

# A Reinvestigation of the Reaction between 2-Acetylbenzenediazonium chloride and Primary Amines. Preparation of 3-Alkyl-4-hydroxy-4-methyl-3,4-dihydro-1,2,3-benzotriazines

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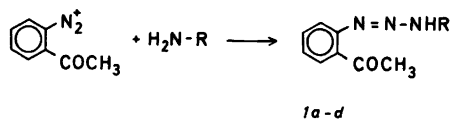
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Disubstituted aryltriazenes with an *ortho*-substituent in the aryl group susceptible to cyclization, have been subject to recent publications.<sup>1,2</sup> The triazene substituent is nucleophilic and able to cyclize to ester, nitrile and oxogroups forming six-membered and five-membered ring systems, namely dihydrobenzotriazines and dihydrobenzotriazoles, respectively.

The reaction between 2-acetylbenzenediazonium chloride and primary amines has been investigated.<sup>2,3</sup> It was found that 4-methylene-3,4-dihydro-1,2,3-benzotriazines were the end products when a primary amine was coupled with the diazonium ion under successive treatment with neutral alumina. By this coupling procedure a bright red compound of unidentified structure<sup>4</sup> was, however, produced with ethyl glycinate.

We have reinvestigated these reactions and have been able to describe them in more detail. In order to obtain pure reaction products, we have changed the reaction conditions of Fong and Vaughan.<sup>5</sup> Instead of adding the amine to the diazonium solution, the diazonium solution was added dropwise to the cooled amine solution. By this procedure we obtained light yellow products of analytical purity with elemental compositions corresponding to the expected triazines. (Scheme 1).

For the reaction product between 2-acetylbenzenediazonium chloride and *p*-toluidine the IR and NMR spectra were in accordance with the expected data for a triazene. (See Experimental).

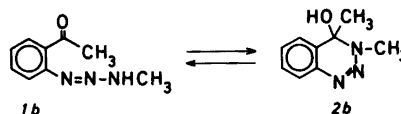


Scheme 1. Compound, R: *a*, *p*-CH<sub>3</sub>C<sub>6</sub>H<sub>4</sub>; *b*, CH<sub>3</sub>; *c*, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>; *d*, C<sub>2</sub>H<sub>5</sub>OCOCH<sub>2</sub>.

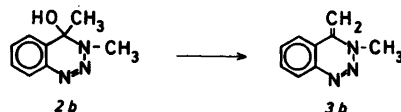
After several months in DMSO-*d*<sub>6</sub> solution the <sup>1</sup>H NMR spectrum was unchanged. In CDCl<sub>3</sub> partial decomposition had occurred after a few weeks.

The tautomeric structure *1a* was established from the <sup>13</sup>C NMR spectrum. The chemical shifts of the two quaternary carbon atoms in the *p*-tolyl group were found at 145.8 and 137.1 ppm. For a *p*-tolylidiazio group the chemical shifts are normally seen<sup>6,7</sup> at 146.3 and 138.8 ppm and for a *p*-tolylamino group at 139.3 and 132.6 ppm. This means that the product contains a *p*-tolylidiazio group and the structure is 1-*p*-tolyl-3-(2-acetylphenyl)-triazene (*1a*).

For the reaction product between 2-acetylbenzenediazonium chloride and methylamine the spectra were quite different. The IR spectrum in CHCl<sub>3</sub> and in KBr were different. In CHCl<sub>3</sub> the usually relatively sharp NH for triazines was seen at 3245 cm<sup>-1</sup> but in KBr, a large broad absorption at 3150 cm<sup>-1</sup> was found. At the same time the carbonyl stretching vibration at 1650 cm<sup>-1</sup> present in CHCl<sub>3</sub> solution was missing in the KBr spectrum. From that evidence it seemed obvious that the product precipitating from the reaction mixture was 3,4-dimethyl-4-hydroxy-3,4-dihydro-1,2,3-benzotriazine *2b* – the ring closed structure. The open chain triazene *1b* predominate in chloroform solution. (Scheme 2).



The NMR spectrum of the reaction product with methylamine showed both *1b* and *2b* present in CDCl<sub>3</sub> solution. The COCH<sub>3</sub> in *1b* was found at 2.55 ppm together with the C-4 methyl in *2b* at 1.84 ppm. The ratio between the two isomers was approximately 1:1. After standing overnight the ratio between *1b* and *2b* was unchanged, but doublets at 3.83 and 4.38 ppm corresponding to structure *3b*<sup>3</sup> appeared. (Scheme 3).



The rate of the dehydration process varied from one day to one week for full dehydration presumably due to varying amounts of impurities. This variation was also seen for *2c* and *2d*. Fong and Vaughan conducted the dehydration by adding neutral alumina to the chloroform solution.

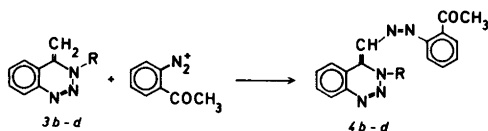
In DMSO- $d_6$  solution no signals corresponding to the triazene structure were seen and the dehydration reaction was much slower than in  $CDCl_3$ -solution. The NMR spectrum showed only one isomer namely **2b** and the methyl group at C-4 was found at 1.73 ppm. After about two weeks at room temperature the dehydration process to **3b** was complete.

The reaction product with benzylamine was different. The solid obtained from the reaction was the hydroxybenzotriazine **2c** seen from the IR-spectrum (KBr). In  $CDCl_3$  solution there was no hydroxybenzotriazine **2c** present but only triazene **1c**. In DMSO- $d_6$  solution there was no triazene but only hydroxybenzotriazine. After standing in  $CDCl_3$  solution for two weeks the dehydration was complete. During the same period only a few percent was dehydrated in DMSO- $d_6$ .

The reaction product with ethyl glycinate was dehydrated rapidly even in the crystalline state. In  $CDCl_3$  both triazene **1d** and hydroxybenzotriazine **2d** were present in the ratio 3:1. In DMSO- $d_6$  the hydroxybenzotriazine was the dominating species, but also the triazene and the dehydrated product **3d** were present. In  $CDCl_3$  the dehydration had proceeded to 50 % in 24h.

It seems plausible that the ring closed hydroxybenzotriazine is precursor for the methylenebenzotriazines. The dehydration proceeded only for **2b–2d** because the tautomeric structure of the corresponding triazenes, which must be expected to be an 1-aryl-3-alkyl-triazene,<sup>5</sup> makes the ring closure possible because N-3 is more nucleophilic than N-1. For the reaction product with *p*-toluidine the tautomeric structure was 1-*p*-tolyl-3-(2-acetylphenyl)-triazene, placing the most nucleophilic N too close to the acetyl group for ring closure.

The procedure used by Fong and Vaughan for coupling the diazonium ion and amine resulted in a mixture of the triazene, hydroxybenzotriazine and a bright red compound, not only for ethyl glycinate but also for methylamine and benzylamine. If the amine is added slowly into the diazonium chloride solution the red compound is the main product. For methylamine we have investigated its structure and found **4b** corresponding to a reaction between the first formed benzotriazine and another mole of diazonium ion. (Scheme 4).



The elemental analysis, MS, IR and NMR spectra were in accordance with structure **4b**. The <sup>1</sup>H NMR showed two methyl signals at 2.48 ppm and 3.91 ppm corresponding to CH<sub>3</sub>CO and CH<sub>3</sub>N and nine protons between 7.2 and 9 ppm. The <sup>13</sup>C NMR spectrum showed two methyl groups, one carbonyl carbon and fourteen closely lying signals in the aromatic region. Finally **4b** could be prepared by adding 2-acetylbenzenediazonium chloride to a solution of 4-methylene-3-methyl-3,4-dihydro-1,2,3-benzotriazine **3b** under neutral to basic conditions.

From the analogous reactions with benzylamine and ethyl glycinate, mixtures were obtained. The spectral data obtained was, however, in accordance with structures **4c** and **4d** as the main products. The reaction product obtained by Baines et al.<sup>2</sup> from the reaction between 2-acetylbenzenediazonium chloride and ethyl glycinate is probably best explained as **4d**. The triazene structure seems less likely, which is supported both by the absence of NH-stretching vibration in the IR-spectrum and the differences in the <sup>1</sup>H NMR chemical shift values for the ethyl group, compared to the other triazene shift-values reported.<sup>2</sup>

**Experimental.** The experimental equipment was reported earlier.<sup>8</sup> Melting points are uncorrected.

**General procedure for preparation of 4-hydroxy-3,4-dihydro-1,2,3-benzotriazines or 3-(2-acetylphenyl)triazenes.** A solution of 2-acetylbenzenediazonium chloride was prepared from 2-aminoacetophenone (0.1 mol), hydrochloric acid (0.3 mol) in water (100 ml) and sodium nitrite (0.1 mol) in water (30 ml). The diazonium chloride solution was added dropwise to a stirred mixture of amine (0.2 mol), sodium carbonate (0.1 mol) and water (100 ml) at 0 °C. After addition the mixture was stirred for 30 min the precipitate was filtered off, washed with cold water and dried.

**1-*p*-Tolyl-3-(2-acetylphenyl)-triazene 1a:** Yield 83 %, m.p. 74–76 °C. Anal. C<sub>15</sub>H<sub>15</sub>N<sub>3</sub>O: C, H, N. <sup>1</sup>H NMR(DMSO- $d_6$ ):  $\delta$  2.35 (3 H, s), 2.65 (3 H, s), 7.00–8.17 (8 H, m), 13.07 (1 H, b). <sup>13</sup>C NMR (DMSO- $d_6$ ):  $\delta$  202.1 145.8, 143.0 137.1, 134.5, 131.9, 129.6, 121.7, 124.4, 114.5, 28.7, 20.6. IR (CHCl<sub>3</sub>, cm<sup>-1</sup>): 3240 (m), 1650 (s), 1600 (m), 1570 (m), 1500 (s), 1460 (s). IR (KBr, cm<sup>-1</sup>): 3220 (m), 1630 (s), 1600 (m), 1570 (s), 1490 (s), 1450 (s).

**3,4-Dimethyl-4-hydroxy-3,4-dihydro-1,2,3-benzotriazine 2b:** Yield 72 %, m.p. 104–107 °C. Anal. C<sub>9</sub>H<sub>11</sub>N<sub>3</sub>O: C, H, N. <sup>1</sup>H NMR(DMSO- $d_6$ ):  $\delta$  1.73 (3 H, s), 3.53 (3 H, s), 6.60 (1 H, s), 7.30–7.70 (4 H, m). IR (KBr, cm<sup>-1</sup>): 3150 (s), 1445 (s), 1400 (m), 1240 (m), 1110 (s), 1010 (s).

IR, mixture of *1b* and *2b*, ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ): 3245 (m), 3000 (m), 1650 (s), 1605 (m), 1570 (m), 1500 (s).

**3-Benzyl-4-hydroxy-4-methyl-3,4-dihydro-1,2,3-benzotriazine 2c:** Yield 96 %, m.p. 78–79 °C. Anal.  $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}$ : C, H, N.  $^1\text{H}$  NMR ( $\text{DMSO}-d_6$ ):  $\delta$  1.65 (3 H, s), 5.12 (2 H, s), 6.84 (1 H, s), 7.25–7.60 (9 H, m).  $^1\text{H}$  NMR, structure *1c*, ( $\text{CDCl}_3$ ):  $\delta$  2.53 (3 H, s), 4.90 (2 H, s), 6.75–8.05 (9 H, m), 12.65 (1 H, s). IR, structure *1c*, ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ): 3240 (m), 3000 (m), 1650 (s), 1600 (m), 1570 (s), 1500 (s), 1450 (m). IR (KBr,  $\text{cm}^{-1}$ ): 3240 (s), 1500 (s), 1450 (s), 1425 (s), 1320 (s).

**3-Ethoxycarbonylmethyl-4-hydroxy-4-methyl-3,4-dihydro-1,2,3-benzotriazine 2d:** Yield 86 %, 65–67 °C. Anal.  $\text{C}_{12}\text{H}_{15}\text{N}_3\text{O}_3$ : C, H, N.  $^1\text{H}$  NMR, mixture of *1d* and *2d*, ( $\text{CDCl}_3$ ):  $\delta$  1.30 (3 H, t), 1.75 (0.7 H, s), 2.60 (2.3 H, s), 4.25 (2 H, q), 4.53 (1.5 H, s), 4.70 (0.5 H, d), 4.95 (0.3 H, s), 6.8–8.00 (4 H, m), 12.7 (0.7 H, s, broad).

**General procedure for preparation of azomethylenedihydrobenzotriazines 4b–4d:** A solution of 2-acetylbenzenediazonium chloride is prepared as described. Sodium acetate (0.2 mol) in water (20 ml) was added to the solution. The amine (0.2 mol) dissolved in water (100 ml) is dropped slowly into the cold diazonium ion solution and the red precipitate filtered off, washed with cold water and dried.

**4-(2-acetylphenylazo)methylene-3-methyl-3,4-dihydro-1,2,3-benzotriazine 4b:** Yield 89 %, m.p. 142 °C. Anal.  $\text{C}_{17}\text{H}_{15}\text{N}_5\text{O}$ : C, H, N.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  2.48 (3 H, s), 3.91 (3 H, s), 7.25–8.00 (8 H, m), 9.00 (1 H, broad).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  151.9, 139.2, 137.7, 136.6, 132.9, 132.6, 132.5, 131.1, 130.2, 129.9, 128.1, 124.3, 124.0, 119.3, 117.6, 42.2, 32.2. IR ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ): 3000 (m), 1680 (s), 1640 (m), 1580 (s), 1550 (s).

**4-(2-acetylphenylazo)methylene-3-benzyl-3,4-dihydro-1,2,3-benzotriazine 4c:** Yield 53 %, m.p. 93–104 °C. Anal.  $\text{C}_{23}\text{H}_{19}\text{N}_5\text{O}$ : C, H, N.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta$  2.33 (2 H, s), 2.57 (1 H, m), 5.49 (1.3 H, s), 6.16 (0.7 H, s), 6.90–9.15 (14 H, m). IR ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ): 3000 (m), 1675 (m), 1640 (m), 1580 (s), 1550 (s), 1490 (s). MS *m/e* (% of base peak): 381(2) $\text{M}^+$ , 353(25), 325(18), 222(42), 221(36), 220(20), 219(36), 218(12), 135(62), 134(20), 133(100), 132(67), 131(68), 120(87), 106(11), 105(18), 104(20), 103(9), 92(67), 91(76), 90(16), 89(27), 78(11), 77(22), 76(13), 65(36), 63(11), 51(16).

**4-(2-acetylphenylazo)methylene-3-ethoxycarbonylmethyl-3,4-dihydro-1,2,3-benzotriazine 4d:** Yield 62 %, m.p. 110–113 °C. Anal. Found: C 63.09; H 5.08; N 18.23. Calc. for  $\text{C}_{20}\text{H}_{19}\text{N}_5\text{O}_3$ : C 63.65; H 5.07; N 18.56.  $^1\text{H}$  NMR, mixture,

( $\text{CDCl}_3$ ):  $\delta$  0.88–1.58 (3 H, m), 2.60 (3 H, s), 3.86–4.82 (3 H, m), 5.5 (1 H, s), 6.4–8.6 (9 H, m). IR ( $\text{CHCl}_3$ ,  $\text{cm}^{-1}$ ): 3000 (m), 1750 (s), 1680 (m), 1640 (m), 1590 (s), 1570 (m), 1555 (s). MS *m/e* (% of base peak): 378(20), 377(34) $\text{M}^+$ , 376(14), 349(14), 305(14), 304(34), 288(26), 287(17), 286(43), 278(29), 143(25), 131(100), 120(43), 117(17), 106(20), 105(25), 92(20), 91(29), 77(58), 65(29), 43(37).

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