Mechanism of Oxidation of 3-Methyl-2-benzothiazolinone Hydrazone by Potassium Ferricyanide in Aqueous Methanol

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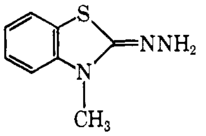
Abstract: Oxidation of 3-methyl-2-benzothiazolinone hydrazone (**1**) by potassium ferricyanide in aqueous methanol produced nitrogen, 3-methyl-2-benzothiazoline azine (**2**), 2-imino-3-methylbenzothiazoline (**3**), and 2,2′-(2-tetrazenediylidene)bis(3-methylbenzothiazoline) (**4**). The amounts of nitrogen, **2**, **3**, and **4** varied with pH and order of addition of reagents. Greatly enhanced yields of **2** were realized when **1** was oxidized in the presence of certain 3-alkylbenzothiazolium salts. Oxidation of 3-methyl-2-benzothiazolinone-2-^{15}N yielded dilabeled nitrogen, monolabeled **2**, and unlabeled **3**. The mechanism of oxidation of **1** is discussed.

The oxidation of 3-methyl-2-benzothiazolinone hydrazone (**1**) yields rather unexpected products which depend markedly upon reaction conditions.[2-5] Oxidation of **1** with potassium ferricyanide evolved only 45–50% nitrogen in the range pH 6–9.[7] In neutral aqueous methanol, the oxidation consumed 1.2 equiv of potassium ferricyanide, yielding 9% 3-methyl-2-benzothiazolinone azine (**2**) and, surprisingly, 65% 2-imino-3-methylbenzothiazoline (**3**).[4] We report a mechanistic study of this oxidation in which ^{15}N labeling of hydrazone **1** was employed.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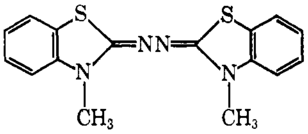
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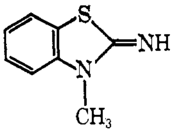
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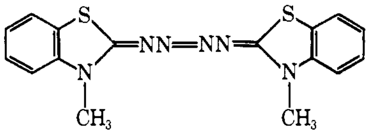
Results

Initial efforts were directed toward a better understanding of the effects of pH,[8] order of addition of reactants, and other reaction variables upon the products of the oxidation of **1** by potassium ferricyanide in aqueous methanol. In addition to the organic products reported previously,[4] 2,2′-(2-tetrazenediylidene)bis(3-methylbenzothiazoline) (**4**) was isolated. The three organic reaction products were shown to be stable under the reaction conditions.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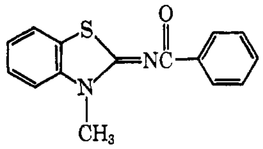
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The normal procedure involved slow addition of 0.5 *N* potassium ferricyanide solution to **1** dissolved in buffered aqueous methanol. A nearly constant pH was maintained by addition of sodium hydroxide when the pH had decreased by 0.1 unit. Alternatively, a solution of 0.5 *N* potassium ferricyanide and sodium hydroxide was added. Nitrogen evolution was measured with a gas buret. When the oxidation was complete, the insoluble azine **2** and tetrazene **4** were removed by filtration and determined spectrophotometrically. The imine **3** was isolated as N-(3-methyl-2-benzothiazolinylidene)benzamide (**5**). Selected results are presented in Table I. The nitrogen evolution observed in run 3 is shown in Figure 1.

Dependence of the amounts of the reaction products upon pH is illustrated in runs 1–7. In the range pH 5.7–8.6, the major products were nitrogen and imine **3**, in agreement with earlier studies.[4] When the oxidizing agent was basic potassium ferricyanide (compare runs 8 and 3), the product mixture contained more azine **2** than imine **3**. Runs 8, 9, and 10, conducted under air, nitrogen, and oxygen, respectively, demonstrate the insensitivity of the reaction products to the nature of the reaction atmosphere. Reverse addition of **1** to a potassium ferricyanide solution (run 11) produced imine **3** and tetrazene **4**, but no azine **2**.[9]

Effect of Benzothiazolium Salts. Oxidation of hydrazone **1** in the presence of certain 3-alkylbenzothiazol-

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[1] N.A.T.O. Postdoctoral Fellow, 1967–1968.

[2] (a) S. Hünig, H. Balli, and H. Quast, *Angew. Chem., Int. Ed. Engl.*, 1, 47 (1962); (b) S. Hünig, *ibid.*, 1, 640 (1962).

[3] Oxidation of **1** with lead tetraacetate in methanol–perchloric acid produces bis(3-methyl-2-benzothiazole)pentaazapentamethinecyanine perchlorate.[4]

[4] S. Hünig and H. Quast, *Justus Liebigs Ann. Chem.*, 711, 139 (1968).

[5] Oxidative coupling of amidrazone systems, such as **1**, with aromatic amines, phenols, and reactive methylene compounds has provided a new approach to azo chemistry.[2b,6]

[6] (a) S. Hünig, *Angew. Chem.*, 70, 215 (1958); (b) S. Hünig, *J. Chem. Educ.*, 46, 734 (1969).

[7] H. Balli, Ph.D. Thesis, Marburg University, Marburg, West Germany, 1961.

[8] Throughout this report, pH refers to the apparent pH observed when a combination glass and silver–silver chloride electrode was immersed in the mixed solvent system of 50% (by volume) aqueous methanol.

[9] This reaction is of possible synthetic utility for preparation of heterocyclic tetrazenes such as **4**, since starting materials are more readily available than for other methods.[10] A 7% yield of **4** was realized from a preparative scale oxidation of 1.05 g of **1**.

[10] H. Balli, *Angew. Chem., Int. Ed. Engl.*, 5, 132 (1966).

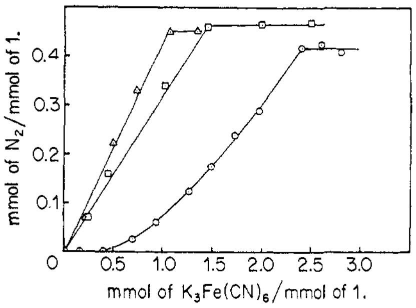


Figure 1. Nitrogen evolution in the oxidation of **1** by potassium ferricyanide: △, run 3; □, run 14; ○, run 17.

ium salts gave greatly enhanced yields of azine **2**. As shown in Table II, oxidation of **1** in the presence of 2,3-dimethyl-, 3-isobutyl-, and 3-methylbenzothiazolium salts (runs 15, 16, and 17, respectively) yielded 44–60% **2** under conditions which produced only a trace of **2** in the absence of benzothiazolium salts (run 12). With 2-*t*-butyl-3-methylbenzothiazolium fluoroborate (run 14), the slight increase in yield of **2** was indistinguishable from a salt effect (run 13).

Table I. Products from Oxidation of 3-Methyl-2-benzothiazoline Hydrazone by Potassium Ferricyanide in Aqueous Methanol at 20°

Run	pH	Equiv of K$_3$Fe(CN)$_6$ required	Products, % N$_2$	2	3	4
1	5.7–5.8	1.4	52	17	56	0
2	6.2–6.3	1.2	53	6	77	0
3	7.0–7.1	1.1	46	T^a	88	T^a
4	7.6–7.7	1.3	47	10	72	1
5	8.5–8.6	1.4	42	7	77	6
6	9.2–9.3	2.7	54	T^a	29	7
7^b	10.5–10.6	3.0	75	T^a	0	1
8^c	7.2–7.3	2.0	56	42	23	T^a
9^{c,d}	7.2–7.3	NM^e	NM^e	38	22	T^a
10^{c,f}	7.2–7.3	NM^e	NM^e	36	25	T^a
11^g	6.3–6.9	NM^e	54	0	15	10

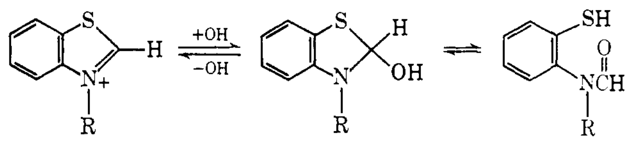
^{a} Trace. ^{b} 15% 3-methyl-2-benzothiazolinone isolated. ^{c} Basic potassium ferricyanide solution. ^{d} Under nitrogen. ^{e} Not measured. ^{f} Under oxygen. ^{g} Reverse addition of **1** to potassium ferricyanide solution.

Table II. Yield of 3-Methyl-2-benzothiazolinone Azine from Oxidation of 3-Methyl-2-benzothiazolinone Hydrazone by Potassium Ferricyanide in the Presence of 3-Alkylbenzothiazolium Salts

Run	pH	Benzothiazolium salt	Yield of **2**, %
12	7.0–7.1	None	T^a
13	7.2–7.3	None (1 equiv of LiClO$_4$)	6
14	7.0–7.1	2-*t*-Butyl-3-methylbenzothiazolium fluoroborate	9
15	6.9–7.0	2,3-Dimethylbenzothiazolium fluoroborate	44
16	6.8–6.9	3-Isobutylbenzothiazolium perchlorate	49
17	6.9–7.0	3-Methylbenzothiazolium perchlorate	60

^{a} Trace.

When the 3-isobutyl- and 3-methylbenzothiazolium salts were dissolved in buffered aqueous methanol, the pH of the solution decreased by approximately one unit. It seems reasonable that the following known equilibrium[11] was occurring. Oxidation of **6** to the disulfide **7** explains the anomalous nitrogen evolution observed during oxidation of **1** in the presence of 3-isobutyl- and 3-methylbenzothiazolium salts (Figure 1, run 17).



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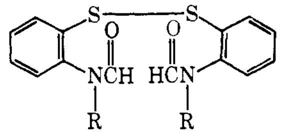

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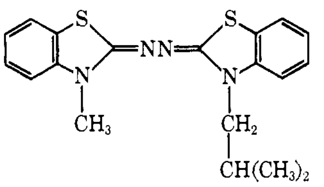
It was demonstrated that oxidation of **1** in the presence of disulfide **7** (R = CH$_3$) under the conditions of run 12 (Table II) produced only a trace of **2**.

That the 3-alkylbenzothiazolium salts were not incorporated into the azine was shown by substituent labeling. Oxidation of **1** in the presence of 3-isobutylbenzothiazolium perchlorate (run 16) yielded azine **2** and not the mixed azine **8**. In addition, when 6-methoxy-3-methyl-2-benzothiazolinone hydrazone was oxidized in the presence of 3-methyl-2-benzothiazolium fluoroborate none of the mixed azine **9** was formed.[12]



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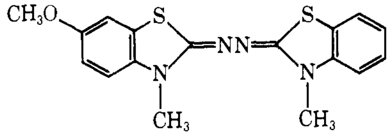

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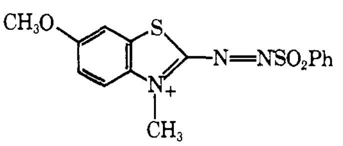

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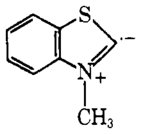

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Oxidation of 3-Methyl-2-benzothiazolinone Hydrazone-2-^{15}N. Results from the oxidation of 3-methyl-2-benzothiazolinone hydrazone-2-^{15}N (**12**) under three sets of conditions are summarized in Scheme I. The isotopic content of reactant and products was determined by mass spectrometry. Under conditions which produced only imine **3** and nitrogen (run 18), **3** was

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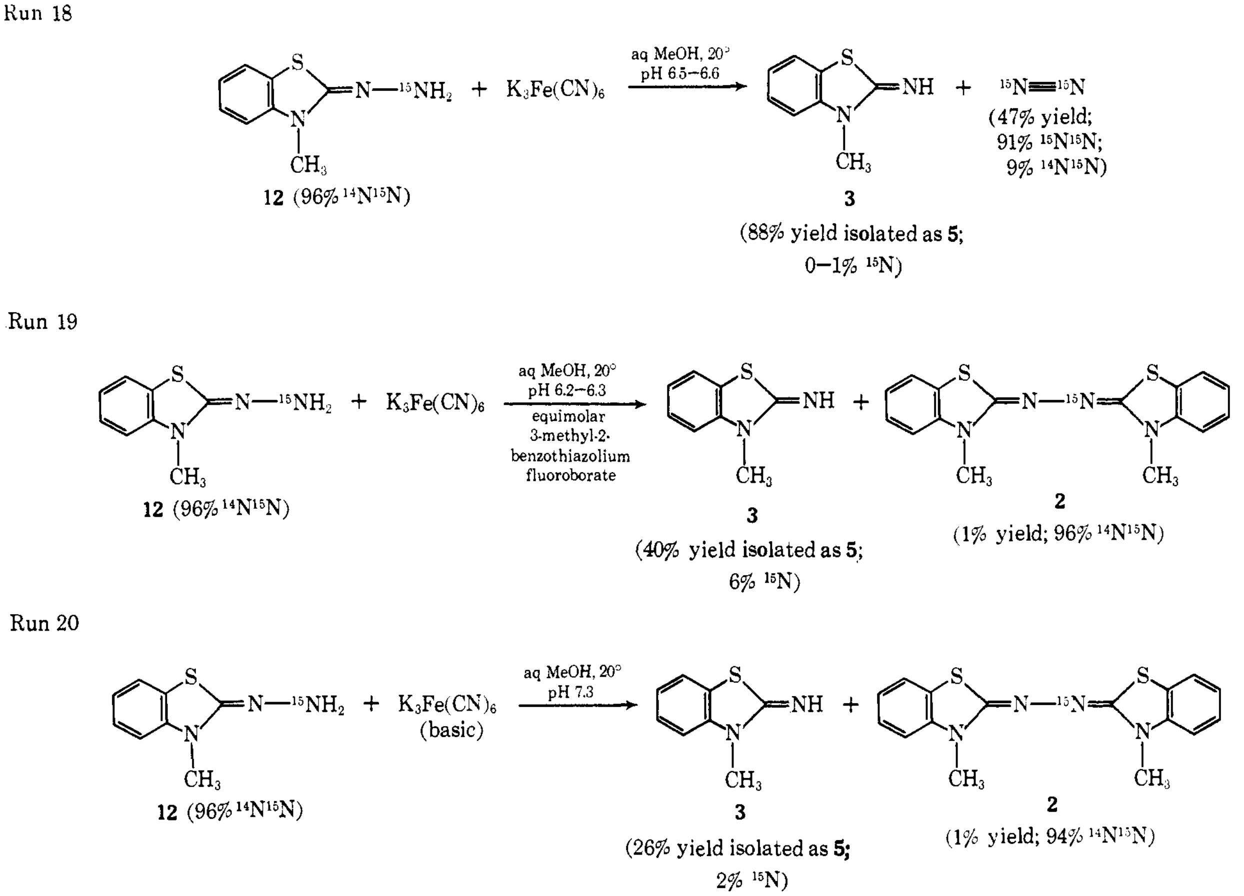
(11) J. Metzger, H. Larivé, R. Dennilauler, R. Baralle, and C. Gaurat, *Bull. Soc. Chim. Fr.*, 2868 (1964).

(12) Reaction of the quaternary azo sulfone **10** with 3-methylbenzothiazolium salt and diisopropylethylamine in acetonitrile yields the mixed azine **9** *via* the ylide **11**.[13]

(13) S. Hünig, H. Geiger, G. Kaupp, and W. Kniese, *Justus Liebigs Ann. Chem.*, 697, 116 (1966).

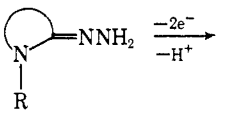
Scheme I



unlabeled and the nitrogen was dilabeled. When both azine **2** and imine **3** were formed (runs 19 and 20), **3** was again essentially unlabeled and **2** contained one label per molecule. It was not possible to isolate sufficient tetrazene **4** from the reaction mixtures to ascertain its isotopic content.

Discussion

Polarographic investigations[14] have revealed that amidrazones **13**, including hydrazone **1**, lose two electrons and one proton on oxidation, thereby forming an electrophilic intermediate **14**, which has been postulated to be the active coupling species in their oxidative coupling reactions.[2a,4,6,15] Conceivable further oxidation of **14** to form a very reactive hypothetical quaternary diazonium ion **15** has been made untenable by chemical evidence.[14] It seems reasonable to propose an intermediate analogous to **14** in the self-coupling of hydrazone **1**.



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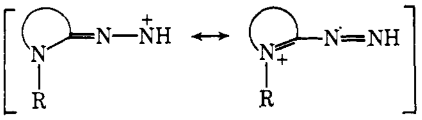

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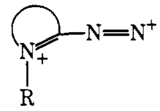

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A mechanism which is consistent with the labeling studies and other experimental evidence is presented in Scheme II. Oxidation of hydrazone **1** produces the resonance-stabilized electrophilic intermediate **14**. The electrophile **14** is ambient and attack by nucleophiles is anticipated at carbon and at the terminal nitrogen.[16] Attack on **14** by **1** at the terminal nitrogen and loss of a proton yields the hypothetical tetrazane intermediate **16**. Further oxidation of **16** produces the tetrazene **4**. Isolation of **4** is in itself good evidence for the intermediacy of **16**. Alternatively, the tetrazane **16** can decompose, forming two molecules of imine **3** and one of nitrogen.[17] An intermediate common to both imine **3** and tetrazene **4** is suggested by the results of oxidation employing reverse addition (*i.e.*, formation of **3** and **4** but no **2**, Table I, run 11). Possible indication of an acid-catalyzed decomposition of **16** to imine **3** and nitro-

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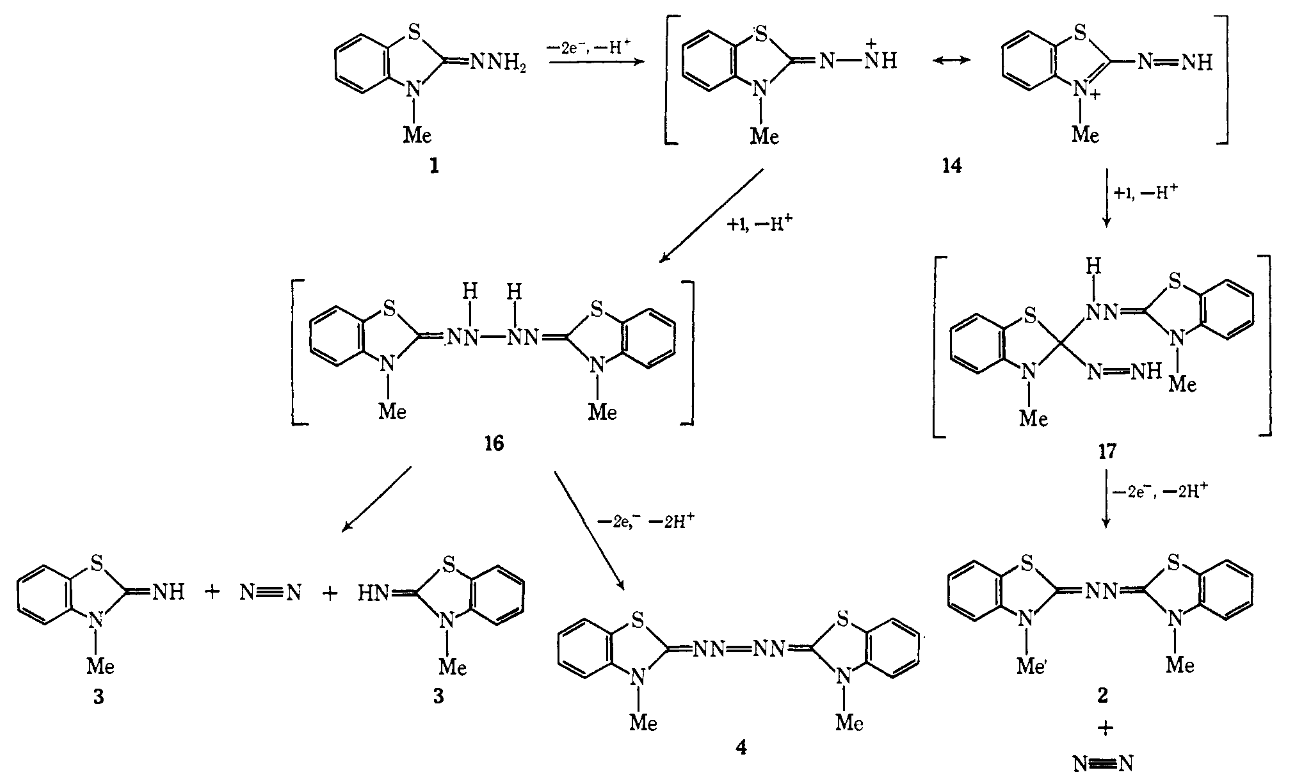
(14) S. Hünig and H. Balli, *Justus Liebigs Ann. Chem.*, **628**, 56 (1959).

(15) An analogous intermediate has been proposed in oxidative coupling reactions of *p*-phenylenediamines: J. Egger and H. Frieser, *Z. Elektrochem.*, **60**, 372 (1956); J. Eggers, *ibid.*, 60, 987 (1956); L. K. J. Tong and M. C. Glesmann, *J. Amer. Chem. Soc.*, **79**, 583, 592 (1957).

(16) The ambient nature of quaternary azo sulfones and other azo quaternary salts has been described: S. Hünig, *Angew. Chem., Int. Ed. Engl.*, 7, 335 (1968).

(17) A similar partitioning of an unisolable tetrazane intermediate between oxidation, forming a tetrazene, and loss of nitrogen, producing phthalimide, has recently been proposed in the oxidation of N-aminophthalimide by lead tetraacetate: L. Hösch and A. S. Dreiding, *Chimia*, **23**, 405 (1969).

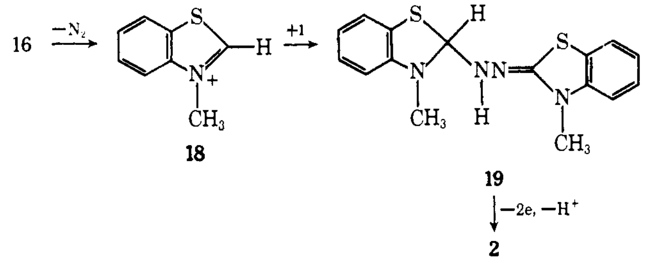
Scheme II



gen may be inferred from the pH-dependence of the relative proportions of **3** and **4** (Table I). Formation of **3** and nitrogen from labeled hydrazone **12** by the mechanism outlined in Scheme II predicts unlabeled imine **3** and doubly labeled nitrogen, as observed (Scheme I, run 18).

Attack of the electrophilic species **14** by **1** at the carbon atom yields intermediate **17**. Azine **2** is produced by further oxidation of **17**. According to this mechanism, oxidation of labeled hydrazone **12** should form **2** with one label per molecule, as found (Scheme I, runs 19 and 20).

Monolabeled azine **2** could also conceivably result from decomposition of the tetrazane intermediate **16**, forming 3-methylbenzothiazolium ion **18**. Combination of **18** with hydrazone **1** would produce **19**, which by oxidation would yield **2**. However, this plausible mechanism is excluded by the absence of mixed azine when **1** was oxidized in the presence of benzothiazolium salts.



The marked enhancement in yield of azine **2** when the oxidation of **1** was performed in the presence of certain 3-alkylbenzothiazolium salts may also be rationalized in terms of the proposed mechanism for formation of **2**. Oxidation of intermediate **17** to azine **2** could also occur by removal of a hydride ion and a proton. Metzger and coworkers have reported hydride abstraction by 3-methylbenzothiazolium iodide.[11,18] Further support for the proposal of hydride abstraction from intermediate **17** by 3-alkylbenzothiazolium salts is derived from the lack of effect of 2-*t*-butyl-3-methylbenzothiazolium fluoroborate upon the yield of azine **2** (Table II, run 14). An attractive explanation is steric hindrance of the bulky *t*-butyl group to hydride abstraction.[19,20]

Experimental Section

Materials. Acetonitrile, ethylene chloride, and dimethylformamide were purified as before.[4] Reagent grade methanol was used directly.

Hydrazone **1**,[22] azine **2**,[4] imine **3**,[23] benzoylated imine **5**,[13] 3-methylbenzothiazolium fluoroborate,[24] and 2,3-dimethylbenzothiazolium fluoroborate[25] were available from other studies. Synthesis of labeled hydrazone **12** will be reported in a paper treating the preparation and infrared spectra of a series of ^{15}N-labeled 3-methyl-2-benzothiazolinone derivatives.[26]

Tetrazene 4 was prepared by modification of the method of Maul for synthesis of the analogous N-ethyl compound.[27] 2-Azido-3-methylbenzothiazolium fluoroborate[4] (0.29 g, 1.0 mmol) and 0.11 g (2.0 mmol) of lithium azide were weighed into the two sides of a "two-hipped" reaction vessel. After the apparatus was evacuated and filled with dry nitrogen several times, 2.0 ml of dimethylformamide was added to each side and the solutions were cooled to

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(18) J. Metzger, H. Larivé, R. Dennilauler, R. Baralle, and C. Gaurat, *Bull. Soc. Chim. Fr.*, 1266 (1969).

(19) No indication of oxidation of tetrazane **16** to tetrazene **4** by hydride abstraction was observed. Steric factors could be involved.

(20) Other hydride acceptors (tropylium fluoroborate,[21] 10-ethylacridinium ethosulfate, and 1,3-dimethylbenzimidazolium perchlorate[21] were uneffective in producing exhalted yields of azine **2**. Apparent coupling of **1** and the hydride acceptor was observed for the first two salts.

(21) A. V. El'tsov and K. L. Muravida-Alexander, *Tetrahedron Lett.*, 739 (1968).

(22) R. Riemschneider, *Monatsh. Chem.*, **89**, 683 (1958).

(23) E. Besthorn, *Chem. Ber.* **43**, 1519 (1910).

(24) H. Quast and S. Hünig, *ibid.*, **99**, 2017 (1966).

(25) H. Quast and E. Schmidt, *ibid.*, **102**, 568 (1969).

(26) R. A. Bartsch, S. Hünig, and H. Quast, to be published.

(27) R. Maul, Ph.D. Thesis, Marburg University, Marburg, West Germany, 1965.

−60°. The solutions were mixed and the reaction mixture was allowed to warm to room temperature overnight. The bright yellow crystals were filtered and recrystallized (acetonitrile), yielding 0.064 g (36%) of **4**: mp 314–316°; $\lambda_{\max}^{\mathrm{DMF}}$ 415 nm (sh), 396 (ϵ 52,100), 380 (sh), 304 (5000).[28]

Anal. Calcd for $C_{16}H_{14}N_6S_2$: N, 23.71; S, 18.09. Found: N, 23.60; S, 18.00.

3-Isobutylbenzothiazolium Perchlorate. Benzothiazole (101.5 g, 0.75 mol) and 194 g of isobutyl tosylate were heated at 100–105° for 5 days in a closed flask. The semisolid reaction product was recrystallized from acetone–acetonitrile (15:1), yielding 207 g of crude 3-isobutylbenzothiazolium tosylate. A portion of the crude tosylate (20 g) in 35 ml of warm ethanol was treated with 10 ml of 70% perchloric acid. After 2 hr, 50 ml of ether was slowly added. Cooling to 0° produced crystals which were repeatedly recrystallized from ethanol, yielding 8.9 g (42%) of the title compound: mp 134–135°; $\delta_{\mathrm{TMS}}^{\mathrm{CH_3CN}}$ doublet (J = 7 Hz) at 1.02 (6 H), doublet (J = 8 Hz) at 4.68 (2 H), multiplet at 7.62–8.50 (4 H), singlet at 10.11 (1 H), tertiary H masked by solvent.

Anal. Calcd for $C_{11}H_{14}ClNO_4S$: Cl, 12.15; S, 10.99. Found: Cl, 12.25; S, 11.01.

2-*t*-Butyl-3-methylbenzolthiazolium Fluoroborate. 2-*t*-Butylbenzothiazole[29] (9.57 g, 50 mmol) and 8.9 g (60 mmol) of trimethyloxonium fluoroborate[30] were stirred in 20 ml of ethylene chloride for 2 hr. The reaction mixture was heated until evolution of dimethyl ether ceased and was cooled overnight. The crude product (10.45 g, 71%, mp 201–212°) was recrystallized from ethanol to give the title compound: mp 218–220°; $\delta_{\mathrm{TMS}}^{\mathrm{CH_3CN}}$ singlet at 1.74 (9 H), singlet at 4.40 (3 H), multiplet at 7.67–8.40 (4 H).

Anal. Calcd for $C_{12}H_{16}BF_4NS$: S, 10.94. Found: S, 11.07.

Apparatus for Oxidation of 1. The general apparatus consisted of a four-necked 200-ml flask containing a Teflon-coated magnetic stirring bar and fitted with two capillary burets, a combination glass and silver–silver chloride electrode, and a small-diameter, thick-walled rubber tube attached to a 100-ml gas buret. A circulating thermostat maintained the jacketed gas buret and the reaction flask bath at 20.0°.

General Procedure for Oxidation of 1. A. By Potassium Ferricyanide. Hydrazone **1** (0.34 g, 1.90 mmol) was washed into the reaction flask with 75 ml of methanol. When **1** had dissolved, 75 ml of buffer (Na_2HPO_4/KH_2PO_4, Na_2CO_3/H_3BO_3 + KCl, or $Na_2HPO_4/C_6H_8O_7$)[31] was added. With vigorous stirring, 0.5 N potassium ferricyanide was added (0.5–1 ml/min) until the pH decreased 0.1 pH unit from the initial value. Sufficient 1.0 N NaOH was added to adjust the pH to the initial value. After each addition of oxidizing agent, gas evolution was followed until a constant reading was obtained (usually 10–15 min). A solvent vapor pressure correction of 35.5 Torr[32] was applied. At the completion of the reaction, the mixture was filtered through a sintered glass funnel. The filtered material was washed with 200 ml of hot water and dried. The content of azine **2** was reckoned from the absorption[4] at 333 nm (or at 321 nm in the presence of **4**) in the spectrum of the residue in acetonitrile; that of tetrazene **4** from absorption at 396 nm in dimethylformamide. Imine **3** was isolated as **5** from the filtrate using the procedure of Hünig and Quast[4] on half-scale. Recovery of azine **2**, imine **3**, and tetrazene **4** from a simulated reaction mixture yielded 97% **2** and **4** and 86–89% **5**.

B. By Basic Potassium Ferricyanide. The procedure was the same as in A, except that only one capillary buret was used to add the oxidizing solution of 0.5 N $K_3Fe(CN)_6$ and 0.5 N NaOH. After addition of 1–2 ml at a slow rate (0.1–0.4 ml/min), the gas evolution was measured as in A.

C. By Potassium Ferricyanide in the Presence of 3-Alkylbenzothiazolium Salts. A solution of 1.00 mmol of 3-alkylbenzothiazolium salt in 75 ml of buffer was added to 0.179 g (1.00 mmol) of hydrazone **1**. The pH was adjusted to the desired value with 1.0 N NaOH and the oxidation was carried out as in A. The insoluble reaction product was recovered as before. With 3-isobutylbenzothiazolium perchlorate, this insoluble residue was shown to be azine **2** by comparison with authentic **2** using uv (in acetonitrile), nmr (in trifluoroacetic acid), and tlc (silica gel).

Oxidation of 6-methoxy-3-methyl-2-benzothiazolinone hydrazone in the presence of 3-methyl-2-benzothiazolium fluoroborate was carried out similarly. The recovered insoluble reaction product was shown by comparison of tlc behavior (silica gel) not to be mixed azine **9** or azine **2**.

D. By Potassium Ferricyanide–Reverse Addition. Run 11. Hydrazone **1** (0.45 g, 2.50 mmol) was dissolved in 50 ml of methanol and the solution was added to 50 ml of 0.1 N NaOH. This solution was added in 10–15-ml portions at a rate of 1–2 ml/min to a vigorously stirred solution of 8.27 g (25 mmol) of potassium ferricyanide in 75 ml of methanol and 75 ml of buffer. Nitrogen evolution was measured after each addition. Initial pH of the ferricyanide solution was 6.3; final pH 6.9. Products were isolated as in A.

Oxidation of Labeled Hydrazone 12. A. By Potassium Ferricyanide. Run 18. The apparatus was modified by substituting a rubber septum for one capillary buret and replacing the gas buret connection with an inlet and outlet tube for flushing the reaction solution with carbon dioxide. The carbon dioxide carrier gas was absorbed by 50% KOH in a nitrogen measuring buret, from which the evolved nitrogen was transferred to and sealed in an ampoule.

Labeled hydrazone **12** (0.048 g, 0.27 mmol) dissolved in 50 ml of methanol and 50 ml of phosphate buffer was oxidized by two 1.0-ml portions of 0.5 N potassium ferricyanide added dropwise through the rubber septum with a syringe.

B. By Potassium Ferricyanide in the Presence of 3-Methylbenzothiazolium Fluoroborate. Run 19. Using the same procedure and apparatus employed in run 18, 0.051 g (0.285 mmol) of **12** was dissolved in 25 ml of methanol and 25 ml of phosphate buffer; 3-methylbenzothiazolium fluoroborate (0.072 g, 0.253 mmol) in 5 ml of water was added with a syringe. During 15 min, 2.5 ml of 0.5 N potassium ferricyanide was then added. Owing to a malfunction of the apparatus the evolved nitrogen could not be measured or collected.

C. By Basic Potassium Ferricyanide Solution. Hydrazone **12** (0.067 g, 0.37 mmol) was dissolved in 15 ml of methanol in a two-necked 50-ml flask. After addition of 15 ml of phosphate buffer, oxidation with 0.5 N potassium ferricyanide and 0.5 N NaOH was carried out as previously.

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(28) The ultraviolet spectrum is in excellent agreement with that reported[10] for the N-ethyl compound.

(29) J. Metzger and H. Clank, *Bull. Soc. Chim. Fr.*, 1692 (1956).

(30) H. Meerwein, *Org. Syn.*, 46, 120 (1966).

(31) Landolt-Börnstein, "Zahlenwerte und Funktionen," Vol. II, 6th ed, Part 7, Springer-Verlag, West Berlin, 1960, p 954.

(32) See ref 31, Part 2a, p 386.