Nitration of Hector's Base

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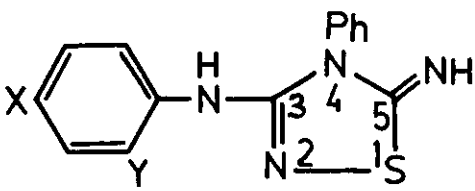
Summary: Nitration of Hector's Base gives both mono and dinitro products. In each case, only one out of two phenyl rings involves in the nitration process and that ring is the 3-anilino portion of the Hector's Base. The protonation of the exocyclic nitrogen of Hector's base seems to deactivate the phenyl ring attached to nitrogen at position 4, which in turn, does not react with nitronium ion. Finally, acetylation of nitrocompounds of Hector's Base and nitration of Hector's Base in acetylating mixture have also been discussed.

Under acid conditions the nitration of aniline leads to 100% mononitroanilines [1]; the product consists mainly of the m and p-isomers with a little of the o-isomer [2]. The dinitro-compound cannot be prepared by direct nitration and is usually synthesised by the action of ammonia on 1-chloro-2,4-dinitrobenzene [3]. However, it is possible to observe the directing effect of the unprotonated but substituted amino-group upon aromatic nitration when the anilino-group is attached to a ring system where protonation occurs elsewhere in the molecule. This is the case in the nitration of Hector's base.

The action of hydrogen peroxide upon 1-phenylthiourea yields a heterocyclic compound, the solid state structure of which has been shown to be (1a) by x-ray crystallography [4].



1a X = Y = H
b X = NO_2; Y = H
C X = Y=NO_2

^{15}N-n.m.r. studies indicate that this structure persists in solution [5]. Nitration of this compound in a mixture of moderately concentrated sulphuric and nitric acids gave a yellow solid which was readily identified by spectroscopic means as (1b), 5-imino-4-phenyl-3-(4-nitrophenylamino)-4H-1, 2,4-thiadiazoline. In the aromatic region of the ^{1}H-n.m.r. spectrum there are two doublets at δ7.83 (2H, J 9Hz) and δ8.21 (2H, J 9Hz). The size of the coupling constants and the value of the chemical shifts shows that the nitro-group is in the p-position. Examination of the product by HPLC showed that there is only one product and not a mixture of the m- and p-compounds as found in the nitration of the anilinium ion. It is known from a previous study [6] that Hector's base preferentially protonates on the imino nitrogen and the charge is delocalised onto the nitrogen at the 4-position. Clearly this renders a second protonation on the anilino-nitrogen at position-3 unfavourable and so, in the reaction of Hector's Base, we are observing the activating effect of an unprotonated -NHR group. If protonation of the anilino-nitrogen is unfavourable it is not immediately obvious why elec-

trophilic attack is not similarly disfavoured. However, by simple resonance theory it is seen that the positive charge occasioned by attack at the p-position is more delocalised and more remote than the charge generated by N-protonation, and so less affected by the charge already present because of protonation of the imino-nitrogen. It appears that the free amin group strongly favours attack at the p-position, rather than at the o-position, although steric factors may complicate the issue in this instance.

The nitration of Hector's base has some similarity with that of acetanilide but in the latter case no dinitro-compound is obtained [7]. However, with a powerful nitrating mixture (concentrated nitric and sulphuric acids) the dinitro derivative of Hector's base is obtained, with both nitro-groups on the same phenyl ring. Examination of the product by HPLC indicated a single compound. In the ^{1}H-n.m.r. spectrum (100 MHz) there were two doublets and one singlet for the protons in the substituted ring, consistent with the disposition of the nitro-groups at the 2- and 4-position (1c). At higher frequency (360 MHz) the unresolved singlet becomes a doublet. Thus, when attached to a thiadiazoline ring the anilino moiety undergoes ready dinitration without oxidation.

By the use of nitric acid in glacial acetic acid and acetic anhydride as a nitrating agent, two products were obtained: the mono- and di-nitrated compounds acylated on the exo-cyclic imino-group. The same compounds were also obtained by acetylation of (1b) and (1c).

Experimental

Materials

Hector's base was prepared by a literature method [8] and acetylated according to a published procedure [6]. All other materials were normal laboratory reagents.

Mononitration

Hector's base (3 g) was stirred at room temperature with a mixture containing 52% w/w H_2SO_4 (50 ml) and 70% w/w HNO_3 (5 ml) for 10 mins and then poured into cold water. After neutralisation (NaOH) a yellow solid precipitated and was crystallised from acetone to give 5-imino-4-phenyl-3-(4-nitrophenylamino)-4H-1,2,4-thiadiazoline (1b), m.p. 208°, m/z 313 (M^+), IR (mull) ν_{max} 3290 (NH), 1630 (C=N), 1500 and 1335 cm^{-1} (NO_2), ^{1}H-NMR (DMSO-d_6, 360 MHz): δ 7.73 (5H, s), 7.8 (1H, s), 7.83 (2H, d, J 9Hz), and 8.21 (2H, d, J 9Hz), ^{13}C-NMR (DMSO-d_6): δ 119.4, 124.7, 128.9, 130.3, 131.1, 132.1(s), 142.2(s), 145.1(s), 148.3(s), and 176.9(s) (Found: C, 54.0; H, 3.7; N, 22.2. $C_{14}H_{11}N_5O_2S$ requires C, 53.7; H, 3.5; N, 22.4%). The same compound was obtained by reaction of Hector's Base with 66% v/v nitric acid at room temperature for 3h.

Dinitration

Hector's base was added a little at a time to a mixture of conc. H_2SO_4 (10 ml) and conc. HNO_3 (5 ml) in an ice bath with stirring during 1 h. The mixture was then poured into cold water, the yellow solid filtered off and crystallised from water to give 5-imino-4-phenyl-3-(2,4-di-nitrophenylamino)-4H-1,2,4-thiadiazoline (1c), m.p. 158° m/z 358 (M^+), IR (mull) ν_{max} 3340-3180 (NH), 1590 (C=N), 1510 and 1345 cm^{-1} (NO_2), ^{1}H-NMR (DMSO-d_6, 100 MHz) δ 7.80 (5H,s), 8.63 (1H,

d, J 2Hz), 8.83 (1H, d, J 2Hz), and 8.70 (1H, s), (Acetone-d_6, 360 MHz) δ7.85-7.88 and 7.93-8.00 (5H, m), 8.65 (1H, d, J 2Hz), 8.68 (1H, dd, J 2Hz), 9.00 (1H, d, J 2Hz), 9.08 (1H, s,), and 9.11 (1H, broad s), ^{13}C-NMR (DMSO-d_6): δ 120.6-132.4, 135.4(s), 138.1(s), 140.7(s), 146.7(s) and 176.2(s) (Found: C, 46.9; H, 2.8; N, 23.2. $C_{14}H_{10}N_6O_4S$ requires C, 46.9; H, 2.8; N, 23.5%).

Nitration and acetylation

Hector's base (2.7 g) was stirred with a mixture of 70% w/w nitric acid (1 ml), glacial acetic acid (2.5 ml) and acetic anhydride (2.5 ml) for 5 h. The mixture was poured into water and the precipitate extracted with acetone to give 5-acetylimino-4-phenyl-3-(4-nitrophenylamino)-4H-1,2,4-thiadiazoline, m.p. 204°, m/z 355 (M^+), IR (Mull): ν_{max} 3230 (NH), 1610 (C=O), 1590 (C=N), 1545 and 1280 cm^{-1} (NO_2), ^{1}H-NMR (DMSO-d_6): δ 2.15 (3H,s), 7.72 (5H,s), 8.20 (2H, d, J 9Hz), 8.75 (2H, d, J 9Hz) and 9.92 (1H), ^{13}C-NMR (DMSO-d_6): δ 28.7, 120.0, 122.4, 125.8, 128.4, 130.4, 130.7, 133.3, 136.2, 145.6, 182.0 and 182.8 (Found: C, 54.2; H, 3.8; N, 19.9. $C_{16}H_{13}N_5O_3S$ requires C, 54.1; H, 3.7; N, 19.7%). The material insoluble in acetone was the dinitrated product, m.p. 310°, m/z 400 (M^+) (Found: C, 48.2; H, 3.0; N, 21.1. $C_{16}H_{12}N_6O_5S$ requires, C, 48.0; H, 3.0, N, 21.0%).

Compound (1b) (2g) in a mixture of glacial acetic acid and acetic anhyde (1:1) was stirred for 24h.

On dilution with water a yellow solid settled out, washed with water, ether and recrystallised from acetone which gave 5-acetylimino-4-phenyl-3-(4-nitro-phenylamino)-4-1,2,4-thiadiazoline, m.p. and mixed m.p. 204°. Compund (1c) was acetylated as described. A yellow solid obtained and after several washings with DMSO gave dinitrated product, m.p. and mixed m.p. 310°.

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