Structure and Synthesis of the Metribuzin Blue Dye. Synthesis and Reactions of 2,5-Dihydrazino-1,3,4-thiadiazole and its Derivatives

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Received November 7, 1989

A blue pigment which sometimes accompanies the manufacture of the triazine herbicide metribuzin (5) was identified as the novel thiadiazole formazan 10 which arises from the reaction of two impurities 3 and 7. The latter compound is a keto acid derivative of 2,4-dihydrazinothiadiazole which in turn is an impurity in carbonothioic dihydrazide. Compound 7 has the interesting property of undergoing a facile oxidative decarboxylation in the presence of alcohols to form hydrazonate esters and in the presence of aliphatic amines to form red amidrazone dyes 9. The N-substituted dyes can be oxidized to ditriazolothiadiazoles 12.

During the manufacture of 4-amino-6-(1,1-dimethylethyl)-3-methylthio-1,2,4-triazin-5(4H)-one (metribuzin) (5) a minor side reaction sometimes occurs and results in metribuzin with an undesirable blue color. Since the occurrence of blue color seemed to be random and could not be controlled by manipulation of plant conditions or duplicated in the laboratory, an investigation of the phenomenon was undertaken.

Compound 5 is made by reaction of an aqueous solution of the sodium salt of triazinethione 4 with methyl bromide [1] (Scheme 1). A singular aspect of "technical" 4 is that dissolution in aqueous base produces a dark green color due to the presence of a small amount of an unknown impurity and it was observed that on rare occasions these green solutions would turn yellow and precipitate a small amount of the blue dye when allowed to stand for a few days in the presence of air. The dye obtained in this way contained at least two sodium atoms. The elemental analysis and mass spectrum of the free acid suggested a compound with MW 494 and a formula $C_{19}H_{30}N_{10}S_2O_2$. These analyses and further losses due to the dye's instability in solution or in contact with silica gel consumed the available material and since it no longer formed by adding air to plant solutions of 4 it was necessary to develop an empirical synthesis.

Scheme 1
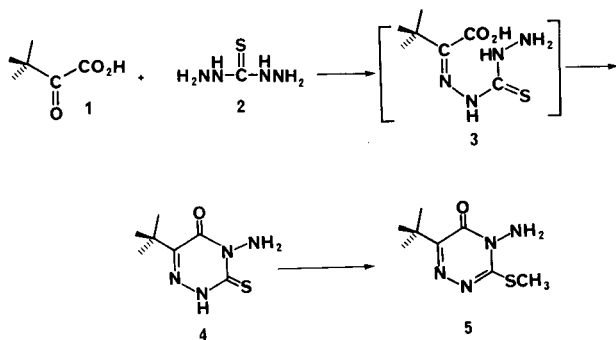
It was supposed that the blue dye could come from the air oxidation of the green impurity, and further, that the green compound might have been formed in an oxidation reaction of 2, given the known tendency of hydrazides and thioamides to oxidize readily [2,3]. Consequently, a solution of 2 hydrochloride was oxidized with hydrogen peroxide and the resulting solution reacted with keto acid 1 (Scheme 2). The product was a mixture of 4 and a new substance $C_{14}H_{22}N_6O_4S$ believed to have structure 7 on the basis of spectral and analytical data, and the known ability of derivatives of 2 to form thiadiazoles [4,5]. An alternative structure for 7 would be the mercaptotriazole isomer related to "purpald" but that structure was eliminated on the basis of ^{13}C nmr of the methyl ester of 7.

Compound 7, a derivative of the heretofore unknown 2,5-dihydrazino-1,3,4-thiadiazole 6, proved to be the desired impurity responsible for the green color of 4 in base. To our consternation, however, oxidation of 7 in base in the presence or absence of 4 produced no blue dye but rather a mixture of purple dyes which have not been characterized. Many subsequent attempts to make the blue dye failed until it was realized that the dye was more likely to form from air oxidation of 4 when 4 was made under conditions of abnormally high pH or low temperature. These conditions would suppress triazine ring formation and so it became apparent that small quantities of 3 would sometimes be present and that might be the missing factor in the formation of the blue dye. Indeed, when hydrazone 3 (easily made by reacting 1 and 2 at 0°) was placed in solution with 7 at elevated pH and air oxidized the elusive blue dye was formed in modest but significant amounts (Scheme 2). The reaction produced a number of other products, one of which was isolated and identified as being the azo compound 11. While 11 was a major product in several of the early blue dye syntheses, it was not produced in later duplicate reactions using different starting materials. The reason for this is unknown.

Scheme 2
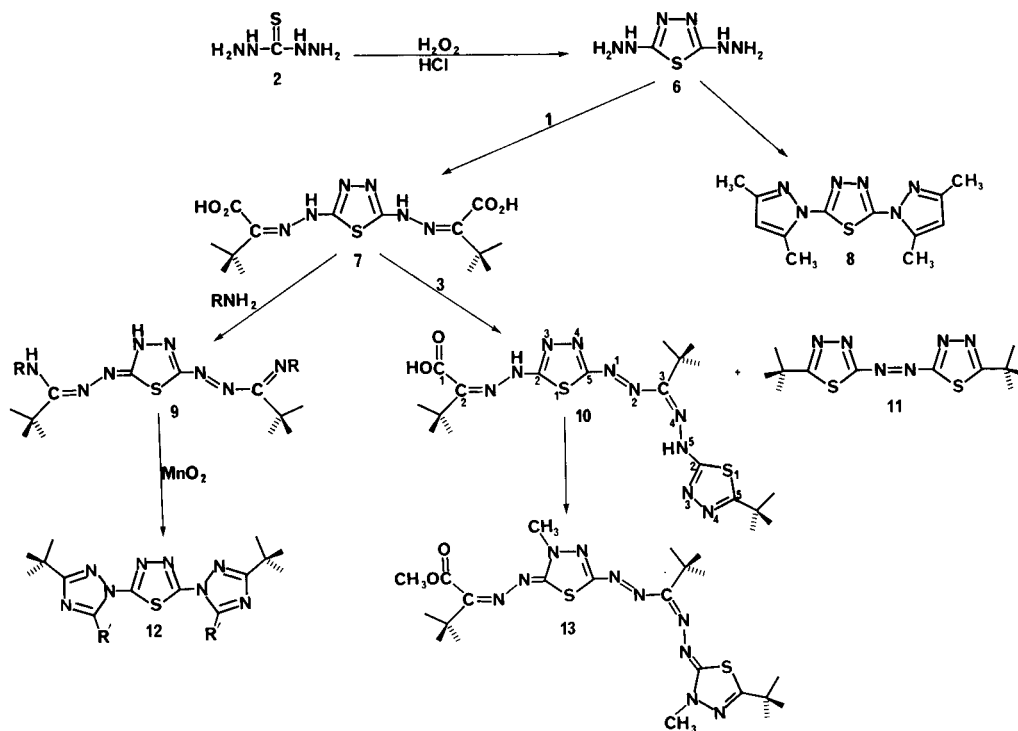
On the basis of the spectral and analytical data for the blue dye, structure **10** seemed to be a reasonable possibility. This was confirmed by X-ray crystallography of **13**, the trimethyl derivative of **10**, and has been reported elsewhere [6]. Compound **10** is envisioned as arising from an initial addition of the amino group of keto-acid hydrazone **3** to bis hydrazone **7** followed by oxidation, decarboxylation and then a second, intra-moleuclar reaction to form the second thiadiazole ring by a similar oxidative decarboxylation process [7].

In the course of trying to prepare the blue dye it was noticed that bishydrazone **7** underwent a dramatic reaction with ammonia, in the presence of air, turning green then rapidly red-brown and finally depositing a bright red compound. This turned out to be a general reaction of **7** with primary amines (Scheme 2) and the bisamidrazone structure **9** is proposed for these compounds. Subsequent experiments showed that a notable yield increase was possible if the reactions were run in alcohol with manganese dioxide. The tautomeric form shown is suggested due to the presence of two different methyl groups in the proton nmr spectrum and the observation that secondary amines do not form red products.

Further oxidation with manganese dioxide in hot toluene of the red compounds with R = R'-CH₂ gave the ditriazolothiadiazoles **12**. The compounds undoubtedly arise from the N-formyl or acyl intermediates, which cyclize to

the triazoles [8]. The oxidation of alkyl amines to amides is known [9,10] but the reaction seems not to have previously been used to form triazoles.

In the absence of amines, reaction of **7** with manganese dioxide in ethanol afforded the analogous ethoxy compound **14** (Scheme 3) which could be converted to **9** by reaction with amines. The methyl ester of **7** underwent a simple oxidation with manganese dioxide in methylene chloride to give the $\triangle^3$-thiadiazoline diester **15**.

Scheme 3
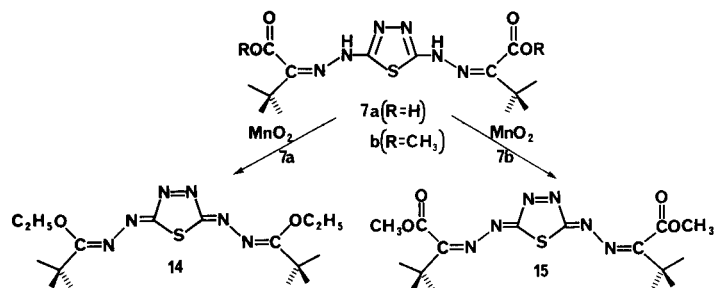
While a few mono-hydrazino-1,2,4-thiadiazoles are known [11,12,13], I can find no literature reference to the dihydrazine **6** except a paper [14], which described the oxidation product of acetone thiosemicarbazone as being the acetone bishydrazone of **6**. This structure assignment was later shown [15] to be in error because the product was actually a 1,2,4-thiadiazolidine. That **6** is unknown is pre-

haps not surprising considering that **6** decomposes rapidly as the free base and more slowly in solution as the dihydrochloride, partly by isomerization to 3-hydrazino-4-amino-5-mercapto-1,2,4-triazole ("purpald") (hplc evidence). In spite of the instability of **6**, it can be stored dry and undergoes typical hydrazine reactions such as the formation of dipyrazolothiadiazole **8** on reaction with pentanedione.

The mechanism for the formation of **6** is unknown, but some possibilities are suggested in Scheme 4. Oxidation of carbonothioic dihydrazide **2** with peroxide seems likely to produce the *S*-oxide **16** [16] which after protonation to the iminosulfenic acid could react with a second molecule of **2** in several ways to form, for example, triaminoguanidine **17** or the bisdihydroformazan disulfide **18** which could go to **17** by reaction with **2** or by rearrangement (cyclization and ring opeing to **20**) followed by loss of sulfur. These various pathways seem convergent on a common intermediate, thiadiazoline **19**, which can lose a molecule of hydrazine to form thiadiazole **6**.

Scheme 4
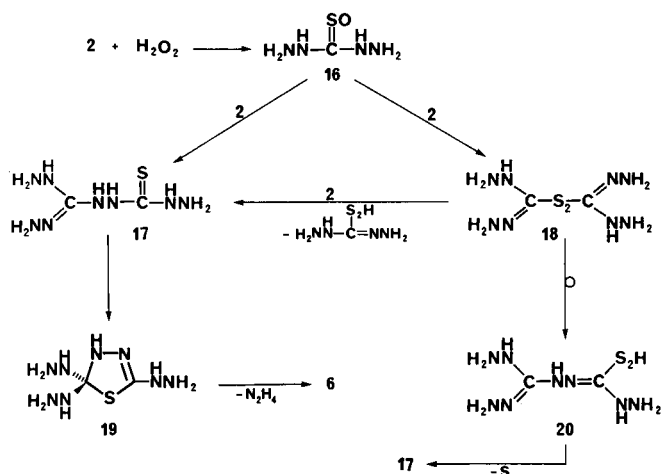
EXPERIMENTAL

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. The nmr spectra were recorded on a Varian VXR 300S spectrometer, the ms spectra on a Nicolet model 740 spectrometer and the ms spectra on a Finnigan model 450 gc/ms at 50 eV.

2-(1-Carboxy-2,2-dimethylpropylidene)carbonothioic Dihydrazide (3).

To a 5° solution of carbonothioic dihydrazide **2** (106 g, 1.0 mole) in water (1 ℓ) containing 100 g of concentrated hydrochloric acid was rapidly added a 6.5% solution of keto acid **1** sodium salt [19] also at 5°. The mixture was stirred ½ hour, filtered and washed with water (1 ℓ). The compound can be dried in air or vacuum without heating but was normally used immediately without drying or purification. It is soluble in bicarbonate as expected and an attempt to crystallize it from ethanol gave pure triazine **4**. Further characterization was deemed unnecessary.

2,5-Dihydrazino-1,3,4-thiadiazole Dihydrochloride (6) [16].

In a 5 ℓ round bottom flask or 4 ℓ beaker was placed ice (500 g), water (400 ml), concentrated hydrochloric acid (300 g) and carbonothioic dihydrazide (159 g, 1.5 mole). Hydrogen peroxide (30%) was added at a rate of 11 g (in one portion) every 15 minutes while the solution was mechanically stirred and maintained at a temperature of 0-5° with a dry ice-2-propanol bath. After 3 hours, the peroxide addition rate was raised to 16 g every 15 minutes. When all of the peroxide was added (330 g, 2.9 moles) the flask was packed in ice and allowed to finish reacting overnight then filtered. If the mixture was stirred during the overnight period, the solid by-product was obtained as a black powder (28 g) [20] while no stirring gave a curious orange-brown plastic sponge which can be lifted out of a beaker in one piece. The aqueous solution was stirred for one hour with 35 g of carbon, filtered, and poured into a shallow 34 x 22 cm enamel pan and allowed to evaporate for about 24 hours until a volume of 900 ml was achieved. The solution was cooled in an ice bath and treated slowly with lithium chloride (165 g) to salt out the product. The cold solution was filtered, washed with cold 20% hydrochloric acid (40 ml) then 200 ml of methanol. The filter cake was placed in about 500 ml of methanol, stirred for one hour and re-filtered to give about 48 g of off-white solid (mp 189° dec) (28% crude yield). The product usually contains some purpald hydrochloride but is sufficiently pure for further reactions. The compound can be crystallized by dissolving in a minimum amount of water (about 3.6 ml/g) and adding two times the volume of acetic acid (gives mp 193°); ir (potassium bromide): 3300, 1685, 1585, 1475, 1125 cm^{-1}; ms: m/e 146 (M$^+$-2HCl), 36 (base peak); uv (methanol): λ max 280 nm; ^{13}C nmr (DMSO-d$_6$) δ 163.346.

Anal. Calcd. for C$_2$H$_8$N$_6$SCl$_2$: C, 10.96; H, 3.65; N, 38.37; Cl, 32.39. Found: C, 10.98; H, 3.69; N, 38.27; Cl, 32.44.

2,5-Bis[2-(1-carboxy-2,2-dimethylpropylidene)hydrazino]-1,3,4-thiadiazole (7a).

Carbonothioic dihydrazide (159 g, 1.5 moles) was oxidized as described above, filtered and treated with 1911 g (1 mole) of a 6.8% aqueous solution of keto acid **1** with vigorous stirring. The mixture was then heated at 70° for 2 hours at pH about 1, then cooled, filtered, and the solid washed with about 1 ℓ of water. After drying, the solid (160 g), which is a mixture of **7** and triazine **4** was triturated with enough hot 95% 2-propanol (about 1500 ml) to remove triazine **4**. Filtration gave crude thiadiazole hydrazone **7**, 90 g (22%) (mp 219° dec), which is pure enough for further reactions. An analytical sample can be obtained by crystallization from dimethylformamide-acetic acid to give a product with mp 223° dec; ir (potassium bromide): 3400, 3160, 1550 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 1.20 (s, 9H); ms: m/e 371 (HM$^+$), 84 (base peak); uv (methanol): λ max 340 nm.

Anal. Calcd. for C$_{14}$H$_{22}$N$_6$SO$_4$: C, 45.39; H, 5.99; N, 22.69; S, 8.66. Found: C, 45.25; H, 5.98; N, 22.62; S, 8.63.

2,5-Bis[2-(1-carbomethoxy-2,2-dimethylpropylidene)hydrazino]-1,3,4-thiadiazole (7b).

To **6** dihydrochloride (4.4 g, 0.02 mole) in 50 ml of water was added **1** methyl ester (7.2 g, 0.05 mole) in methanol (15 ml). After stirring for one hour, the solid was filtered, washed with water, 2-propanol, and toluene then recrystallized from methanol to give 6.9 g (87%) of pale yellow product, mp 198-199°; ^{13}C nmr

(deuteriochloroform): δ 28.63, 37.28, 51.88 (OCH₃) 142.14 (propylidene), 163.45 (C-2,5 or CO), 164.04 (CO or C-2,5); ¹H nmr (deuteriochloroform): δ 1.26 (s, 9H), 3.83 (s, 3H); ms: m/e 398 (M⁺), 141 (base peak); uv (methanol): λ max 334 nm; ir (potassium bromide): 1734 cm⁻¹ (CO), 1550 cm⁻¹.

Anal. Calcd. for C₁₆H₂₆N₆SO₄: C, 48.22; H, 6.58; N, 21.09; S, 8.05. Found: C, 48.34; H, 6.48; N, 21.01; S, 7.36.

2,5-Bis(3,5-dimethylpyrazolo)-1,3,4-thiadiazole (8).

To dihydrazinothiadiazole hydrochloride (6) (4.4 g, 0.02 mole) in water (50 ml) was added a 60° solution of 2,4-pentanedione (4.4 g, 0.044 mole) in ethanol (40 ml). The mixture was stirred for 2 hours, filtered, washed with ethanol and the solid chromatographed on silica gel (50 g) eluting with toluene. The chromatographed product was recrystallized from ethyl acetate to give 3.9 g (71%) of white crystals, mp 171-172°; ¹H nmr (deuteriochloroform): δ 2.20 (s, 3H), 2.67 (s, 3H), 5.96 (s, 1H); ms: m/e 274 (M⁺), 95 (base peak); ¹³C nmr (deuteriochloroform): δ 31.467 (CH₃), 109.946 (C-4), 142.183 (C-5), 152.490 (C-3), 161.266 (C-2,5).

Anal. Calcd. for C₁₂H₁₄N₆S: C, 52.53; H, 5.15; N, 30.64; S, 11.69. Found: C, 52.52; H, 5.09; N, 30.59; S, 11.76.

2-(1-Imino-2,2-dimethylpropylazo)-5-[2-(1-amino-2,2-dimethylpropylidene)-1-hydrazono]-4H-△²-1,3,4-thiadiazoline (9a, R = H).

Method A.

Hydrazone 7 (3.7 g, 0.01 mole) was reacted exactly as described for compound 9b except 10 g of concentrated ammonium hydroxide was used instead of methyl amine. Workup gave 2.0 g (64%) of the red dye as a green solid, mp 244-246° and after crystallization from ethanol (45 ml) mp 254-255°; ms: m/e 310 (M⁺), 157 (base peak); ¹H nmr (deuteriochloroform): δ 1.32 (s, 9H), 5.9 (s, 2H); ir (nujol): 3500, 3450, 1610, 1590 cm⁻¹; ms (high resolution): m/e 310.1665 (corresponds to C₁₂H₂₂N₈S); uv (methanol): λ max 250, 528 nm.

Anal. Calcd. for C₁₂H₂₂N₈S: C, 46.43; H, 7.15; N, 36.10; S, 10.33. Found: C, 46.72; H, 7.38; N, 36.01; S, 9.95.

Method B.

About 0.1 gm of compound 15 was placed in 2 ml of methanol and 0.3 ml of concentrated ammonium hydroxide added. The solution rapidly turned red and tlc (2 toluene: 1 ethyl acetate) indicated conversion of 15 to compound 9. The product was not isolated nor characterized further.

2-(Methylimino-2,2-dimethylpropylazo)-4-methyl-5-[2-(1-amino-2,2-dimethylpropylidene)-1-hydrazono]-4H-△²-1,3,4-thiadiazoline (9b, R = CH₃).

A slurry of hydrazone 7 (3.7 g, 0.01 mole) in methanol (200 ml) was treated with 40% aqueous methyl amine (10 g, 0.13 mole) and when all the solid dissolved activated manganese dioxide (2 g, 0.022 mole) was added and the mixture stirred at room temperature for 20 hours. The solution was filtered and the solid washed with methanol until the washings showed no color then the filtrate was evaporated and the residue triturated with water (50 ml). Filtration and water washing gave the nearly pure (by tlc) product (3.2 g, 95%) mp 195-196°. Further purification can be achieved by stirring for one hour with 20 ml of a 1:1 mixture of toluene:ethyl acetate followed by recrystallization from ethanol. The last traces of the lower Rf pigments (1:1 toluene:ethyl acetate) can be removed by chromatography on silica with 2:1 toluene:ethyl acetate. The compound appears as a dark green solid

with gold colored reflections, mp 197-198°; ¹H nmr (deuteriochloroform): δ 1.48 (s, 18H), 2.56 (s, 3H, N–Me), 2.31 (s, 3H, N–Me), 3.12 (bs, 2H); ms: m/e 338 (M⁺), 30 (base peak).

Anal. Calcd. for C₁₄H₂₆N₈S: C, 49.68; H, 7.74; N, 33.11; S, 9.47. Found: C, 49.41; H, 7.71; N, 32.73; S, 9.31.

(Z,E,Z)-2-[5-[3-(1,1-Dimethylethyl)-5-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-1-formazano]-1,3,4-thiadiazol-2-ylhydrazono]-3,3-dimethylbutanoic Acid (10).

A mixture of 7 (37 g, 0.1 mole), hydrazone 3 (43.6 g, 0.2 mole), potassium chloride (50 g) and water (1.5 ℓ) was stirred and dissolved at pH 10 with potassium hydroxide (20%) while bubbling oxygen through the solution at about 100 ml per hour. Oxygen addition was continued for 4 hours while the pH was allowed to drop, then the solution was filtered and the solid washed with 1% potassium chloride, ½% potassium hydroxide (20 ml) then 1% potassium chloride (20 ml). The crude dye (5.9 g) was triturated with 100° toluene (100 ml), filtered, then heated at the boiling point in ethanol (35 ml) for 10 minutes, cooled to room temperature, filtered and washed with ethanol to give 5.3 g (8.2%) of 12 which analyses approximately as the tripotassium salt dihydrate (mp 226-229°), one spot on tlc (65 chloroform, 30 methanol, 4 ammonium hydroxide). The free acid is made by adding 1 gm of dye to 100° acetic acid (10 ml), cooling to 20°, filtering and washing with acetic acid and water to give 0.71 g orange solid, mp 195°; ms: m/e 495 (MH⁺), 158 (base peak); uv (methanol): λ max 267, 500 nm; ¹H nmr (deuteriomethanol): δ 1.33 (s, t-Bu), 1.40 (s, t-Bu), 1.50 (s, t-Bu), 3.33 (bs); ¹³C nmr (DMSO-d₆): δ 28.150, 28.453, 30.579, 35.922; 36.043, 36.651, 156.997 (C3), 162.401 (C5 on t-Bu thiadiazole), 165.437, 166.954, 167.379, 167.744 (C2 butanoic acid), 170.537 (CO).

Anal. Calcd. for C₁₉H₃₀N₁₀S₂O₂: C, 46.13; H, 6.11; N, 28.32; S, 12.96; O, 6.47. Found: C, 46.22; H, 6.13; N, 28.31; S, 13.07; O, 6.50.

1,2-Bis[5-(1,1-dimethylethyl)-1,3,4-thiadazol-2-yl]diazene (11).

A mixture of water (3 ℓ), triazine 4 (200 g, 1 mole), and lithium hydroxide (48 g, 2 mole) was stirred for 1 hour then added to thiadiazole 7 (68 g, 0.18 mole) suspended in water (1 ℓ). After adjusting the pH to 12.5 with lithium hydroxide the solution was divided equally into 3 shallow enamel pans (22 x 34 cm) and allowed to stand for 3 days then filtered, washed with water, and the solid then stirred in water (1 ℓ) for one-fourth hour while maintaining pH 12.5 with lithium hydroxide. The solid was then re-filtered, washed with water, dried and triturated with enough 100° toluene to remove the yellow compound from the crude blue dye (13.8 g). Evaporation of the toluene gave 10.3 g of crude 11 which was chromatographed on 60-200 mesh silica using 7:1 toluene:ethyl acetate and then crystallized from ethanol to give 6.7 g of yellow crystals, mp 223-224°; ms: m/e 310 (M⁺), 57 (base peak); ¹H nmr: δ 1.23; ¹³C nmr: δ 30.91, 37.28, 177.12 (C-5), 184.22 (C-2).

Anal. Calcd. for C₁₂H₁₈N₆S₂: C, 46.45; H, 5.81; N, 27.10; S, 20.65. Found: C, 46.46; H, 5.81; N, 27.01; S, 20.57.

2,5-Bis[3-(1,1-dimethylethyl)-1,2,4-triazolo]-1,3,4-thiadiazole (12).

A mixture of red dye 9 (R = CH₃) (2 g, 6.45 mmoles) and activated manganese dioxide (3.5 g, 40 mmoles) was stirred and heated at 100° in toluene (30 ml) until the red color was discharged (about 20 minutes) then filtered and the filtrate stirred for one-half hour with activated carbon. Re-filtration and evapora-

tion gave a product which was crystallized from ethanol to give 1.5 g (76%) of white needles, mp 164-165°; ^{1}H nmr (deuteriochloroform): δ 1.43 (s, 9H), 8.97 (s, 1H); ^{13}C nmr (deuteriochloroform): δ 29.080 (CH$_3$), 33.176 (t-BuC), 141.674 (C-5), 158.102 (C-3), 174.761 (C-2,5); ms: m/e 332 (M$^+$), 317 (base peak).

Anal. Calcd. for C$_{14}$H$_{20}$N$_8$S: C, 50.58; H, 6.06; N, 33.71; S, 9.65. Found: C, 50.27; H, 5.79; N, 33.46; S, 9.40.

Methyl (Z,Z,E,Z,Z)-2-[5-[3-(1,1-Dimethylethyl)-5-[5-(1,1-dimethylethyl)-3-methyl-1,3,4-thiadiazol-2(3H)-ylidene]-1-formazano]-3-methyl-1,3,4-thiadiazol-2(3H)-ylidenehydrazono]-3,3-dimethylbutanoate (13).

A mixture of compound 10 (494 mg, 1 mmole), dimethyl sulfate (0.5 g, 4 mmoles), potassium carbonate (1.39 g, 10 mmoles), aliquat (0.1 g), and methylene chloride (100 ml) was stirred for 65 hours then filtered, evaporated, and chromatographed on silica (35 g) eluting with 9:1 toluene:ethyl acetate. Evaporation of the reddish-brown fractions and crystallization of the residue by slow evaporation of a 5 ml 2-propanol solution gave 0.31 g (58%) of the trimethyl compound 13 as brown crystals, mp 111-112°; ms: m/e 536 (M$^+$), 253 (base peak); ^{1}H nmr (deuteriochloroform): δ 1.23 (s, 9H, t-Bu), 1.30 (s, 18H, t-Bu), 3.55 (s, 3H), 3.78 (s, 3H), 3.88 (s, 3H, OCH$_3$).

Anal. Calcd. for C$_{22}$H$_{36}$N$_{10}$S$_2$O$_2$: C, 49.24; H, 6.76; N, 26.09; S, 11.95. Found: C, 49.34; H, 6.76; N, 25.96; S, 12.04.

2,5-Bis[2-(1-ethoxy-2,2-dimethylpropylidene)hydrazono]-△^{3}-1,3,4-thiadiazoline (14).

To a solution of 7 (3.7 g, 0.01 mole) in absolute ethanol (150 ml) and triethylamine (3 g) was added activated manganese dioxide (4 g, 0.045 mole) and the mixture was then refluxed for two hours. Filtration and evaporation gave a solid which was triturated with boiling cyclohexane. The cyclohexane was evaporated and the residue chromatographed on silica eluting with toluene. The orange toluene fractions were evaporated to near dryness and after cooling the toluene-crystal mixture was diluted with an equal volume of heptane and filtered to give 1.7 g (46%) of brick colored plates mp 130-132°, mp 132-134° after recrystallization from heptane; ms: m/e 368 (M$^+$), 57 (base peak); ^{1}H nmr: δ 1.35 (t, 3H), 1.37 (s, 9H), 4.24 (q, 2H); ^{13}C nmr (deuteriochloroform): δ 13.902 (Et-CH$_3$), 27.820 (t-Bu-CH$_3$), 38.785 (t-Bu-C), 64.208 (CH$_2$), 171.849 (imino ether C), 177.399 (C-2,5).

Anal. Calcd. for C$_{16}$H$_{28}$N$_6$O$_2$S: C, 52.17; H, 7.61; N, 22.83. Found: C, 51.98; H, 7.67; N, 23.14.

2,5-Bis[2-(1-carbomethoxy-2,2-dimethylpropylidene)hydrazono]-△^{3}-1,3,4-thiadiazoline (15).

A mixture of 7b (2.0 g, 5 mmoles), activated manganese dioxide (1.5 g, 17 mmoles), and methylene chloride (40 ml) was stirred overnight, filtered, evaporated, and the residue recrystallized from cyclohexane to give 1.65 g (83%) of orange crystals, mp 142°; ms: m/e 340 (M$^+$-t-butyl), 57 (base peak); ir: 1737 (CO), 1604 cm^{-1}; uv (methanol): λ max 392 nm; ^{1}H nmr (acetone): δ 1.28 (s, 9H), 3.86 (s, 3H); ^{13}C nmr (deuteriochloroform): δ 27.85, 37.48, 52.15 (OCH$_3$), 164.61 (propylidine), 175.66 (C-2,5 or CO), 175.75 (CO or C-2,5).

Anal. Calcd. for C$_{16}$H$_{24}$N$_6$O$_4$S: C, 48.47; H, 6.1; N, 21.19; S, 8.09. Found: C, 48.40; H, 6.06; N, 21.20; S, 7.77.

REFERENCES AND NOTES

[1] F. R. Haglid, U. S. Patent 3,890,317 (1975), E. I. DuPont de Nemours; *Chem. Abstr.*, **83**, 164243 (1976).

[2] H. Paulsen and D. Stoye, The Chemistry of Amides, J. Zabicky, ed, Interscience Publishers, 1970, p 566.

[3] W. Walter and J. Voss, The Chemistry of Amides, J. Zabicky, ed, Interscience Publishers, 1970, p 449.

[4] W. Sherman, Heterocyclic Compounds, Vol 7, R. Elderfield, ed, Wiley, New York, 1961, p 165.

[5] J. Sandstrom, Advances in Heterocyclic Chemistry, Vol 9, A. Katritzky and A. Boulton, eds, Academic Press, New York, 1968, p 165.

[6] F. Takusagawa and D. Jackman, *Acta Cryst.*, **C44**, 1418 (1988).

[7] G. Werber and F. Maggio, *Anal. Chem. (Rome)*, **49**, 2124 (1959).

[8] M. Atkinson and J. Polya, *J. Chem. Soc.*, 3319 (1954).

[9] H. Henbest and A. Thomas, *J. Chem. Soc.*, 3032 (1957).

[10] O. Meth-Cohn and H. Suschitzky, *Chem. Ind. (London)*, 443 (1969).

[11] S. Turner, M. Meyers, B. Gadie, A. J. Nelson, R. Pape, J. F. Saville, J. C. Doxey and T. L. Berridge, *J. Med. Chem.*, **31**, 902 (1988).

[12] M. Kanaoka, *Pharm. Bull.*, **5**, 385 (1957).

[13] R. Stolle and K. Fehrenbach, *J. Prakt. Chem.*, [2], **122**, 289 (1929).

[14] De and Roy-Choudhury, *J. Indian Chem. Soc.*, **5**, 269 (1928).

[15] Bambas, The Chemistry of Heterocyclic Compounds, Vol 4, Interscience Publishers, 1952.

[16] W. Walter, Organosulfur Chemistry, M. Janssen, ed, Interscience Publishers, New York, NY, 1967, p 241.

[17] J. Schaeffer, C. Goodhue, H. Risley and R. Stevens, *J. Org. Chem.*, **32**, 392 (1966).

[18] This reaction should be carried out exactly as described by an experienced research. Failure to properly control the temperature or peroxide addition rate can result in a runaway reaction due to a strong exotherm and vigorous foaming.

[19] D. E. Jackman, U. S. Patent 4,614,822 (1986), Mobay Chemical Corp.; *Chem. Abstr.*, **93**, 204077k (1980).

[20] The solid gave the following elemental analysis: C, 7.67; H, 0.68; N, 17.32; S, 67.00, which corresponds roughly to CHN$_2$S$_3$. It is believed to be mostly polymeric sulfur.