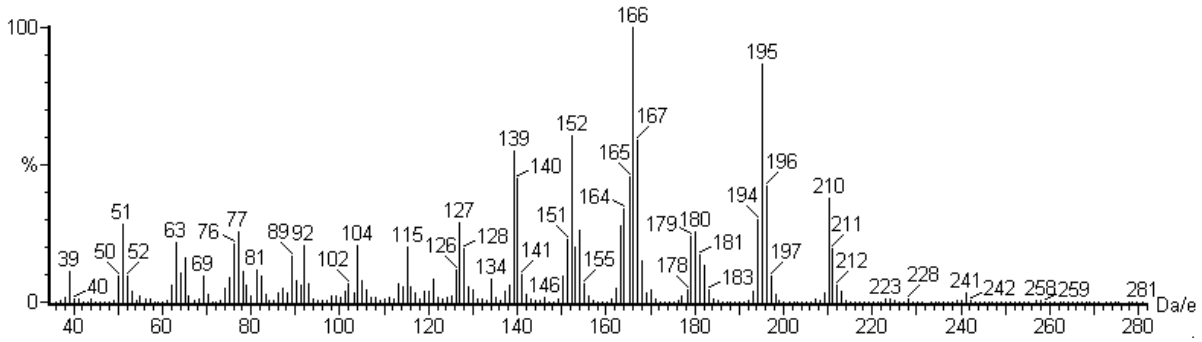

Figure 5. The positive EI mass spectrum of *o*,*o'*-dinitrodiphenylmethane.

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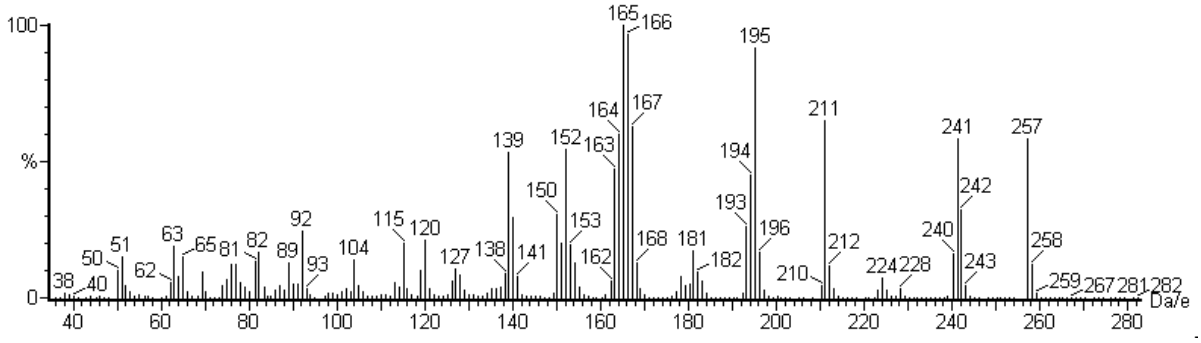

Figure 6. The positive EI mass spectrum of *o*,*p*′-dinitrodiphenylmethane.

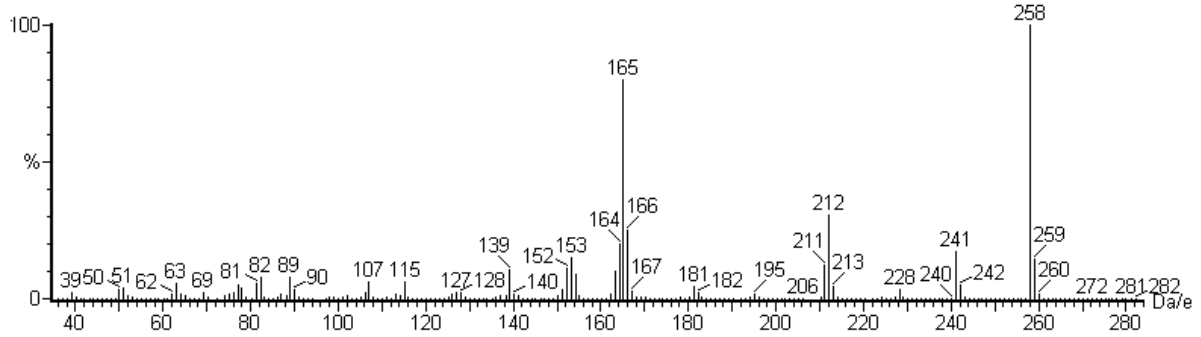

Figure 7. The positive EI mass spectrum of *p*,*p*′-dinitrodiphenylmethane.

GC (GC–MS) analysis at intermediate stages of the process shows the unexpected feature of the *p*-isomer being less reactive than the *o*-isomer, which is consumed more rapidly, although present in much smaller concentration.

Analytical Notes

GC–MS analyses were performed with a Fisons TRIO 2000 gas chromatograph–mass spectrometer, operating in the electron impact mode at 70 eV. A 30-m silica gel capillary column (Supelco MDN-5S, i.d. 0.25 mm, film thickness 0.50 μm) was operating between 100 and 310 ºC with a temperature program of 10 ºC min^{-1} (injector at 250 ºC). Mass spectra of all isomeric mono- and dinitroderivatives of diphenylmethane were recently reported [26]. The GC quantitative data were utilized as a double check for the more reliable ^{1}H-NMR data, based on the integral values for the individual peaks, which, owing to concentration effects, showed some fluctuation of location causing overlapping. When this problem showed up for a particular mixture we reverted to the GC quantitative data. NMR spectra were recorded at room temperature on a Bruker AC-F 200 spectrometer at 50 MHz, using $CDCl_3$ as solvent for the samples.

Figures 2 through 7 show the recorded electron impact mass spectra of *o*-nitrodiphenylmethane, *m*-nitrodiphenylmethane, *p*-nitrodiphenylmethane, *o*,*o*′ -dinitrodiphenylmethane, *o*,*p*′-dinitrodiphenylmethane, and *p*,*p*′-dinitrodiphenylmethane.

Some safe basic considerations may be made on the basis of a systematic observation of the fragmentation patterns. Only the *p*-nitro and *p*,*p*′-dinitroderivatives exhibit their parent ions, which are the base peaks. Loss of NO_2 from the parent peak is a common feature, except for the *o*- and *o*,*p*′-derivatives, where the apparent loss is that of HNO_2. Conspicuously, the parent ion of *o*-nitrodiphenylmethane does not find a fast enough route for the formation of $C_7H_7^+$ (91 m/z). A simple study of the electron impact induced fragmentations of the three main products, that is, the *o*,*o*′-, *o*,*p*′- and *p*,*p*′-derivatives, may be proposed.

A simplified version of the above experiment may be performed using *p*-nitrodiphenylmethane (easily prepared by a conventional Friedel–Crafts reaction between *p*-nitrobenzyl chloride and benzene according to the method described for the preparation of diphenylmethane [27]) utilizing half the nitric acid employed with diphenylmethane. The three products produced are *o*,*p*′-dinitrodiphenylmethane (25 %), *m*,*p*′-dinitrodiphenylmethane (5 %) and *p*,*p*′-dinitrodiphenylmethane (70 %).

Discussion

The following interesting aspects of this experiment should be noted by students:

The need for using H_2SO_4 as the solvent–catalyst is eliminated using an innovative procedure. This procedure improves safety, facilitates process control, and simplifies disposal methods.

The low boiling point and low enthalpy of evaporation of dichloromethane results in a large savings in energy requirements; the endothermic process of mixing HNO_3 and CH_2Cl_2 eliminates the need to cool the reaction mixture.

This experiment only goes as far as separating *p*,*p*′-dinitrodiphenylmethane in an adequate state of purity by

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crystallization. In principle, the two other main isomers produced, *o*,*p*′-dinitrodiphenylmethane and *o*,*o*′-dinitrodiphenylmethane, can be also separated. This experiment yields some products of interest as intermediates, like the corresponding diamines [28], which can be isolated by more complicated and expensive procedures.

The spent HNO_3 (modest amount of water) may be reconcentrated (bp 83.4 °C); 69% aqueous nitric acid is left behind (azeotrope, bp 120 °C [29]).

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References and Notes

1. *For example [2] details the nitrations of benzene, bromobenzene, nitrobenzene and p-nitrobenzyl cyanide, [3] presents the nitration of bromobenzene and [4] proposes the nitration of methylbenzoate. All use nitric acid in concentrated sulfuric acid. The use of both acids can be avoided [5] by employing nitronium tetrafluoroborate in sulfolane in the nitration of toluene and mesitylene.*
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