

713. *The Action of Nitric Acid–Acetic Anhydride Mixtures on Some Methylbenzenes.*

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When toluene, *o*-xylene, and hemimellitene are treated with nitric acid in acetic anhydride at 0°, nitration is accompanied by acetoxylation. From an examination of aryl acetate : nitro-hydrocarbon product ratios under varied experimental conditions, it is suggested that protonated acetyl nitrate is responsible for both acetoxylation and nitration.

MIXTURES of acetic anhydride and nitric acid have been widely used both for preparative mononitrations and for rate-comparisons, but the mechanism of their reaction with aromatic hydrocarbons is uncertain. In addition, we have briefly reported¹ that nitration is accompanied by acetoxylation when the substrate is toluene, *o*-xylene, or hemimellitene. The present paper describes this work.

EXPERIMENTAL

Analytical Reactions.—The hydrocarbon (8.2 mmole) was dissolved in acetic anhydride (2 ml.) at 0° in a 5-ml. flask fitted with stirrer and dropping funnel. A chilled mixture of anhydrous nitric acid (4.8 mmole) and acetic anhydride (1 ml.) was added dropwise to the stirred hydrocarbon solution over 1 hr. and the mixture stirred for a further 15 min. The temperature remained between 0 and 2° in all reactions. The mixture was quenched by pouring it into water (50 ml.), the product was extracted with ether, washed three times with water and dried (MgSO₄). The ether was removed under vacuum and the remaining material was analysed by gas chromatography.

Preparative Reactions.—In preparative runs with larger quantities of material the extraction

¹ Fischer, Packer, Vaughan, and Wright, *Proc. Chem. Soc.*, 1961, 369.

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technique was the same as for the analytical runs, except that the product was washed with 10% aqueous sodium carbonate and distilled before being chromatographed.

Chromatography.—With one exception (specified below) all chromatographic work was carried out in a Beckman Megachrom, fitted with eight standard 6 ft. \times $\frac{3}{8}$ in. U-tube columns in parallel, packed with 35% (w/w) Apiezon J on C-22 firebrick. The carrier gas was helium and the detector was the standard four-filament katharometer. All chromatograms were run at a column temperature of 180°, an inlet pressure of 16 lb./in.², and a back pressure of 1 lb./in.². A specially-constructed stainless-steel demountable inlet assembly was used in place of the commercial inlet because of a small amount of decomposition which always occurred in the inlet, particularly during preparative runs. Peak areas for analytical measurement were calculated as the product of peak height and width at half-height. This method is rapid; checks on peak areas with a planimeter showed it to be satisfactory.

Reagents.—**Hydrocarbons.** AnalaR toluene and Halewood Chemicals "Research" grade hemimellitene were used without further purification. Commercial *o*-xylene was purified by Clarke and Taylor's sulphonation method.² The product after hydrolysis was fractionated; it had b. p. 66°/37 mm. and a gas chromatogram showed no detectable impurity.

Anhydrous nitric acid. This was prepared by distillation of a mixture of 1 part fuming nitric acid ($\rho = 1.52$) and 2 parts concentrated sulphuric acid at room temperature and 1 mm. pressure, in an all-glass apparatus. The colourless product was collected in a cold trap and could be stored indefinitely at dry-ice temperature in the dark.

Acetic anhydride. AnalaR acetic anhydride was stored over sodium for 1 week, refluxed for 4 hr., and then distilled under reduced pressure.

Acetyl peroxide was prepared by Slagle and Shine's method.³

3-Nitro-*o*-xylene. The commercial material was fractionated (b. p. 96.5°/5 mm., f. p. 14.8°); the gas chromatogram of the product showed no detectable impurities.

4-Nitro-*o*-xylene. The commercial material, when recrystallised from ethanol, had m. p. 29—30° (lit.,⁴ 29—30°) and showed no detectable impurities on the gas chromatograph.

3,4-Dimethylphenyl acetate. This was prepared from 4-nitro-*o*-xylene by successive reduction to 3,4-xylidine (tin and hydrochloric acid), diazotization and hydrolysis to 3,4-dimethylphenol, and acetylation in acetic anhydride.

***p*-Tolyl acetate** was prepared from recrystallised *p*-cresol by acetylating with acetic anhydride.

Identification of Reaction Products.—***o*-Xylene.** Three products were separated on the gas chromatograph. Of these, 3-nitro-*o*-xylene and 4-nitro-*o*-xylene were identified by infrared spectrum and retention time, which were, for each compound, identical with those of an authentic sample. 3,4-Dimethylphenyl acetate was isolated as a white solid, m. p. 22° (after recrystallisation from methanol), b. p. 240—242° (lit.,⁴ m. p. 22—25°; b. p. 241°). The infrared spectrum showed intense bands at 5.6 and 8.2—8.4 μ , characteristic of vinylic and phenolic esters, and was identical with that of an authentic sample (Found: C, 73.2; H, 7.9; O, 19.3. Calc. for C₁₀H₁₂O₂: C, 73.2; H, 7.3; O, 19.5%). The ester was hydrolysed by 10% aqueous sodium hydroxide to 3,4-dimethylphenol, m. p. 62.5° [after recrystallisation from light petroleum (b. p. 50—70°)] (lit.,⁵ m. p. 62.5°) (Found: C, 78.4; H, 8.0; O, 13.3. Calc. for C₈H₁₀O: C, 78.7; H, 8.2; O, 13.1%). The i.r. spectrum was as published.⁶ The Pye Argon chromatograph completely separates 2,3- and 3,4-dimethylphenyl acetates on Apiezon L at 125°, and reaction mixtures run under these conditions showed no detectable 2,3-dimethylphenyl acetate.

Toluene. Of the four products, *o*-, *m*-, and *p*-nitrotoluenes were identified through their i.r. spectra.⁷ *p*-Tolyl acetate was isolated (Megachrom) as an oil whose retention time and i.r. spectrum were identical with those of authentic material. The acetate was hydrolysed (10% aqueous sodium hydroxide) to *p*-cresol, m. p. 33—34° (lit.,⁵ 34°).

Hemimellitene. Four products were separated on the gas chromatograph. 4-Nitro- and 5-nitro-hemimellitenes were identified through their i.r. spectra.⁸ 4-Hemimellitanyl acetate has b. p. 239—241° (lit.,⁵ 239—241°) and its i.r. spectrum showed the strong characteristic 5.6 μ peak

² Clarke and Taylor, *J. Amer. Chem. Soc.*, 1923, **45**, 830.

³ Slagle and Shine, *J. Org. Chem.*, 1959, **24**, 107.

⁴ "Beilsteins Handbuch der Organischen Chemie," Springer-Verlag, Berlin, Vol. 6, Part II, p. 455.

⁵ Heilbron and Bunbury, "Dictionary of Organic Compounds," Eyre and Spottiswoode, London, 1946, 2nd edn.

⁶ Barnes, Liddel, and Williams, *Ind. Eng. Chem., Analyt.*, 1943, **15**, 685.

⁷ Pristera and Halik, *Analyt. Chem.*, 1955, **27**, 217.

⁸ Dolinsky, Jones, Ritchie, Yates, and Hall, *J. Assoc. Offic. Agric. Chemists*, 1959, **42**, 709.

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of phenolic esters. Hydrolysis in methanol-sulphuric acid gave 4-hemimellitenol, m. p. 80.5° (lit.,⁵ m. p. 81°); its phenylurethane melted at 127° (lit.,⁵ m. p. 127°). *sym*-Hemimellitenyl acetate had m. p. 59° [after recrystallisation from light petroleum (b. p. 30–40°)] (lit.,⁵ m. p. 59–60°) (Found: C, 73.4; H, 8.1; O, 19.0. Calc. for C₁₁H₁₄O₂: C, 74.2; H, 8.1; O, 17.9%). Hydrolysis in methanol-sulphuric acid gave hemimellitenol, m. p. 106.5–107.5° (lit.,⁵ m. p. 107°) (Found: C, 79.4; H, 8.8; O, 11.8. Calc. for C₉H₁₂O: C, 78.8; H, 8.5; O, 12.1%).

Check on Extraction Procedure.—To ensure that no change in product composition occurred during extraction, several synthetic mixtures were analysed by gas chromatography before and after the extraction procedure. No measurable change in composition occurred.

Product Distribution.—The product compositions given in Table 1 were obtained with the Megachrom. The figures ($\pm 1\%$) are uncalibrated, but are means of values from at least three reactions. Two chromatograms were run on each reaction.

TABLE 1.

Product analysis for reaction of aromatic hydrocarbon (2.7M) with nitric acid (1.6M) in acetic anhydride at 0°.

Toluene:	<i>o</i> -nitro 63, <i>m</i> -nitro 3, <i>p</i> -nitro 31, <i>p</i> -acetoxy 3%
<i>o</i> -Xylene:	3-nitro 16, 4-nitro 33, 3-acetoxy 0, 4-acetoxy 51%
Hemimellitene:	4-nitro 55, 5-nitro 9, 4-acetoxy 9, 5-acetoxy 27%

Nitrite Production.—We wished to learn whether formation of acetoxy-product is accompanied by equivalent nitrite production. For such comparison, with *o*-xylene as substrate, we required an accurate figure for the aryl acetate produced. A series of mixtures was made from the two nitro-*o*-xylenes and 3,4-dimethylphenyl acetate. Then, with *o*-dichlorobenzene as internal standard, the following recorder responses (peak area per mmole of sample injected into the chromatograph under identical conditions of temperature, flow rate, and recorder sensitivity and speed in units of mm.² mmole⁻¹) were obtained: 3-nitro-*o*-xylene, 60.5 \pm 3; 4-nitro-*o*-xylene, 57.7 \pm 3; 3,4-dimethylphenyl acetate, 81.3 \pm 1; *o*-dichlorobenzene, 415 \pm 10. (These response figures allow the calculation of corrected figures for the composition of *o*-xylene reaction products. They are: 3-nitro, 18%; 4-nitro, 39%; 4-acetoxy, 43%).

Nitrite was determined through a modified Griess-Ilosvay test,^{9,10} in which the colorimetric comparison with sodium nitrite standards was made at 520 m μ by the Hilger "Uvispek" spectrophotometer. Amounts of other products were calculated (making use of the recorder response figures) and the nitrite: aryl acetate molar ratio (over three runs) was 0.6 \pm 0.1. A typical product analysis when the added nitric acid was 5.85 mmole was: 3-nitro-*o*-xylene, 0.65; 4-nitro-*o*-xylene, 1.36; 3,4-dimethylphenyl acetate, 2.28; nitrite, 1.4 mmole.

Effect of Variation in Reactant Concentrations.—In Table 2 are listed the molar ratios of acetoxy: nitro products obtained under the given experimental conditions.

TABLE 2.

Acetoxylation of *o*-xylene in acetic anhydride at 0°.

[<i>o</i> -Xylene] mmole l. ⁻¹	[HNO ₃] mmole l. ⁻¹	[Other reagents] mmole l. ⁻¹	Acetoxy: nitro ratio
2.73	0.2	—	0.76
2.73	1.6	—	0.76
2.73	1.6	AcOH, 16.3	0.76
2.73	1.6	H ₂ SO ₄ , 0.016	0.86
2.73	1.6	H ₂ SO ₄ , 0.032	0.99
2.73	—	H ₂ SO ₄ , 1.1	No reaction
2.73	—	Acetyl peroxide, 1.6; H ₂ SO ₄ , 1.6	No reaction

DISCUSSION

The figures in Table 1 illustrate the marked dependence of acetoxylation on activation of the substrate to electrophilic substitution, and this form of attack is strongly suggested

⁹ Lunge and Lwoff, *Z. angew. Chem.*, 1898, **7**, 348.

¹⁰ Benford and Ingold, *J.*, 1938, 929.

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by the results. Free-radical attack, under the reaction conditions, would seem unlikely, and treatment of *o*-xylene with acetyl peroxide and sulphuric acid produced no detectable reaction (Table 2). Considerable acetoxylation occurs at the more activated 4-position in *o*-xylene but none can be detected at the 3-position. The 4-position in hemimellitene is more highly activated to electrophilic attack than the 4-*o*-xylene position but is considerably more sterically hindered, and here only 4½% acetoxylation occurs in each position; the bulk of attack (in contrast to nitration) occurs at the less activated 5-position. These facts imply a large attacking entity, and it would appear that acetoxylation is more subject to steric hindrance than is nitration. (This conclusion applies to acetoxylation and nitration under our reaction conditions. However, such nitration in acetic anhydride is in its turn, subject to greater steric hindrance than nitration with nitronium tetrafluoroborate in sulpholane.¹¹) Additional support for this conclusion is provided by the fact that only 4% acetoxylation occurs with *m*-xylene.¹² If it were not for the greater steric hindrance in its most activated positions, *m*-xylene, being more activated to electrophilic attack, should be acetylated to a greater extent than *o*-xylene (see below).

Consideration of the ratio of acetoxylation to nitration in the more activated unhindered positions of toluene (4-), *o*-xylene (4-), and hemimellitene (5-), indicates that acetoxylation is more sensitive to activation in the substrate than is nitration (*i.e.*, the value of the Hammett rho function for acetoxylation is greater than that for nitration). Thus the acetoxyating species is less active and presumably more selective than the nitrating species. Paul¹³ showed that the rate of nitration of benzene in acetic anhydride–nitric acid mixtures (of similar concentration to ours) is markedly increased by the addition of 0.01M-sulphuric acid. Rates of both acetoxylation and nitration of *o*-xylene are more sensitive to addition of sulphuric acid, acid concentrations as low as 10⁻⁵M having a significant effect.¹² Addition of 0.01M-sulphuric acid to our reaction mixtures (Table 2) had only a slight effect on the ratio of acetoxy- to nitro-products. The proposition that protonated acetyl nitrate is both the acetoxyating and nitration entity is consistent with these observations. Furthermore it will be noted that the general requirement of greater steric hindrance to acetoxylation than to nitration is qualitatively met if it be assumed that acetoxylation occurs by attack at the more hindered central oxygen of protonated acetyl nitrate rather than at carbonylic oxygen. The existence of protonated acetyl nitrate as a reactive species in nitric acid–acetic anhydride mixtures was demonstrated by Bordwell and Garbisch¹⁴ who showed that it is the reactive entity in the formation of β-nitro-acetates from alkenes.

The reaction between this species and hydrocarbon to produce acetylated hydrocarbon requires the release of an equivalent amount of nitrite. We have been able to account for about 60% of the theoretical amount of nitrite and must assume that during the period of reaction (about 1.5 hr.), some nitrite is lost from the solution. The suggestion that the aryl acetate arises from the replacement of a nitro-group of a previously-formed mononitro-compound may be discounted by the fact that neither 3-nitro- nor 4-nitro-*o*-xylene yields an acetoxy-product on treatment with nitric acid and acetic anhydride.

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¹¹ Olah, Kuhn, and Flood, *J. Amer. Chem. Soc.*, 1961, **83**, 4575.

¹² Fischer, Read, and Vaughan, following Paper.

¹³ Paul, *J. Amer. Chem. Soc.*, 1958, **80**, 5329.

¹⁴ Bordwell and Garbisch, *J. Amer. Chem. Soc.*, 1960, **82**, 3588.