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Diazotization of 2,6-Diaminobenzothiazole. A New Process for the Preparation of 2-Chlorobenzothiazole Reactive Azo Dyes

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ABSTRACT

The diazotization of 2,6-diaminobenzothiazole was studied. In contrast with the literature data, it was found that the two amino groups can be diazotized to yield a 2-chlorobenzothiazole-6-diazonium intermediate when reacted in a standard manner. A small comparative study on the diazotization of 6-substituted 2-aminobenzothiazoles using these standard conditions is presented. Finally, the usefulness of the reaction for the preparation of 2-chlorobenzothiazole reactive dyes is outlined.

1 INTRODUCTION

The diazotization of substituted 2-aminobenzothiazoles has been well studied.[1] In many cases, the amino group, which is in equilibrium with an imino tautomer (Scheme 1), is difficult to diazotize and the obtained diazonium salt is often unstable, leading to hydrolysis and decomposition products.[1,2] The standard diazotization methods often have to be adjusted to match the solubility and reactivity of the amine or to minimize the decomposition of the diazonium salt. There appears to be no general method to prepare the desired diazonium salt in good yield.[1] A literature review, whilst showing numerous studies on the diazotization of substituted 2-aminobenzothiazoles, afforded only two references pertaining to the diazotization of 2,6-diaminobenzothiazole.[3,4] In the first,[3] dating from 1935, only the 6-amino group was diazotized, using 1.2 equivalents of

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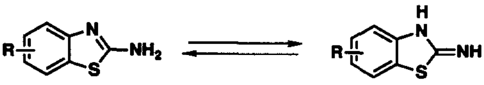


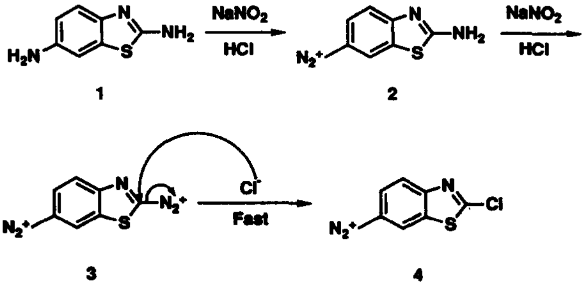
Scheme 1

sodium nitrite in hydrochloric acid. The second,[4] dating from 1937, claims that only the 6-amino group of 2,6-diaminobenzothiazole can be diazotized and that the 2-amino group is unreactive because of the imino tautomer. These results may have inhibited further studies on the subject. In this paper, the authors report their findings on the diazotization of 2,6-diaminobenzothiazole using standard conditions and also compare the reactivity of the 2-amino group with those of some other 6-substituted 2-aminobenzothiazoles. The authors also report on some coupling products of the diazonium salt obtained and on the usefulness of the reaction for the preparation of 2-chlorobenzothiazole reactive azo dyes.

2 RESULTS AND DISCUSSION

During these studies on the diazotization of substituted 2-aminobenzothiazoles, it was found that when 2,6-diaminobenzothiazole 1 is diazotized in a standard manner, using 2 equivalents of sodium nitrite in 6 M hydrochloric acid at 0°C followed by the addition of hexafluorophosphoric acid, the hexafluorophosphate salt of 2-chlorobenzothiazole-6-diazonium 4 is obtained in 61% yield (Scheme 2). The diazonium hexafluorophosphate salt seems relatively stable. After 24 h under vacuum, it shows an unchanged infrared spectrum. The structure of the intermediate was shown by reducing the diazonium salt to 2-chlorobenzothiazole with hypophosphorous acid[5] and comparing with an authentic sample obtained from Aldrich Chemical Company, Inc.

When the diazotization mixture was quenched with hypophosphorous



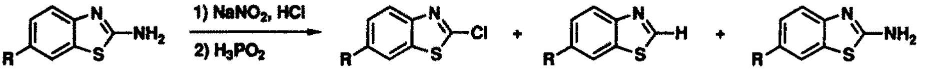
Scheme 2

acid, 2-chlorobenzothiazole was obtained in 49% yield, together with 2-aminobenzothiazole in 26% yield. This result shows that the 2-amino group is indeed, less reactive than the 6-amino group.

The reaction is outlined in Scheme 2. Because of its higher reactivity, the 6-amino group is diazotized first. The slower diazotization of the 2-amino group then takes place, followed by a rapid chloride displacement of nitrogen at the activated 2-position. The displacement reaction does not seem to proceed by a displacement of ammonia because both 2,6-diaminobenzothiazole and 2-amino-6-nitrobenzothiazole were recovered unchanged after stirring in 6 M hydrochloric acid.

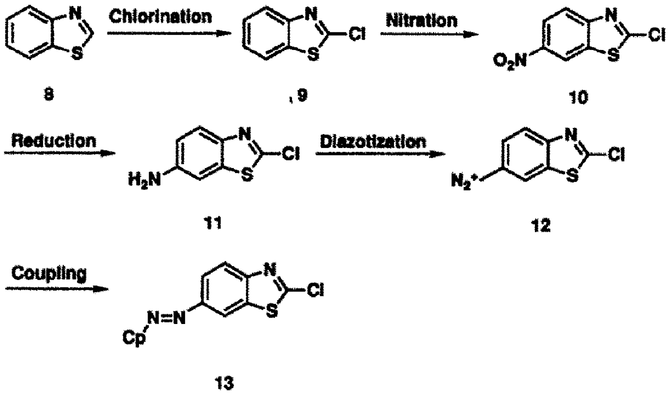
Substitutions of this type on diazonium ions are known as the Sandmeyer reaction but they require copper (II) chloride as the reagent (or copper (II) and a source of chloride ion) and they proceed through a mechanism involving radical intermediates and redox reactions.[6-8] Most 2-chlorobenzothiazole derivatives prepared from the corresponding 2-aminobenzothiazoles use the Sandmeyer conditions[2,9] but since carbon-2 can act as a nucleophilic acceptor if properly activated, the reaction can proceed without any catalyst and there are some procedures in the literature which take advantage of this uncatalyzed reaction for the preparation of substituted 2-chlorobenzothiazoles.[10-15]

In contrast with the observations of Drozdov[4] in which he claims that the 2-amino group of 2,6-diaminobenzothiazole cannot be diazotized, the authors found that it was the most reactive 2-amino group in a series of four 2-aminobenzothiazole derivatives (Scheme 3). In this short series, the diamino derivative **1** seems to achieve the delicate balance between reactivity of the 2-amino group towards diazotization and activation of carbon-2 towards nucleophilic attack, which increases with the presence of the conjugated electron withdrawing diazonium group in the benzene ring. In the case of compounds **5** and **6** with R = H or NO_2, the amine is not soluble/reactive enough (high recovery of starting material) but carbon-2 seems to be adequately activated towards nucleophilic attack once the diazotization has occurred because all of the diazonium ion present reacted to form the 2-chlorobenzothiazole derivative and no reduction products were isolated



1 R = NH_2	R = H	49%	—	26%
5 R = H	R = H	26%	—	45% (starting material)
6 R = NO_2	R = NO_2	20%	—	68% (starting material)
7 R = MeO	R = MeO	13%	12%	46% (starting material)

Scheme 3

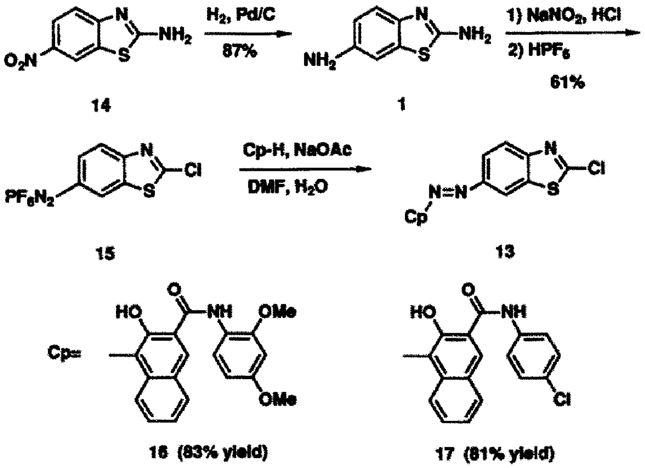


Scheme 4

after reaction with hypophosphorous acid. In the case of compound **7**, with R = MeO, the material also has a low solubility/reactivity towards diazotization but carbon-2 is now deactivated by the conjugated, electron donating, methoxy group since about half of the diazotized material did not undergo the chloride substitution and was reduced in the second step.

The authors thought that this chloride displacement reaction could be useful for the preparation of 2-chlorobenzothiazole reactive azo dyes of formula **13** (Scheme 4) where Cp is a coupler residue of a naphthol, phenol, pyrazolone, aniline or other standard coupling components. These reactive dyes are useful for the colouration of fibers such as cellulose, polypeptides, polyesters and nylons in a wide range of colors.[16-21]

The reactive dyes can be prepared in five steps from the commercially available benzothiazole as described in Scheme 4. Because the reaction



Scheme 5

described earlier leads to a diazotization and chlorination in a single step, this allows a shorter, more economical process for the preparation of the dyes. They can be prepared in three steps from the commercially available 2-amino-6-nitrobenzothiazole **14** (Scheme 5). For example, dyes **16** and **17** were prepared in excellent yield by this process and they were fully characterized by ^{1}H-NMR spectroscopy, mass spectrometry, IR spectroscopy, UV/visible spectroscopy and elemental analysis.

3 EXPERIMENTAL

3.1 Instrumentation

Melting points were determined using a Thomas Hoover capillary melting point apparatus and are uncorrected. ^{1}H-NMR spectra were obtained at 400 MHz with a Bruker AMX-400 instrument. Mass spectrometry was carried out with a Finnigan instrument by the electron impact method. IR spectra were recorded on a Nicolet 20DX FT-IR spectrophotometer. UV/visible spectra measurements were performed using a Hewlett-Packard HP 8450A spectrophotometer.

3.2 Preparation of 2,6-diaminobenzothiazole

One gram of 10% palladium on charcoal was added to a stirred suspension of 10·1 g of 2-amino-6-nitrobenzothiazole in 250 ml ethanol and hydrogen was bubbled into the solution for 22 h. The mixture was then filtered on celite and and the celite was washed with 600 ml methanol by portions. After evaporation of the solvent and recrystallization from acetonitrile, 7·47 g (87%) of 2,6-diaminobenzothiazole was obtained. The material had a melting point of 204–206°C (lit.[3]; 207°C) and was fully characterized by ^{1}H-NMR and IR spectroscopy.

3.3 Preparation of 2-chlorobenzothiazole-6-diazonium hexafluorophosphate

Sodium nitrite (3·07 g) dissolved in 10 ml water was slowly added to 3·50 g of 2,6-diaminobenzothiazole in suspension in 60 ml 6 M aqueous hydrochloric acid at 0°C under nitrogen. After 1·5 h stirring, 1·2 g urea dissolved in water was added and the solution was stirred for 10 min. The mixture was filtered and 16 ml of 60% aqueous hexafluorophosphoric acid was added to the cold filtrate. The precipitate was filtered, washed with cold water and dried under high vacuum. 4·42 g (61%) of 2-Chlorobenzothiazole-6-diazonium hexafluorophosphate was obtained as an orange-red solid. IR (Nujol): $\nu =$ 2267, 1586, 1549, 1415, 1341, 1111, 1055, 1030 cm^{-1}.

3.4 Reduction of 2-chlorobenzothiazole-6-diazonium hexafluorophosphate

2-Chlorobenzothiazole-6-diazonium hexafluorophosphate (1·89 g) was added to 80 ml water at 0°C and 4·7 ml of 50% aqueous hypophosphorous acid was added dropwise over 20 min while stirring. After 45 min stirring, the flask was allowed to stand in the refrigerator with a loose stopper for 16 h. The solution was warmed up to room temperature with stirring for 2 h and aqueous sodium hydroxide was added until a pH of 9 was reached. The mixture was extracted twice with 250 ml ether and the ether phases were combined, washed three times with 100 ml water and dried over magnesium sulfate. After evaporation of the solvent, the red oil was purified by flash chromatography with hexanes/ethyl acetate to give 0·338 g (36%) of 2-chlorobenzothiazole, identical to a sample obtained from Aldrich Chemical Company, Inc. by TLC, ^{1}H-NMR and IR spectroscopy.

3.5 Direct preparation of 2-chlorobenzothiazole from 2,6-diaminobenzothiazole

2,6-Diaminobenzothiazole was diazotized as above and 10 equivalents of hypophosphorous acid were directly added to the mixture after stirring for 1·5 h. The reduction was then carried out as described earlier and 2-chlorobenzothiazole was isolated in 49% yield, together with 2-aminobenzothiazole in 26% yield (Scheme 3).

3.6 Procedure used for the comparative study

The amines **5**, **6** and **7** were diazotized as described in the direct preparation of 2-chlorobenzothiazole from 2,6-diaminobenzothiazole, using 1·05 equivalents of sodium nitrite instead of 2·1 equivalents. The reduction was carried out using 5 equivalents of hypophosphorous acid instead of 10 equivalents. After separation, the products were characterized by ^{1}H-NMR spectroscopy, mass spectrometry and IR spectroscopy. The yields are reported in Scheme 3.

3.7 Preparation of the reactive azo dyes 16 and 17

N-(2,4-Dimethoxyphenyl)-3-hydroxy-2-naphthalenecarboxamide (2·91 g) (obtained from Hoechst and recrystallized from acetonitrile) dissolved in 30 ml *N*,*N*-dimethylformamide was added to 2·10 g 2-chlorobenzothiazole-6-diazonium hexafluorophosphate in 10 ml *N*,*N*-dimethylformamide at 0°C. Sodium acetate (1·47 g) dissolved in 7 ml water was slowly added. The temperature was allowed to rise to 25°C and after 19 h stirring, the suspension was filtered and the solid washed with *N*,*N*-dimethylformamide, water and acetone. Azo pigment **16** (2·66 g, 83%) was obtained after drying under high vacuum. mp 255–257°C. IR (KBr): $\nu = 3441$, 3229, 1671, 1601, 1537, 1497, 1449, 1279, 1262, 1219, 1179, 1155, 1012 cm^{-1}. UV/visible (1-methyl-2-pyrrolidinone): $\lambda(\varepsilon) = 370$ (13 200 liters $\mathrm{mol}^{-1}\,\mathrm{cm}^{-1}$), 556 nm (20 100 liters $\mathrm{mol}^{-1}\,\mathrm{cm}^{-1}$). ^{1}H-NMR (DMSO-d6, 80°C): $\delta = 16{\cdot}4$ (broad s, 1H, OH), 11·6 (broad s, 1H, NH), 8·89 (s, 1H, H_1 of naphthalenecarboxamide), 8·61 (d, 1H, $J_{5-7} = 2{\cdot}1$ Hz, H_7 of benzothiazole), 8·54 (d, 1H, $J = 8{\cdot}1$ Hz, H_5 or H_8 of naphthalenecarboxamide), 8·18 (d, 1H, $J_{3-5} = 3{\cdot}0$ Hz, H_3 of phenyl), 8·07 (A of AB, 1H, $J_{4-5} = 8{\cdot}8$ Hz, H_4 of benzothiazole), 7·99 (coupled B of AB, 1H, $J_{4-5} = 8{\cdot}8$ Hz, $J_{5-7} = 2{\cdot}2$ Hz, H_5 of benzothiazole), 7·95 (d, 1H, $J = 7{\cdot}4$ Hz, H_5 or H_8 of naphthalenecarboxamide), 7·71 (~td, 1H, $J \approx 7{\cdot}6$ and 1 Hz, H_6 or H_7 of naphthalenecarboxamide), 7·52 (~td, 1H, $J \approx 7{\cdot}6$ and 1 Hz, H_6 or H_7 of naphthalenecarboxamide), 7·03 (d, 1H, $J_{5-6} = 8{\cdot}9$ Hz, H_6 of phenyl), 6·67 (dd, 1H, $J_{5-6} = 8{\cdot}9$ Hz, $J_{3-5} = 3{\cdot}1$ Hz, H_5 of phenyl), 3·97 (s, 3H, OCH_3), 3·76 ppm (s, 3H, OCH_3). MS: $m/e = 520$, 518 (M^+), 368, 366 (M^+–C_6H_3 $(OCH_3)_2NH$). Analysis, calculated for $C_{26}H_{19}ClN_4O_4S$: C 60·17, H 3·69, Cl 6·83, N 10·80, S 6·18; found: C 59·04, H 3·79, Cl 7·03, N 10·67, S 5·81.

Similar conditions were used for the preparation of the reactive azo dye **17** and it was obtained in 81% yield. mp 288–288°C. IR (KBr): $\nu = 3453$, 3243, 1678, 1608, 1593, 1553, 1535, 1489, 1449, 1329, 1283, 1263, 1202, 1175, 1157, 1015, 818 cm^{-1}. UV/visible (1-methyl-2-pyrrolidinone): $\lambda(\varepsilon) = 363$ (11 400 liters $\mathrm{mol}^{-1}\,\mathrm{cm}^{-1}$), 547 nm (17 900 liters $\mathrm{mol}^{-1}\,\mathrm{cm}^{-1}$). ^{1}H-NMR (DMSO-d6, 80°C): $\delta = 16{\cdot}3$ (broad s, 1H, OH), 11·3 (broad s, 1H, NH), 8·73 (s, 1H, H_1 of naphthalenecarboxamide), 8·66 (d, 1H, $J_{5-7} = 2{\cdot}0$ Hz, H_7 of benzothiazole), 8·59 (d, 1H, $J = 8{\cdot}1$ Hz, H_5 or H_8 of naphthalenecarboxamide), 8·08 (A of AB, 1H, $J_{4-5} = 8{\cdot}8$ Hz, H_4 of benzothiazole), 8·04 (coupled B of AB, 1H, $J_{4-5} = 8{\cdot}8$ Hz, $J_{5-7} = 2{\cdot}1$ Hz, H_5 of benzothiazole), 7·95 (d, 1H, $J = 7{\cdot}5$ Hz, H_5 or H_8 of naphthalenecarboxamide), 7·79 (AA′ of AA′BB′, 2H, H_2, H_6 or H_3, H_5 of phenyl), 7·72 (~td, 1H, $J \approx 7{\cdot}1$ and 1 Hz, H_6 or H_7 of naphthalenecarboxamide), 7·53 (~td, 1H, $J \approx 7{\cdot}5$ and 1 Hz, H_6 or H_7 of naphthalenecarboxamide), 7·43 ppm (BB′ of AA′BB′, 2H, H_2, H_6 or H_3, H_5 of phenyl). MS: $m/e = 494$, 492 (M^+), 368, 366 (M^+–ClC_6H_4NH). Analysis, calculated for $C_{24}H_{14}Cl_2N_4O_2S$: C 58·43, H 2·86, Cl 14·37, N 11·36, S 6·50; found: C 58·27, H 2·91, Cl 15·12, N 11·30, S 6·54.

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