

Formation of Adducts in the Nitration of Toluene in Acetic Anhydride

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cis- and *trans*-4-Nitro-1,4-dihydro-*p*-tolyl acetate are formed as minor products when toluene is nitrated in acetic anhydride. Decomposition of these adducts gives *p*-tolyl acetate.

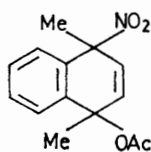
FORMATION of acetyl nitrate adducts such as (I) when aromatic compounds are reacted with nitric acid in acetic anhydride has been observed for a variety of substrates.¹ Adducts are formed when an aromatic carbon atom carrying a substituent is not substantially

less activated than one carrying a hydrogen atom. *ipso*-Attack² by the nitronium ion or incipient nitronium ion at the substituted position is then competitive with attack at the unsubstituted position and the resulting phenonium ion, which loses neither nitro-group nor substituent as a cation, adds a nucleophile to generate a pair of diastereoisomeric adducts. Adduct formation thus has a similar initial phenonium ion-forming step as substitution and the ratio of addition to substitution product is presumably determined by the relative rates of

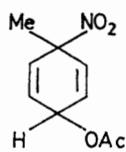
¹ (a) D. J. Blackstock, A. Fischer, K. E. Richards, J. Vaughan, and G. J. Wright, *Chem. Comm.*, 1970, 641; (b) D. J. Blackstock, J. Cretny, A. Fischer, M. P. Hartshorn, K. E. Richards, J. Vaughan, and G. J. Wright, *Tetrahedron Letters*, 1970, 2793; (c) A. Fischer, C. C. Greig, A. L. Wilkinson, and D. R. A. Leonard, *Canad. J. Chem.*, 1972, **50**, 2211; (d) A. Fischer and D. R. A. Leonard, *ibid.*, p. 3367; (e) A. Fischer and A. L. Wilkinson, *ibid.*, in the press.

² C. L. Perrin and G. A. Skinner, *J. Amer. Chem. Soc.*, 1971, **93**, 3389.

attack by the electrophile at *ipso* and unsubstituted positions. Thus 1,4-dimethylnaphthalene gives only



(I)



(II)

a; NO₂, OAc *trans*
b; NO₂, OAc *cis*

minor amounts of nitro-substitution product,^{1e} the major product being the diastereoisomeric adducts (I). Here the substituted 1-position is a much more reactive site than the unsubstituted 2-, 5-, and 6-positions. The 5-position should not be much less activated than the 1-position, but attack in the 5-position should be sterically inhibited by the *peri*-methyl substituent. The 2- and 6-positions (β) are much less activated than the 1-position (α). Consequently attack at the substituted 1-position is much preferred and thus adduct formation is the predominant reaction. In contrast mesitylene gives only nitromesitylene.³ In mesitylene the unsubstituted positions, being *ortho* and *para* to the methyl groups, are much more activated than the substituted positions (*meta* and *ipso* to the methyl groups); consequently attack at the unsubstituted position leading to the normal nitro-substitution product is dominant.

It has been shown in the case of 1,4-dimethylnaphthalene,^{1e} and it is probably generally so, that the initially formed adduct is that resulting from addition of nitronium nitrate rather than nitronium acetate (acetyl nitrate), the acetyl nitrate adduct being formed by a subsequent reaction. Decomposition of the acetyl nitrate adducts normally gives an aryl acetate by loss of nitrous acid^{1a-c} or other products including α -nitroarenes are sometimes formed and may even predominate.^{1a,e} *p*-Tolyl acetate has been observed as a minor product in the nitration of toluene with nitric acid in acetic anhydride⁴ and a recent investigation of this reaction⁵ has revealed that α -nitrotoluene is also formed in small amounts. It seemed to us that these products might arise by decomposition of the acetyl nitrate adducts of toluene and we have reinvestigated the nitration of toluene in acetic anhydride in a search for the adducts.

The crude product isolated from the nitration of toluene in acetic anhydride exhibited absorption in the τ 3.5–4.5 region characteristic of the vinylic and allylic protons of the 1,4-cyclohexadiene system of the expected

adduct. Integration of the diene and aromatic regions indicated that adduct constituted *ca.* 3–4% of the product. Chromatography of the product on alumina afforded *trans*- and *cis*-4-nitro-1,4-dihydro-*p*-tolyl acetate (II). Integration of the methyl region of the n.m.r. spectrum of the product mixture showed that the *trans*-adduct was formed in *ca.* twice the amount of the *cis*-adduct. Analogous arguments to those given for related adducts¹ in support of the assigned structural formula can be made. Two points specific to the case in hand are the highly symmetrical n.m.r. spectra (AA'BB'C) and the fact that the protons of the nuclear methyl group appear as a singlet. The former point is only consistent with the assigned structure and its isomer in which the nitro- and acetate groups are interchanged and the latter is only consistent with structures [such as (II)] in which the methyl group is not attached to a double bond. The stereochemical assignment is based on dipole-moment measurements, the *cis*-structure being assigned to the isomer of lower dipole moment.^{1e} This assignment is supported by the comparative downfield shifts of the protons of the methyl group at C(4), induced by addition of the shift reagent tris-(1,1,1,2,2,3,3-heptafluoro-7,7-[²H₆]dimethyl-4,6-[²H₃]octanedionato)-europium(III) {Eu([²H₉]fod)₃}.⁶ The gradient of a plot of the shift against mole ratio of reagent to substrate is 0.46 p.p.m. for the *cis*-adduct and 1.04 p.p.m. for its *trans*-isomer. The decrease in paramagnetic shift of a proton with increase in distance between complexed europium ion and the proton is well established.⁷ In the present case there are two potential complexing sites, the nitro- and acetoxy-groups. However, nitro-groups are only very weakly complexed and the dominant complexing should be with the acetoxy-group.^{7c} This is confirmed by the observation that the shift of the acetate methyl protons (gradient 6.9 and 5.9 p.p.m. for *cis*- and *trans*-adducts, respectively) is six or more times as sensitive to the addition of the reagent than the C(4)-methyl protons. Clearly the europium is complexed at the acetoxy-group and closer to the acetate methyl rather than at the nitro-group where it would be closer to the C(4)-methyl. The different gradients for the C(4)-methyl shifts in the two isomers show that the europium, complexed at the ester function, is closer to the C(4)-methyl group in the *trans*-adduct (IIa) than in its *cis*-isomer (IIb), in accordance with predictions from models.

Further confirmation that the 1,4-cyclohexadiene ring is planar^{1a,8} is provided by the calculated values of the dihedral angles between the H(1)–C(1)–C(2) and C(1)–C(2)–H(2) planes in the isomers (IIa) and (IIb). These angles can be calculated from the three- and four-bond coupling constants of the vinylic allylic

³ D. J. Blackstock, Ph.D. Thesis, University of Canterbury, Christchurch, New Zealand, 1970.

⁴ A. Fischer, J. Packer, J. Vaughan, and G. J. Wright, *Proc. Chem. Soc.*, 1961, 369; A. Fischer, J. Vaughan, and G. J. Wright, *J. Chem. Soc. (B)*, 1967, 368.

⁵ S. R. Hartshorn, R. B. Moodie, and K. Schofield, *J. Chem. Soc. (B)*, 1971, 1256.

⁶ R. E. Sievers and R. E. Rondeau, *J. Amer. Chem. Soc.*, 1971, **93**, 1522.

⁷ (a) C. C. Hinckley, *J. Amer. Chem. Soc.*, 1969, **91**, 5160; (b) P. V. Demarco, T. K. Elzey, R. B. Lewis, and E. Wenkert, *ibid.*, 1970, **92**, 5734; (c) J. K. M. Sanders and D. H. Williams, *ibid.*, 1971, **93**, 641; (d) C. C. Hinckley, M. R. Klotz, and F. Patil, *ibid.*, p. 2417.

⁸ E. W. Garbisch, jun., and M. G. Griffin, *J. Amer. Chem. Soc.*, 1968, **90**, 3590.

system.^{1c,9} The angles are 70° (from ³J) or 66° (from ⁴J) with a mean of 68° for (IIa) and 67° (³J) or 61° (⁴J) with a mean of 64° for (IIb). Planar 1,4-cyclohexadiene with tetrahedral bond angles at C(1) and C(4) would have a dihedral angle of 60°.

The dienes were decomposed both thermally and in the presence of acid. The isomeric dienes gave rise to the same product, *p*-tolyl acetate. The *trans*-isomer decomposed more rapidly than its *cis*-counterpart. Any α -nitrotoluene formed could not have amounted to 5% of the *p*-tolyl acetate since it could not be detected in the n.m.r. spectrum of the decomposition product. There was an unassigned peak in the gas chromatogram of diene decomposition product but its area was *ca.* 2–3% of the acetate peak. In the decomposition of the 1,4-dimethylnaphthalene adducts (I) the highest yield of α -nitro-derivative is obtained when the decomposition is carried out in the presence of nitric acid in acetic anhydride. Even under these conditions we could not detect any α -nitrotoluene in the decomposition product of the toluene adducts (II).

Although the α -nitro-derivative has been obtained as a product in the nitration of several arenes,^{1a,e,3,10} in all of these examples the substrate contains two methyl or methylene groups in a *para*-relationship. The adduct, which is the intermediate in the formation of the α -nitro-product, thus has a methyl or methylene group attached to the carbon to which the acetate group has added as well as the normal methyl (methylene) on the carbon bearing the nitro-group. Thus elimination of acetic acid to generate an exocyclic methylene (methylidyne) can occur, a key step in the formation of the α -nitro-derivative.¹¹ Clearly this pathway is not open to the adducts (II) and it is not surprising that α -nitro-compound is not obtained as a decomposition product. We conclude that the α -nitrotoluene observed by Hartshorn *et al.*⁵ as a minor product from the nitration of toluene in acetic anhydride was not formed *via* the acetyl nitrate adducts (II). However the previously observed ⁴*p*-tolyl acetate is formed *via* the adducts and this is confirmed by the fact that the yield of acetate measured then by g.l.c. of the nitration products is equal within experimental error to the yield of adducts as determined in the present work by n.m.r.

EXPERIMENTAL

U.v. spectra were determined on a Unicam SP 700 spectrometer. I.r. spectra were obtained with a Perkin-Elmer 337 spectrometer calibrated with polystyrene. N.m.r. spectra were determined on Varian HA-60-IL and Perkin-Elmer R12A spectrometers with tetramethylsilane as internal standard. Spectra at 220 MHz were determined on a Varian HR200 instrument by the Canadian 220 MHz Centre. Mass spectra were obtained with a Perkin-Elmer Hitachi RMU-7 spectrometer. Molecular weights were determined in methylene dibromide by use of a Perkin-Elmer-Hitachi 115 molecular weight apparatus. Dipole

⁹ E. W. Garbisch, jun., *J. Amer. Chem. Soc.*, 1964, **86**, 5561.

¹⁰ R. Robinson and H. W. Thompson, *J. Chem. Soc.*, 1932, 2015.

¹¹ R. Robinson, *J. Chem. Soc. (B)*, 1970, 1289.

moments were derived by use of Higasi's equation¹² from dielectric-constant measurements^{1c} of benzene solutions of the dienes. The dielectric constants were measured with a Sargent Chemical Oscillometer model V with inductive cell-compensator. Nitric acid was purified by distilling 'fuming' acid (300 cm³) at 1 mmHg from urea (10 g) and sulphuric acid (500 cm³). Alumina was deactivated with 3% or 10% acetic acid.

Formation of the Adducts (II).—A cold solution of nitric acid (94 g, 1.5 mol) in acetic anhydride (250 cm³) was added slowly with stirring to a solution of toluene (92 g, 1 mol) in acetic anhydride (250 cm³) at –30 °C. Stirring was continued for 30 min. The solution was then cooled in solid carbon dioxide–acetone, ether (500 cm³) was added, and ammonia was condensed into the solution. Excess of ammonia was removed with an aspirator, more ether added, and the mixture was poured on ice. The combined ether layer and ether extract of the aqueous layer was dried (MgSO₄) and the ether was then evaporated at 14 °C. Chromatography on alumina at –30 °C and elution first with pentane and then with ether gave an enriched diene-containing (35%) mixture in the ether fraction. Repeated chromatography gave a fraction enriched to 60% diene. Further chromatography and elution with pentane and ether–pentane gave in the 15% ether fraction *trans*-4-nitro-1,4-dihydro-*p*-tolyl acetate (IIa) as an oil, λ_{\max} (MeOH) 197 nm (ϵ 920 m² mol⁻¹); ν_{\max} (CCl₄) 1750 and 1230 (OAc) and 1550 and 1345 cm⁻¹ (NO₂); τ (220 MHz; CD₂Cl₂) 3.76 (2H, m, 3- and 5-H), 3.85 (2H, m, 2- and 6-H), 4.31 (1H, m, *J*_{1,2} 3.1, *J*_{1,3} –1.9, *J*_{2,3} 10.1, *J*_{2,5} –0.2, *J*_{2,6} 1.9, *J*_{3,5} 1.9 Hz, 1-H), 7.91 (3H, s, OAc), and 8.21 (3H, s, Me), *m/e* (relative intensity) 151 (3, *M* – NO₂), 150 (5), 109 (100), 92 (20), 91 (38); μ 3.69 D (12.3 aC pm) (Found: *M*, 199. C₉H₁₁NO₄ requires *M*, 197). Elution with 50% ether–pentane afforded *cis*-4-nitro-1,4-dihydro-*p*-tolyl acetate (IIb) as an oil, λ_{\max} 198 nm (ϵ 930 m² mol⁻¹), ν_{\max} (CCl₄) 1750 and 1235 (OAc) and 1555 and 1345 cm⁻¹ (NO₂), τ (220 MHz; CCl₄) 3.75 (2H, m, 3- and 5-H), 3.96 (2H, m, 2- and 6-H), 4.48 (1H, m, *J*_{1,2} 3.2, *J*_{1,3} –1.7, *J*_{2,3} 10.3, *J*_{2,5} –0.1, *J*_{2,6} 1.5, *J*_{3,5} 1.6 Hz, 1-H), 7.97 (3H, s, OAc), and 8.31 (3H, s, Me), *m/e* (relative intensity) 151 (2, *M* – NO₂), 150 (3), 109 (100), 92 (33), 91 (52); μ 2.96 D (9.9 aC pm) (Found: *M*, 201. C₉H₁₁NO₄ requires *M*, 197).

Decomposition of the Adducts (II).—Decomposition was carried out by refluxing in benzene, by refluxing in 10% acetic acid–benzene, by treatment with an equimolar amount of nitric acid in acetic anhydride, and thermally (250 °C) on injection into a gas chromatograph. Under each condition and with both dienes (IIa) and (IIb) *p*-tolyl acetate was obtained as the sole product. The *p*-tolyl acetate had identical mass, *i.e.*, and n.m.r. spectra with a sample prepared from *p*-cresol. In the case of the decomposition induced on injection into the gas chromatograph identity of retention time with authentic *p*-tolyl acetate was observed.

Effect of Shift Reagent.—Increments (*ca.* 15 mg) of Eu([²H₉]fod)₃ were added to a solution of mixed adducts (IIa) and (IIb) (50 mg) in carbon tetrachloride (0.3 cm³) in an n.m.r. tube. The weight of reagent added and the n.m.r. spectrum (tetramethylsilane reference) were determined after each addition. Excellent linear plots (nine points) of the chemical shift of the two sets of methyl

¹² K. Higasi, *Bull. Inst. Phys. Chem. Res. (Tokyo)*, 1943, **22**, 805; B. Krishna and K. Srivastava, *J. Chem. Phys.*, 1960, **32**, 663.

protons in each isomer against mole ratio of shift reagent to substrate were obtained. The effect of the shift reagent depends both on the equilibrium constant for complex formation and the distance between proton and europium ion in the complex.¹³ However the equilibrium constants for complexation of the stereoisomers should be very similar and hence the observed variation in the C(4)-methyl proton shifts is properly attributed to a variation in the proton-europium distances. This assumption is supported by the observation that the shifts of the acetate methyl groups for the two isomers, in which the proton-europium distances would be expected to be closely similar, differ by only 14%.

The distance between the carbonyl oxygen, the site of complexation by the europium ion,¹⁴ and the protons of the C(4)-methyl group in the adducts was calculated for a planar cyclohexadiene system by assuming a positive distortion of 3.5° from the normal ($109\frac{1}{2}$ and 120°) ring bond angles in order to obtain a planar ring. The internuclear distance is 0.63 nm for the *cis*-isomer (IIb) with *trans*-acetate and

methyl groups and 0.54 nm for the *trans*-isomer (IIa) with methyl *cis* to acetate.

Kinetics Studies.—The disappearance of the C(4)-methyl peaks corresponding to (IIa) and (IIb) and the appearance of the C(4)-methyl peak of *p*-tolyl acetate in carbon tetrachloride containing 3% by volume of trifluoroacetic acid were followed at 37 °C by n.m.r. Linear first-order plots of the logarithm of the peak integrals of compounds (IIa) and (IIb) were obtained and gave the rate constants $12 \times 10^{-5} \text{ s}^{-1}$ for (IIa) and $2 \times 10^{-5} \text{ s}^{-1}$ for (IIb). The sum of the (IIa), (IIb), and *p*-tolyl acetate peak integrals was constant through the run.

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¹³ C. C. Hinckley, *J. Org. Chem.*, 1970, **35**, 2834.

¹⁴ H. Hart and G. M. Love, *Tetrahedron Letters*, 1971, 625.