3-Methyl-2,1-benzisoxazolium, Benzisothiazolium, and Indazolium Salts as New Active-Methyl Compounds

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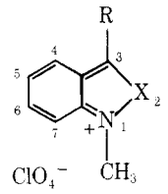
The 3-CH_3 group of the title salts has been shown to be quite reactive (nucleophilic) by condensing with aldehydes, ketones, orthoesters, and diazonium salts, forming new styryl, cyanine, and azo dyes, respectively. The 3 position of the title salts has also been found to be electrophilic, and the consequence of this bifunctionality (adjacent nucleophilic and electrophilic centers) has been utilized in the syntheses of potential thermochromic materials.

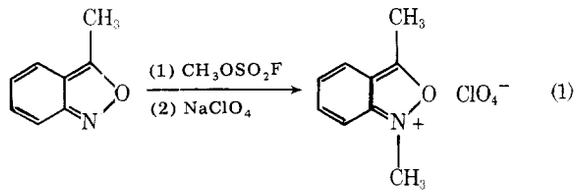
Recently both Olofson and Nakagawa have utilized the exceptionally low electron density at the carbon atom in the 3 position of *N*-alkyl-2,1-benzisoxazolium salts 1 as a synthon



1a, R = H; X = O
b, R = CH_3; X = O
c, R = CH_3; X = S
d, R = CH_3; X = NCH_3

for both the highly strained benzoazetinone and the well-known tranquilizer Valium.[1,2] Olofson utilized the high acidity of the C-3 proton for his synthesis and Nakagawa the electrophilic behavior of the C-3 carbon itself toward attack by nucleophiles. We report now the activation of the methyl group attached to the 3 position of 1,3-dimethyl-2,1-benzisoxazolium salt **1b** and its utility as a *nucleophile* in dye-forming reactions. Similarly, we also report and compare the reactivity of the corresponding 3-methyl-2,1-benzisothiazolium and indazolium salts (**1c, 1d**).

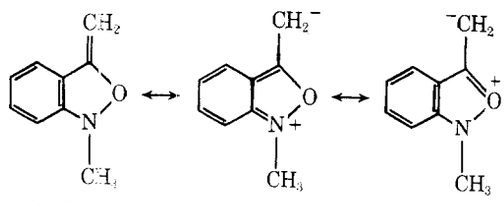
1,3-Dimethyl-2,1-benzisoxazolium perchlorate (**1b**) was prepared according to eq 1 in the expectation that it would



(1)

1b

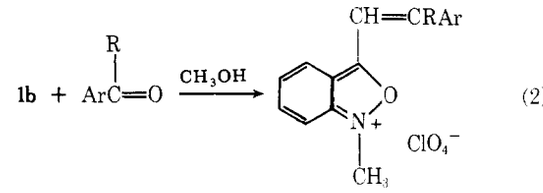
react as a nucleophile (high electron density) at the C-3 methyl carbon atom and an electrophile (low electron density) at the C-3 ring carbon atom. In fact, resonance contributors **2** and



anhydro base 2 3

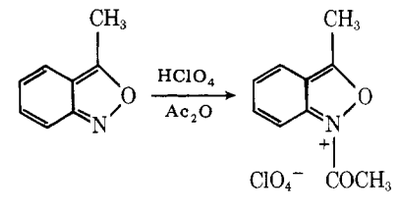
3 of the anhydro base of **1b** show that the exocyclic carbon atom at C-3 is not only the terminal atom of a vinylogous enamine but of a vinyl ether as well; therefore, considerable negative charge should be located at this site as shown by resonance form **2.**

We have found that both 3-methyl-2,1-benzisoxazole and 1,3-dimethyl-2,1-benzisoxazolium perchlorate (**1b**) condense with aromatic aldehydes and ketones to form highly colored styryl derivatives as shown in eq 2 and 3. The condensation



(2)

R = H, CH_3



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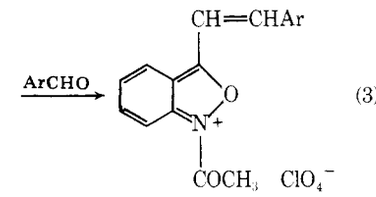

(3)

of **1b** proceeds in the absence of added base, whereas 3-methyl-2,1-benzisoxazole condenses with aromatic aldehydes in a strong acid medium such as $HClO_4$–Ac_2O, probably via the *N*-acetyl derivative **4** (eq 3).

The mechanism for the formation of the styryl compounds shown in Table I probably involves the anhydro base, which is in rapid equilibrium with the protonated form (**1b**). In methanol–D_2O the hydrogen–deuterium exchange of the C-3 methyl protons of **1b** is complete within 15 min. This rapid rate of exchange with deuterium oxide as well as the rates of reaction of **1b** with aromatic aldehydes is noteworthy when compared with the much slower reaction rates of the corresponding benzthiazole and indazole derivatives which will be discussed later.

1,3-Dimethyl-2,1-benzisoxazolium perchlorate (**1b**) also reacts as a nucleophile via the C-3 methyl group with diazonium salts (eq 4). The product **5,** formally the *p*-nitrophenylhydrazone of 1-methyl-3-formyl-2,1-benzisoxazolium perchlorate, deprotonates easily in basic medium yielding the azo derivative **6.**

Cyanine dyes **7** and **8** were also synthesized from **1b** to illustrate its utility as a dye-forming reagent. With triethyl orthoformate the symmetrical cyanine dye **7** is readily formed, whereas **1b** and Fischer's aldehyde readily yield the unsymmetrical cyanine **8.**

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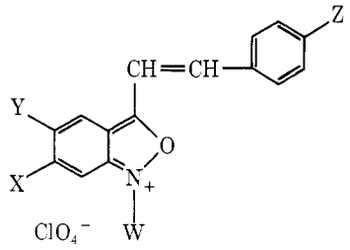
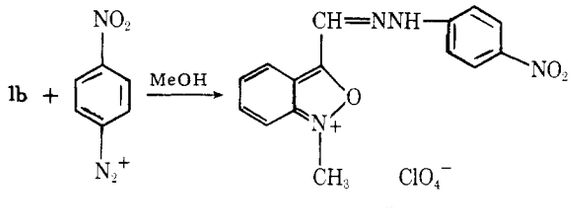
Table I. 3-Styryl-2,1-benzisoxazolium Salts

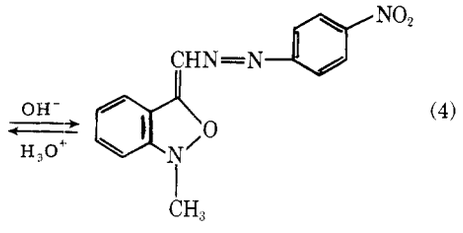


Compd	Registry no.	W	X	Y	Z	λ_{max} (CH_3CN), nm	(log ε)	Yield, %	Mp, °C
20	64872-09-9	CH_3	H	H	H	414			
21	64872-11-3	CH_3	H	H	OH	465	(4.49)	86	210 dec
22	64872-13-5	CH_3	H	H	$N(CH_3)_2$	584	(4.77)	100	173-174 dec
23	64872-15-7	CH_3	H	NO_2	$N(CH_3)_2$	635	(4.82)	62	177-178 dec
24	64872-17-9	CH_3	OCH_2	O	$N(CH_3)_2$	530	(4.52)	80	192 dec
25	64872-19-1	$COCH_3$	H	H	$N(CH_3)_2$	650	(4.45)	19	174 dec
26	64872-21-5	$C(CH_3)_3$	H	H	$N(CH_3)_2$	590	(4.99)	95	130-131 dec



5

λ_{max} (CH_3CN) 485 nm

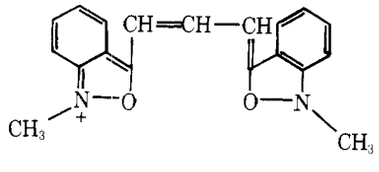


(4)

6

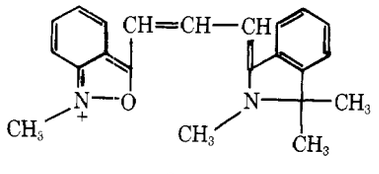
λ_{max} (CH_3CN) 555 nm

Reaction of dimethyl salt **1b** with base (Et_3N) instantaneously gives dimer **9**; further addition of base deprotonates



7

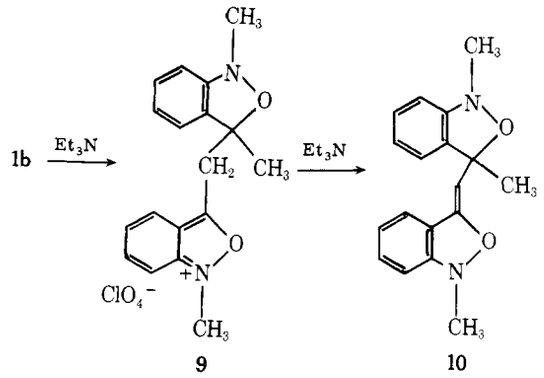
λ_{max} (CH_3CN) 617 nm



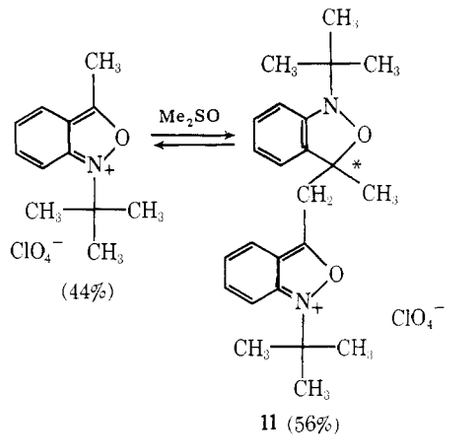
8

λ_{max} (CH_3CN) 557 nm

the dimer yielding anhydro base **10**, itself a dye-forming agent. The entire reaction sequence can be followed conveniently by NMR. Dimer formation is best accomplished simply by dissolving **1b** in Me_2SO (rather than treating with Et_3N) followed by precipitation with water. Structure **9** for the dimer is supported by spectral evidence and microanalysis. However, we were concerned that the diastereotopic methylene protons in **9** appeared only as a broadened singlet rather than an AB quartet in the NMR spectrum. Examination by NMR of dimer **11** formed from the *N-tert*-butyl analogue of **1b** in Me_2SO-d_6 shows that a facile equilibrium is formed between monomer and dimer, but more importantly, the methylene



9 **10**



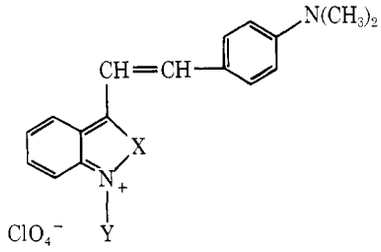
(44%)

11 (56%)

group of the dimer (**11**) appears as an AB quartet. Apparently the broadened singlet found for the methylene protons in **9** is fortuitous.

For comparison purposes, we prepared 3-methyl-2,1-benzisothiazolium and indazolium salts **1c** and **1d** to ascertain whether they are similar in reactivity to **1b**. A priori, based only on simple electronegativity differences, one would predict an increase in electron density at the C-3 carbon atom if oxygen is replaced with sulfur or nitrogen. Thus, the reactivity

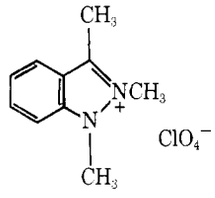
Table II. Effect of Heteroatom and N-Substituent on Styryl-2,1-benzisoxazolium Dyes



Compd	Registry no.	X	Y	λ_{max} (CH_3CN), nm	(log ϵ)	Mp, °C	Yield, %
20		O	CH_3	585	(4.77)	173-174 dec	100
27	64872-23-7	S	CH_3	592	(4.58)	255-256 dec	92
28	64872-25-9	NCH_3	CH_3	428	(4.55)	245-247 dec	40
25		O	$COCH_3$	650[a]	(4.45)	174 dec	19
29	64872-27-1	S	$COCH_3$	705[a]	(4.74)	212-213 dec	60

[a] In CH_2Cl_2 as solvent.

of the C-3 carbon atom (electrophilic site) and its bonded methyl group (nucleophilic site) should be less in **1c** and **1d** compared to **1b**. Furthermore, **1d** should be less reactive than **1c** since it has a more energetically favorable resonance form, **12**. In **12** the benzenoid character of one ring has been restored,

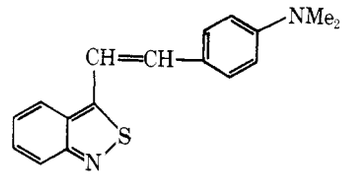


12

while **1c** still possesses an orthoquinoid electronic structure. In fact, **1d**'s reactivity should be similar to that of a methylated indoxazene.

Although the reaction rates are much slower, the isothiazolium and indazolium salts **1c** and **1d** undergo nucleophilic addition with aromatic aldehydes in a manner analogous to the behavior of **1b** (eq 2). For example, with *p*-*N*,*N*-dimethylaminobenzaldehyde, **1b** gave styryl dye **22** in 99% yield in less than 1 min at room temperature, benzisothiazolium **1c** gave a 92% yield of **27** after 30 min at reflux, and indazolium **1d** gave a 40% yield of **28** only after 24 h at reflux temperature (methanol). Also, **1c** shows no hydrogen–deuterium exchange at the C-3 methyl group after 72 h in MeOH–D_2O. A comparison of styryl dyes **22**, **27**, and **28** (Table II) shows the effect of heteroatom substitution on the long-wavelength absorption maxima. Exchange of oxygen by sulfur results in a small bathochromic shift, whereas substitution of nitrogen gives a large hypsochromic shift. Perhaps a resonance form such as **12** is becoming more important. Exchange of the *N*-methyl group for acetyl also produces a large bathochromic shift in absorption wavelength (Table II). In fact, the benzisothiazolium dye **29** shows a shift of 113 nm when the N substituent is changed from methyl to acetyl. Evidently, the chromophore has changed dramatically; however, treatment of the acetyl dyes with any base instantaneously yields merocyanine dyes such as **13**, indicating no gross structural differences among dyes from **1b**, **1c**, and 3-methyl-2,1-benzisoxazole.

As indicated earlier, the C-3 position of **1b** should be the site for nucleophilic attack. Several reports have appeared[1-3] which describe such chemistry; consequently, we will limit our discussion to new chemistry involving nucleophilic attack and subsequent reactions of **1b** and **1c**. 1,3-Dimethyl-2,1-benzisoxazolium perchlorate is unique in that the 3-methyl group



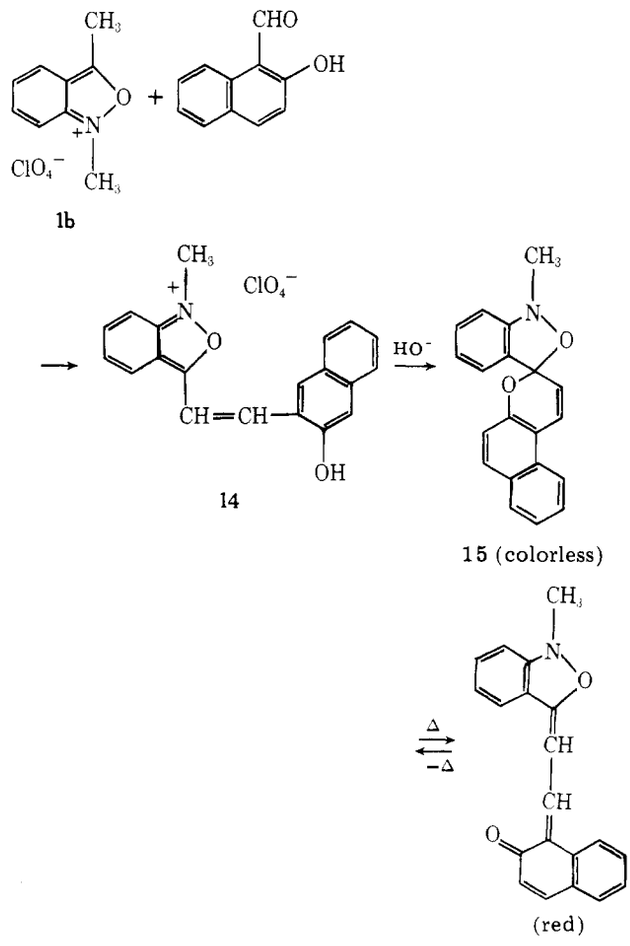
13

λ_{max} (CH_3CN) 435 nm

can serve as a nucleophile and the C-3 carbon as an electrophile in successive reactions.

An example of its bifunctionality is shown in Scheme I. The

Scheme I



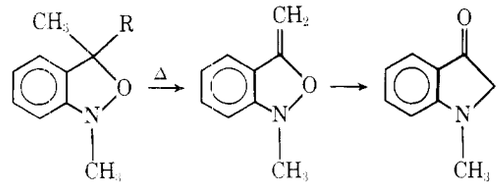
1b

14

15 (colorless)

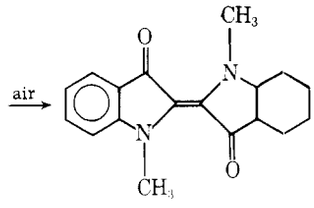
(red)

Scheme II



16 17

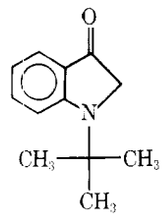
R = CN, N_3, OCH_3



18

styryl dye **14**, formed from 2-hydroxy-1-naphthaldehyde, cyclizes in base to the thermochromic spiropyran **15**. Dimerization of **1b** to dimer **9** is another example of the bifunctional behavior of **1b**.

Cyanide, azide, and methoxide ions react with **1b** to give 3-substituted benzisoxazolines (**16**, Scheme II). Similar reactions have been described by Olofson;[1] however, subsequent reactions of our resulting benzisoxazolines are quite different. Whereas Olofson's benzisoxazolines undergo thermal ring opening to *o*-acyl anilines, our derivatives (**16**) lose HCN, HN_3, or CH_3OH on heating (130 °C) to yield what is believed to be *N,N'*-dimethylindigo **18** (identical UV–vis spectrum).[4] We propose that the formation of indigo **18** arises via the mechanism outlined in Scheme II. Support for the mechanism is based on the following information: (1) the formation of HCN or HN_3 was observed spectroscopically, (2) *N-tert*-butyl-3-cyano-3-methyl-2,1-benzisoxazoline yielded *N-tert*-butylindoxyl **19** on heating to 130 °C, (3) pyrolysis of 3-cyano-



19

1,3-dimethyl-2,1-benzisoxazoline under a nitrogen atmosphere gave a compound whose NMR spectrum is consistent with *N*-methylindoxyl **17**, and (4) the oxidation of **17** to indigo **18** is a known reaction.[5]

Experimental Section

Melting points are uncorrected. IR spectra were obtained with a Perkin-Elmer 137 spectrophotometer and NMR spectra with a Varian T-60 spectrometer using Me_4Si as an internal standard. UV spectra were taken with a Cary 17 spectrophotometer. All compounds included in this paper gave satisfactory microanalyses and IR, NMR, UV–vis, and mass spectra consistent with the proposed structures.

***N*-Alkyl-2,1-benzisoxazolium Salts. Typical Procedures. 1,3-Dimethyl-2,1-benzisoxazolium Perchlorate (1b):** To a solution of 3-methyl-2,1-benzisoxazole (13.3 g) in diethyl ether (100 mL) was added methyl fluorosulfonate (12.0 g) in 1 portion. The reaction mixture was stirred for 1 h at room temperature. The precipitated white solid was collected, washed with diethyl ether, and then dissolved in a minimum amount of water. To this aqueous solution was added sodium perchlorate monohydrate (15.0 g) dissolved in water (20 mL). A white crystalline solid precipitated immediately and was collected and washed with cold water. Recrystallization from hot water gave 21.9 g (89%) of 1,3-dimethyl-2,1- benzisoxazolium perchlorate: mp 152–153 °C (explodes at 154 °C); NMR (CD_3CN) δ 7.8 (m, 4 H), 4.4 (s, 3 H), 3.0 (s, 3 H); IR (KBr) 1630, 1500, 1420, 1090, 755 cm^{-1}; UV λ_{max} (H_2O) 335 nm (log ϵ 3.54), 201 (4.40).

Anal. Calcd for $C_9H_{10}ClNO_5$: C, 43.7; H, 4.1; N, 5.7. Found: C, 44.1; H, 4.0; N, 5.9.

***N*-*tert*-Butyl-3-methyl-2,1- benzisoxazolium Perchlorate:** Nitromethane (20 mL) containing 3-methyl-2,1-benzisoxazole (13 g), *tert*-butyl alcohol (8 g), and 70% perchloric acid (16 g) was stirred at room temperature for 48 h. To the solution was added diethyl ether (200 mL), and the precipitated white solid was collected and washed with diethyl ether. Recrystallization from methanol gave *N-tert*-butyl-3-methyl-2,1- benzisoxazolium perchlorate (20 g): mp 183 °C dec; NMR (CD_3CN) δ 8.0 (m, 3 H), 7.4 (m, 1 H), 3.0 (s, 3 H), 1.9 (s, 9 H); IR (KBr) 1625, 1450, 1090, 760 cm^{-1}; UV λ_{max} (H_2O) 335 nm (log ϵ 3.72), 268 (3.68), 205 (4.43).

Anal. Calcd for $C_{12}H_{16}ClNO_5$: C, 49.7; H, 5.6; N, 4.8. Found: C, 49.4; H, 5.6; N, 5.1.

1,3-Dimethyl-2,1-benzisothiazolium Perchlorate (1c): 83%; mp 161–162 °C; NMR (CD_3CN) δ 3.2 (s, 3 H), 4.4 (s, 3 H), 8.0 (m, 4 H); UV λ_{max} (CH_3CN) 350 nm (log ϵ 3.69), 300 (4.09).

Anal. Calcd for $C_9H_{10}ClNO_4S$: C, 41.0; H, 3.8; N, 5.3; S, 12.2. Found: C, 40.9; H, 3.7; N, 5.5; S, 12.5.

1,2,3-Trimethylindazolium Perchlorate (1d): 75%; mp 219–220 °C; NMR (CD_3CN) δ 2.8 (s, 3 H), 4.2 (s, 6 H), 7.8 (m, 4 H).

Anal. Calcd for $C_{10}H_{13}ClN_2O_4$: C, 46.1; H, 5.0; N, 10.8. Found: C, 46.4; H, 5.1; N, 10.6.

Condensation of 1b–d with Aromatic Aldehydes, Ketones, Diazonium Salts, and Orthoesters. Typical Procedures. 3-(*p*-Dimethylaminostyryl)-1-methyl-2,1-benzisoxazolium Perchlorate (22): *p*-Dimethylaminobenzaldehyde (1.5 g, 0.01 mol) and **1b** (2.5 g, 0.01 mol) were dissolved in methanol (25 mL) and refluxed briefly. Cooling followed by filtration gave 3.7 g (100%) of blue crystals: mp 173–174 °C dec; NMR (CF_3CO_2H) δ 8.3–7.5 (m, 10 H), 4.5 (s, 3 H), 3.5 (s, 6 H).

Anal. Calcd for $C_{18}H_{19}ClN_2O_5$: C, 57.1; H, 5.1; N, 7.4. Found: C, 57.1; H, 4.8; N, 7.7.

1,3-Dimethyl-2,1-benzisothiazolium perchlorate (**1c**) and 1,2,3-trimethylindazolium perchlorate (**1d**) required 0.5 and 24 h reflux times, respectively.

3-(*p*-Dimethylamino-α-methylstyryl)-1-methyl-2,1-benzisoxazolium Perchlorate (eq 2, R = CH_3, Ar = C_6H_5): *p-N,N*-Dimethylaminoacetophenone (1.6 g, 0.01 mol) and **1b** (2.5 g, 0.01 mol) were dissolved in methanol (50 mL) and refluxed for 1 h. Cooling followed by filtration gave 3.6 g (92%) of blue crystals: mp 168–169 °C; NMR (CF_3CO_2H) δ 7.9–7.0 (m, 9 H), 4.2 (s, 3 H), 3.2 (s, 6 H), 2.5 (s, 3 H); UV–vis λ_{max} (CH_3CN) 574 nm (log ϵ 4.71), 305 (4.01).

Anal. Calcd for $C_{19}H_{21}ClN_2O_5$: C, 58.1; H, 5.4; N, 7.1. Found: C, 57.9; H, 5.4; N, 7.0.

3-Formyl-1-methyl-2,1-benzisoxazolium Perchlorate *p*-Nitrophenylhyrazone (5) and Its Conversion to 6: *p*-Nitrobenzenediazonium tetrafluoroborate (0.24 g, 1 mmol) and **1b** (0.25 g, 1 mmol) were dissolved in methanol (30 mL), and the solution was stirred at room temperature for 18 h. Filtration gave 0.27 g (68%) of red crystals: mp 216 °C dec; UV–vis λ_{max} (CH_3CN) 485 nm (log ϵ 4.48); IR (KBr) 3175 (NH), 1620 (C=N), 1090 cm^{-1} (ClO_4).

Anal. Calcd for $C_{15}H_{13}ClN_4O_7$: C, 45.4; H, 3.3; N, 14.1. Found: C, 45.2; H, 3.4; N, 14.0.

A solution of **5** (1.0 g) in methylene chloride (100 mL) was stirred overnight with 0.1 N NaOH (100 mL). Chromatography of the organic phase on silica gel eluting with EtOAc–benzene (25:75) gave **6** as a cherry-red solid (0.51 g, 68%): mp 250–252 °C; UV–vis λ_{max} (CH_3CN) 555 nm (log ϵ 4.06), 395 (4.15).

Anal. Calcd for $C_{15}H_{12}N_4O_3$: C, 60.8; H, 4.1; N, 18.9. Found: C, 60.4; H, 4.2; N, 18.9.

1-Methyl-2,1-benzisoxazolium Trimethinecyanine Perchlorate (7): **1b** (0.5 g, 0.02 mol) and triethyl orthoformate (15 mL) were heated on a steam bath for 1 h. The solution was cooled, and 0.3 g (75%) of blue crystalline solid was collected by filtration: mp 138 °C dec; UV–vis λ_{max} (CH_3CN) 615 nm (log ϵ 4.56).

Anal. Calcd for $C_{19}H_{17}ClN_2O_6$: C, 56.4; H, 4.2; N, 6.9. Found: C, 56.3; H, 4.0; N, 6.6.

***N*-Acetyl-3-(*p-N,N*-dimethylaminostyryl)-2,1-benzisothiazolium Perchlorate (29):** 3-Methyl-2,1-benzisothiazole (1.5 g, 0.01 mol) and acetic anhydride (15 mL) were cooled to −20 °C and treated dropwise with 70% perchloric acid (1.5 g, 0.11 mol). This procedure was followed by the addition of *p*-dimethylaminobenzaldehyde (1.5 g, 0.01 mol) at room temperature, and the resulting solution soon deposited metallic green crystals. Filtration yielded 2.5 g (60%) of material: mp 212–213 °C dec; UV–vis λ_{max} (CH_2Cl_2) 705 nm (log ϵ

4.74), 660 (4.47); IR (KBr) 1724 (C=O), 1613 (C=N), 1087 cm^{-1} (ClO_4); NMR (TFA) δ 8.4–7.4 (m, 10 H), 3.3 (s, 6 H), 2.9 (s, 3 H).

Anal. Calcd for $C_{19}H_{19}ClN_2O_5S$: C, 54.0; H, 4.5; N, 6.6; S, 7.6. Found: C, 53.7; H, 4.8; N, 6.8; S, 7.5.

***N*-Acetyl-3-(*p*-*N*,*N*-dimethylaminostyryl)-2,1-benzisoxazolium Perchlorate (25):** This was prepared as above from 3-methyl-2,1-benzisoxazole in 20% yield: mp 174 °C dec; UV–vis λ_{max} (CH_2Cl_2) 650 nm (log ϵ 4.45), 605 (4.20); IR (KBr) 1724 (C=O), 1081 cm^{-1} (ClO_4).

Anal. Calcd for $C_{19}H_{19}ClN_2O_6$: C, 56.1; H, 4.7; N, 6.9. Found: C, 55.8; H, 5.0; N, 7.0.

Dimerization of 1b with Me_2SO and Deprotonation with Triethylamine to 10: A solution of **1b** (1.0 g, 0.004 mol) in dimethyl sulfoxide (5 mL) was stirred for 15 min. Water (15 mL) was added, and the orange solid was collected by filtration and recrystallized from methanol, giving 0.7 g (44%) of **9:** mp 140 °C dec; IR (Nujol) 1640 (C=N), 1090 cm^{-1} (ClO_4); NMR (TFA) δ 8.4–7.5 (m, 8 H), 4.5 (s, 3 H), 4.3 (br s, 2 H), 3.8 (s, 3 H), 2.1 (s, 3 H).

Anal. Calcd for $C_{18}H_{19}ClN_2O_6$: C, 54.8; H, 4.9; N, 7.1. Found: C, 55.0; H, 5.1; N, 7.4.

The NMR spectrum of *N*-*tert*-butyl-3-methyl-2,1-benzisoxazolium perchlorate in Me_2SO-d_6 shows it is in a 44:56 (dimer) equilibrium with dimer **11:** NMR (Me_2SO-d_6) δ 8.3–6.8 (aromatic), 4.2 (d, J = 14 Hz, HCH dimer), 3.9 (d, J = 14 Hz, HCH dimer), 3.1 (s, $=CCH_3$ monomer), 1.9 (s, $N^+C(CH_3)_3$ monomer), 1.8 (s, CCH_3 dimer), 1.7 (s, $N^+C(CH_3)_3$ dimer), 1.0 (s, $NC(CH_3)_3$ dimer). Addition of D_2O results in a loss of resonance at δ 4.2, 3.9, 3.1, and 1.8, indicating the two species are in equilibrium.

Dimer **9** (1 g) was suspended in methylene chloride (25 mL), and triethylamine was added until the color was discharged. The resulting solution was extracted three times with water (25-mL portions), dried over anhydrous $MgSO_4$, filtered, and evaporated under vacuum. The residual pale yellow oil **10** (0.5 g) which slowly crystallized was analytically pure: NMR ($CDCl_3$) δ 7.2–6.6 (m, 8 H), 5.1 (s, 1H), 3.1 (s, 6 H), 1.9 (s, 3 H); IR (KBr) 1690 cm^{-1} (C=C).

Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.4; H, 6.2; N, 9.5. Found: C, 73.2; H, 6.1; N, 9.4.

3-(*p*-Dimethylaminostyryl)-2,1-benzisothiazole (13): *N*-Acetyl-3-(*p*-dimethylaminostyryl)-2,1-benzisothiazolium perchlorate (1 g) was stirred for 6 h with triethylamine (10 mL), water (50 mL), and diethyl ether (100 mL). The organic phase was separated and dried ($MgSO_4$). Evaporation under vacuum yielded 0.6 g of **13,** a red yellow solid: mp 150–152 °C; UV–vis λ_{max} (CH_3CN) 435 nm (log ϵ 4.41), 308 (4.15); NMR ($CDCl_3$) δ 7.6–6.5 (m, 10 H), 3.0 (s, 6 H).

Anal. Calcd for $C_{17}H_{16}N_2S$: C, 72.8; H, 5.8; N, 10.0; S, 11.4. Found: C, 72.6; H, 5.8; N, 9.8; S, 11.3.

Cyclization of 14 to Spiropyran 15: 2-Hydroxy-1-naphthaldehyde (1.7 g, 0.01 mol) and **1b** (2.5 g, 0.01 mol) were dissolved in methanol (25 mL) and stirred for 2 h at 40 °C. Cooling followed by filtration yielded 3.5 g (87%) of red styryl dye **14:** mp 215–216 °C; IR (KBr) 3125 (OH), 1087 cm^{-1} (ClO_4); UV–vis λ_{max} (CH_3CN) 520 nm (log ϵ 4.52).

Anal. Calcd for $C_{20}H_{16}ClNO_6$: C, 59.8; H, 4.0; N, 3.5. Found: C, 59.5; H, 4.3; N, 3.2.

Styryl dye **14** (1.0 g) was stirred in diethyl ether (50 mL), ammonium hydroxide (10 mL), and water (20 mL) until all the solid had dissolved. The organic phase was separated, dried ($MgSO_4$), and evaporated under vacuum to yield 0.6 g (80%) of **15,** a white solid: mp 160–163 °C (turns red at 155 °C); NMR ($CDCl_3$) δ 8.2–6.8 (m, 11 H), 5.9 (d, J = 9 Hz, 1 H), 3.2 (s, 3 H).

Anal. Calcd for $C_{20}H_{15}NO_2$: C, 79.7; H, 5.0; N, 4.6. Found: C, 79.6; H, 4.9; N, 4.4.

General Procedure for Addition of Cyanide, Azide, Hydride, or Methoxide to 1b, Yielding 16. Sodium cyanide solution (0.5 g in 10 mL water) was added to **1b** (2.5 g, 0.01 mol) slurried in diethyl ether (50 mL). The mixture was stirred for 1 h and diluted with water (50 mL); the ether layer was separated, dried ($MgSO_4$), and evaporated under vacuum. Distillation of the residual yellow oil at 0.05 Torr gave 1.4 g (80%) of 3-cyano-1,3-dimethyl-2,1-benzisoxazoline: bp 50–54 °C; NMR ($CDCl_3$) δ 7.3–6.8 (m, 4 H), 3.1 (s, 3 H), 1.9 (s, 3 H).

Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.9; H, 5.8; N, 16.1. Found: C, 68.8; H, 5.9; N, 16.0.

3-Azido-1,3-dimethyl-2,1-benzisoxazoline from **1b** and NaN_3 (58% yield, yellow oil which was not distilled): IR (neat) 2083 cm^{-1} (N_3); NMR ($CDCl_3$) δ 7.6–6.8 (m, 4 H), 3.1 (s, 3 H), 1.9 (s, 3 H).

Anal. Calcd for $C_9H_{10}N_4O$: C, 56.8; H, 5.3; N, 29.5. Found: C, 56.4; H, 5.0; N, 28.9.

1,3-Dimethyl-2,1-benzisoxazoline from **1b** and $NaBH_4$ (ethanol was used as solvent instead of ether–water, 68%): bp 91–93 °C (18 Torr); NMR ($CDCl_3$) δ 7.2–6.4 (m, 4 H), 5.3 (q, J = 7 Hz, 1 H), 3.0 (s, 3 H), 1.5 (d, J = 7 Hz, 3 H).

Anal. Calcd for $C_9H_{11}NO$: C, 72.5; H, 7.4; N, 9.4. Found: C, 72.4; H, 7.4; N, 9.4.

1,3-Dimethyl-3-methoxy-2,1-benzisoxazoline from **1b** and methanol–triethylamine (methanol was used as solvent instead of ether–water, and 1 equiv of triethylamine was added, 54%): NMR ($CDCl_3$) δ 7.3–6.8 (m, 4 H), 3.1 (s, 6 H), 1.9 (s, 3 H).

Anal. Calcd for $C_{10}H_{13}NO_2$: C, 62.0; H, 7.3; N, 7.8. Found: C, 66.7; H, 7.0; N, 7.7.

Pyrolysis of 3-Cyano-1,3-dimethyl-2,1-benzisoxazoline (16, R = CN). 3-Cyano-1,3-dimethyl-2,1-benzisoxazoline (1 g) was heated at 130 °C for 3 min under N_2. NMR ($CDCl_3$) of the dark blue liquid showed a mixture of (1) starting material at δ 1.8 (s, CCH_3) and 3.10 (s, $N—CH_3$), (2) *N*-methylindoxyl **17** at δ 3.3 (s, CH_2) and 2.6 (s, $N—CH_3$), and (3) *N*,*N*′-dimethylindigo **18** at δ 2.9 (s, $N—CH_3$). The IR spectrum (neat) showed absorption at 3400 and 2250 cm^{-1} due to HCN and at 1715 and 1645 cm^{-1} due to *N*-methylindoxyl and dimethylindigo, respectively. The UV–vis spectrum showed a maximum absorption at 640 cm with a shoulder at 600 nm; the spectrum is identical to that of *N*,*N*′-dimethylindigo.[4]

N-*tert*-Butyl-3-cyano-3-methyl-2,1-benzisoxazoline when treated as above gave only *N*-*tert*-butylindoxyl **19:** NMR ($CDCl_3$) δ 7.5–6.5 (m, 4 H), 3.4 (s, 2 H), 1.1 (s, 9 H); IR (neat) 1715 (C=O), 3400 and 2250 cm^{-1} (HCN).

Registry No.—**1b,** 63609-41-6; **1c,** 64872-29-3; **1d,** 64872-31-7; **5,** 64872-33-9; **6,** 64872-34-0; **7,** 64871-88-1; **8,** 64872-07-7; **9,** 64871-90-5; **10,** 64871-91-6; **11,** 64871-93-8; **13,** 64871-94-9; **14,** 64871-96-1; **15,** 64871-97-2; **17,** 3260-62-6; **18,** 64871-98-3; **19,** 64871-99-4; 3-methyl-2,1-benzisoxazole, 4127-53-1; methyl fluorosulfonate, 421-20-5; sodium perchlorate, 7601-89-0; *tert*-butyl alcohol, 75-65-0; perchloric acid, 7601-90-3; *N*-*tert*-butyl-3-methyl-2,1-benzisoxazolium perchlorate, 63609-46-1; 3-methyl-2,1-benzisothiazole, 20712-09-8; 2,3-dimethylindazole, 50407-18-6; *p*-dimethylaminobenzaldehyde, 100-10-7; *p*-*N*,*N*-dimethylaminoacetophenone, 2124-31-4; *p*-nitrobenzenediazonium tetrafluoroborate, 456-27-9; triethyl orthoformate, 122-51-0; 2-hydroxy-1-naphthaldehyde, 708-06-5; sodium cyanide, 143-33-9; 3-cyano-1,3-dimethyl-2,1-benzisoxazoline, 64872-00-0; 3-azido-1,3-dimethyl-2,1-benzisoxazoline, 64872-01-1; sodium azide, 26628-22-8; 1,3-dimethyl-2,1-benzisoxazoline, 64872-02-2; 1,3-dimethyl-3-methoxy-2,1-benzisoxazoline, 64872-03-3; *N*-*tert*-butyl-3-cyano-3-methyl-2,1-benzisoxazoline, 64900-50-1; $NaBH_4$, 16940-66-2; 3-(*p*-dimethylamino-α-methylstyryl)-1-methyl-2,1-benzisoxazolium perchlorate, 64872-05-5.

References and Notes

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