ml of ethanol was held for 4 days at reflux. The solution was allowed to cool. The resultant solid, 36.1 g, mp 204–215° dec, was crystallized from ethanol to give 33.9 g (76% based on ethoxymethylenemalononitrile) of solid, mp 225–226° dec. The ir spectrum of this material was identical with that of the product obtained by method A.

Method C.—A solution of 60 g (0.231 mol) of [*o*-phenylenebis(iminomethylidyne)]dimalononitrile in 600 ml of N,N-dimethylacetamide was stirred at 100° under nitrogen for 3 hr. The solution was concentrated under vacuum, and the residue was poured into 700 ml of water. The resultant solid, 51.6 g, mp 212–213° dec, was crystallized from 3 l. of hot water (filtration) to give 41.3 g (69%) of product, mp 223–224° dec. The ir spectrum of this material was identical with that of the products obtained by methods A and B.

2-Amino-4-(5,6-dimethyl-1-benzimidazolyl)-1,3-butadiene-1,1,-3-tricarbonitrile (3b).—Reaction of equimolar amounts of 5,6-dimethylbenzimidazole, ethoxymethylenemalononitrile, and malononitrile in ethanol at reflux for 5 days gave white needles, mp 255–256° dec (from ethanol with charcoal treatment), in 75% yield: ir 3.03 sh, 3.20 (NH), 4.58 (CN), 6.20 (weak), 6.46 (C=C) μ; nmr τ −3.95 (s, 2, NH_2), 0.57 (s, 1, N=CHN), 2.42 (s, 2, ArH), 2.93 (s, 1, NCH=C), 7.59 (s, 6, CH_3).

Anal. Calcd for $C_{16}H_{12}N_6$: C, 66.66; N, 4.20. Found: C, 66.50; H, 4.20.

2-Amino-4-(5,6-dichloro-1-benzimidazolyl)-1,3-butadiene-1,1,-3-tricarbonitrile (3c).—*Caution: skin irritant.* By a procedure similar to that employed for **3b** (reaction time, 1 day), the product, mp 268° dec (placed in melting point apparatus at 261°; melting point dependent on rate of heating), was obtained in 71% yield: ir 3.20 (NH), 4.56 (CN), 6.20 (weak), 6.50 μ.

Anal. Calcd for $C_{14}H_6Cl_2N_6$: C, 51.09; H, 1.84; N, 25.53. Found: C, 51.01; H, 1.75; N, 25.57.

2-Amino-4-(1-imidazolyl)-1,3-butadiene-1,1,3-tricarbonitrile (6a).—From equimolar amounts of imidazole, ethoxymethylenemalononitrile, and malononitrile in ethanol solution was obtained, after 18 hr at 23°, a solid product, mp 163–165°, in 46% yield: ir 3.1, 3.2 (NH), 4.58 (CN), 6.35, 6.48 μ; nmr τ −3.75 (bs, 2, NH_2), 0.70 (t, 1, J = 1 Hz, N=CHN), 2.07 (d, 2, J = 1 Hz, HC=CH), 2.82 (s, 1, NCH=C).

Anal. Calcd for $C_{10}H_6N_6$: C, 57.14; H, 2.87; N, 39.98. Found: C, 56.88; H, 2.94; N, 39.79.

2-Amino-4-(4,5-diphenyl-1-imidazolyl)-1,3-butadiene-1,1,3-tricarbonitrile (6b).—A solution of 11.0 g (0.050 mol) of 4,5-diphenylimidazole and 12.2 g (0.10 mol) of ethoxymethylenemalononitrile in 150 ml of ethanol was held for 4 days at reflux. The solvent was removed under vacuum, and the residual solid was crystallized from aqueous ethanol (charcoal) to give 4.3 g (24%) of product: mp 204–205° dec; ir 3.20 (NH), 4.57 (CN), 6.50 μ.

Anal. Calcd for $C_{22}H_{14}N_6$: C, 72.92; H, 3.89. Found: C, 72.82; H, 3.93.

Diethyl 3-Amino-4-(1-benzimidazolylmethylene)-2-cyanoglutaconate (7a).—A solution 11.8 g (0.10 mol) of benzimidazole, 16.9 g (0.10 mol) of ethyl 2-cyano-3-ethoxyacrylate, and 11.3 g (0.10 mol) of ethyl cyanoacetate in 100 ml of ethanol was held for 4 days at reflux and then was allowed to cool. The resultant solid, 28.0 g (79%), mp 193–195°, was collected: ir 3.2 (NH), 4.56 (CN), 5.90, 6.12, 6.20, 6.50 μ; nmr τ −3.19 (bs, 2, NH_2), 0.43 (s, 1, N=CHN), 1.93 (s, 1, NCH=C), 2.25 (multiplet, 4, ArH), 5.90 (q, 4, OCH_2CH_3), 8.80 (t, 6, OCH_2CH_3).

Anal. Calcd for $C_{18}H_{18}N_4O_4$: C, 61.01; H, 5.11; N, 15.81. Found: C, 60.77; H, 5.20; N, 15.64.

Diethyl 3-Amino-2-cyano-4-[(5,6-dimethyl-1-benzimidazolyl)-methylene]glutaconate (7b).—Prepared by the procedure for **7a** with a reaction time of 19 hr, the product, mp 203–204°, was obtained in 65% yield: nmr τ −3.51 (bs, 2, NH_2), 0.57 (s, 1, N=CHN), 1.94 (s, 1, NCH=C), 2.37 (s, 2, ArH), 5.92 (q, 4, OCH_2CH_3), 7.59 (s, 6, CH_3), 8.82 (t, 6, OCH_2CH_3).

Anal. Calcd for $C_{20}H_{22}N_4O_4$: C, 62.82; H, 5.80; N, 14.65. Found: C, 62.55; H, 5.84; N, 15.00.

Diethyl 3-Amino-2-cyano-4-[(1-imidazolyl)methylene]glutaconate (8a).—Prepared by the procedure for **7a**, the product obtained after removal of the solvent was crystallized from water to give a yellow solid, mp 152–154°, in 59% yield: nmr τ −3.62 (bs, 2, NH_2), 0.91 (t, 1, J = 1 Hz, N=CHN), 1.91 (s, 1, NCH=C), 2.31 (d, 2, J = 1 Hz, HC=CH), 5.91 (q, 4, OCH_2CH_3), 8.82 (t, 6, OCH_2CH_3).

Anal. Calcd for $C_{14}H_{16}N_4O_4$: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.14; H, 5.38; N, 18.20.

Diethyl 3-Amino-2-cyano-4-[(2-methyl-1-imidazolyl)methylene]glutaconate (8b).—Prepared by the procedure for **7a**, the product, mp 183–185°, was obtained in 91% yield: nmr τ −2.11 (b, 2, NH_2), 1.91 (s, 1, NCH=C), 2.43 (s, 2, HC=CH), 5.90 (q, 4, OCH_2CH_3), 7.41 (s, 3, CH_3), 8.82 (t, 6, OCH_2CH_3).

Anal. Calcd for $C_{15}H_{18}N_4O_4$: C, 56.60; H, 5.70; N, 17.60. Found: C, 56.62; H, 5.82; N, 17.40.

Registry No.—**3a**, 20406-91-1; **3b**, 20406-92-2; **3c**, 20546-01-4; **4**, 20406-93-3; **6a**, 20406-98-8; **6b**, 20406-94-4; **7a**, 20406-99-9; **7b**, 20406-95-5; **8a**, 20406-96-6; **8b**, 20406-97-7.

The Synthesis of Substituted 2,1-Benzisothiazoles

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2,1-Benzisothiazole (**3**) and nine substituted 2,1-benzisothiazoles have been synthesized by the reaction of thionyl chloride with an appropriately substituted 2-aminotoluene (*o*-toluidine) in xylene at reflux temperature. Yields as high as 80% may be obtained. Liquid benzisothiazoles are conveniently isolated as picrate salts. The mechanism of formation of **3** is discussed and an intermediate benzylidenesulfinyl compound (**8**) is postulated. Nmr and uv data are presented.

2,1-Benzisothiazole (**3**) and its derivatives have received little attention from chemists in the 70 years since the parent compound was prepared by Gabriel and Stelzner.[1] The original method, reduction by stannous chloride and hydrochloric acid of 2-nitrotoluene-α-thiol, was recently supplemented by a procedure involving the iodine oxidation of an alkaline solution of 2-aminotoluene-α-thiol.[2]

Both of these methods suffer from the disadvantage of requiring relatively inaccessible, air-sensitive thiols, and, although in principle such methods could be extended to the synthesis of many substituted 2,1-benzisothiazoles, in practice such an approach is tedious. In exploratory work, we prepared 5-bromo-2,1-benzisothiazole by the oxidative cyclization of the corresponding aminothiol, but the yield was low. The only substituted 2,1-benzisothiazoles so far reported are those with 3-amino substituents, prepared by peroxide oxidation of 2-aminophenylthioamides.[3,4] By contrast,

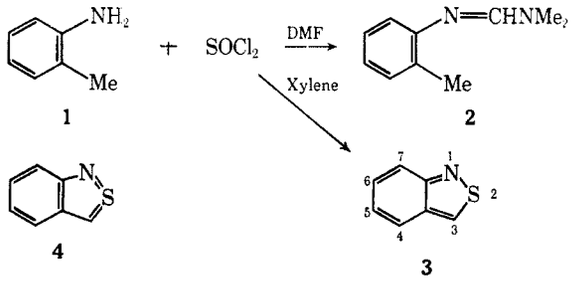
(1) S. Gabriel and R. Stelzner, *Chem. Ber.*, **29**, 160 (1896).
(2) J. Goerdeler and J. Kandler, *ibid.*, **92**, 1679 (1959).
(3) Parke, Davis & Co., Netherlands Patent Application 6408290 (1965); *Chem. Abstr.*, **63**, 1768b (1965).
(4) R. F. Meyer, B. L. Cummings, P. Bass, and H. O. J. Collier, *J. Med. Chem.*, **8**, 515 (1965).

there exists a considerable literature on 2,1-benzisoxazoles[5] and on 1,2-benzisothiazoles.[6]

Recent reports by Naito and coworkers[7,8] on the use, in dimethylformamide solution, of thionyl chloride and sulfur monochloride for construction of the isothiazole ring from compounds containing an amino group and a relatively activated methylene group three carbon atoms removed suggested to us the possibility that 2,1-benzisothiazole might be obtained from a reaction between 2-aminotoluene (**1**) (*o*-toluidine[9]) and thionyl chloride. Although in this latter case the methyl group is not activated, earlier studies in our laboratory[10] on the chemistry and nmr spectrum of 2,1-benzisothiazole had indicated that this compound is surprisingly stable and might well be formed under vigorous reaction conditions.

In view of the current interest in valence-shell expansion in sulfur heterocycles,[11] we note in passing that the properties of 2,1-benzisothiazole indicate a substantial contribution from the tetracovalent sulfur structure **4**.

Reaction between **1** and thionyl chloride in DMF under the general conditions used by the Japanese workers[7,8] afforded the amidine **2** as the main product. No 2,1-benzisothiazole (**3**) could be detected. However, we found that, if xylene were used as the solvent, **3** was formed in reasonable yield, as reported by us in an earlier communication.[12]



We now find that this reaction is a general one, and that substituted 2,1-benzisothiazoles may be prepared from the corresponding substituted 2-aminotoluenes in yields as high as 80%. So far, only 2-amino-5-nitrotoluene has failed to yield the desired product.

The greater basicity of the 2-aminotoluenes and the usually slight solubility of their hydrochlorides in hydrochloric acid can be exploited for a simple separation of the 2,1-benzisothiazoles from the reaction mixtures, which usually contain sulfur and an N-sulfinylarylamine as well as the desired product. 2,1-Benzisothiazoles that are liquids or low-melting solids are conveniently isolated as their picrates. The 2,1-benzisothiazoles and their picrates prepared by the new method are listed in Tables I and II.

TABLE I

MELTING POINTS, BOILING POINTS, NMR DATA, AND MICROANALYSES OF SOME 2,1-BENZISOTHIAZOLES

Registry no.	Substituent	Mp or bp, °C (mm)	τ, H-3[a]	Analyses (calcd, % / found, %) C	H	N	S
271-6-4	None	68 (0.5)[b]	1.07 d	...	...	...	...
20712-04-3	4-Cl	41–42	0.67 d	49.6	2.4	8.2	18.9
20728-40-9 (picrate)				49.8	2.4	8.1	18.7
20712-05-4	5-Cl[c]	72	0.98 d	49.6	2.4	8.2	18.9
				49.7	2.6	8.1	19.0
20712-06-5	6-Cl	71	0.84 d	49.6	2.4	8.2	18.9
				49.7	2.1	8.0	18.6
20712-07-6	5-Br[d]	85	0.91 d	39.3	1.9	6.5	14.9
				39.4	1.9	6.7	14.4
20712-08-7	6-Br[e]	81	0.82 d	39.3	1.9	6.5	14.9
				39.4	1.9	6.7	14.9
20712-09-8	3-CH_3	103	...	64.4	4.7	9.4	21.5
				64.6	4.6	9.1	21.2
20728-41-0	4-CH_3	116 (2)	1.03 d	64.4	4.7	9.4	21.5
20728-42-1 (picrate)				64.3	4.8	9.1	21.0
20712-10-1	7-CH_3	106 (1)	0.91 s	64.4	4.7	9.4	21.5
20728-43-2 (picrate)				64.2	4.7	9.1	21.4
20712-11-2	6-NO_2	149	0.65 d	46.7	2.3	15.5	17.8
				46.8	2.5	15.4	17.5

[a] In $CDCl_3$. [b] Lit.[1] bp 238° (760 mm). [c] Cl: calcd 20.9, found 20.8%. [d] Br: calcd 37.4, found 37.7%. [e] Br: calcd 37.4, found 37.6%.

TABLE II

MELTING POINTS AND MICROANALYSES OF SOME 2,1-BENZISOTHIAZOLE PICRATES

Substituent	Mp, °C	Analyses (calcd, % / found, %) C	H	N	S
None	121[a]	...	...	...	...
4-Cl[b]	99	39.2	1.8	14.1	8.0
		39.5	1.9	13.9	8.0
4-CH_3	135	44.5	2.7	14.8	8.5
		44.6	2.8	14.4	8.2
7-CH_3	98	44.5	2.7	14.8	8.5
		44.5	2.7	14.7	8.8

[a] Lit.[1] mp 123°. [b] Cl: calcd 8.9, found 8.9%.

The known formation of N-sulfinylarylamines from the reaction of arylamines with thionyl chloride[13,14] and evidence of N-sulfinylamines in crude reaction mixtures suggested that 2-methyl-N-sulfinylarylamines, such as (**6**), are intermediates that undergo thermal cyclodehydration. We have found, however, that such compounds, when heated on their own or in high-boiling inert solvents, do not yield 2,1-benzisothiazoles. When heated in the presence of excess thionyl chloride, 2,1-benzisothiazoles are formed, indicating that thionyl chloride—or a product of thermal decomposition of thionyl chloride—is implicated in the cyclodehydration reaction which generates the heterocyclic ring. The following reaction scheme is suggested (Scheme I).

The initial vigorous reaction between **1** and thionyl chloride produces a yellow crystalline compound which is probably the sulfinyl chloride **5**; this, on heating, loses HCl forming the N-sulfinylamine **6**. Continued heating with excess thionyl chloride yields a sulfinyl chloride, **7**, which similarly loses a molecule of HCl. The resulting benzylidenesulfinyl compound **8** eliminates a

(5) K.-H. Wünsch and A. J. Boulton, *Advan. Hetsrocycl. Chem.*, **8**, 303 (1967).

(6) L. L. Bambas in "The Chemistry of Heterocyclic Compounds," "5-Membered Heterocyclic Compounds with Nitrogen and Sulfur, or Nitrogen, Sulfur, and Oxygen (except Thiazoles)," A. Weissburger, Ed., Interscience Publishers, Inc., New York, N. Y., 1952, p 227.

(7) T. Naito, S. Nakagawa, J. Okumura, K. Takahashi, and K. Kasai, *Bull. Chem. Soc. Jap*, **41**, 959 (1968).

(8) T. Naito, S. Nakagawa, J. Okumura, K. Takahashi, K. Masuko, and Y. Narita, *ibid.*, **41**, 965 (1968).

(9) The literature betrays some ambiguity in the numbering of substituted *o*-toluidines. We prefer to name all of our compounds as derivatives of 2-aminotoluene to avoid confusion.

(10) M. Davis, B. Ternai, and A. W. White, unpublished results.

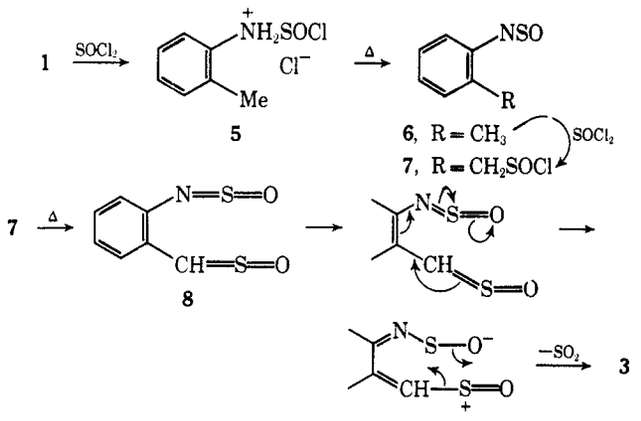
(11) W. G. Salmond, *Quart. Rev.* (London), **22**, 253 (1968).

(12) M. Davis and A. W. White, *Chem. Commun.*, 1547 (1968).

(13) G. Kresze, *Angew. Chem. Intern. Ed. Engl.*, **1**, 89 (1962).

(14) G. Kresze and W. Wucherpfennig, *ibid.*, **6**, 149 (1967).

SCHEME I



molecule of SO_2, generating 2,1-benzisothiazole (**3**). This mechanism is supported by the failure of 5-nitro-2-aminotoluene to form a 2,1-benzisothiazole, even under forcing conditions, suggesting that an intramolecular nucleophilic attack of the N-sulfinyl group upon its *ortho*-substituent is the critical reaction. A *p*-nitro group might reasonably be expected to inhibit such an attack.

Optimum yields of 2,1-benzisothiazoles are obtained when the solvent used has a boiling point between 140 and 170°. Below 140° the reaction is too slow, and above 170° the reaction mixture becomes very black and viscous and the product is then difficult to isolate. We have found xylene (mixed isomers, bp 141–144°) convenient, although bromobenzene (bp 155°) and mesitylene (bp 163°) can also be used with success. Even at 140° some thermal decomposition occurs, and by-products isolated include not only sulfur and N-sulfinylamine, but also chlorinated derivatives of the 2-aminotoluene and of the product 2,1-benzisothiazole.

An attempt to form a novel isothiazolopyridine from 2-amino-3-methylpyridine yielded 2-amino-3-methyl-5-chloropyridine as the only isolated product.

Spectral Data.—The nmr spectrum of **3** shows a complex group of lines between τ 2 and 3, derived from the protons on the carbocyclic ring, and a doublet at τ 1.07 from the proton on the heterocyclic ring. This latter proton is weakly coupled with H-7 ($J \approx 1$ Hz). This doublet (or singlet if position 7 is substituted) is a characteristic feature of the spectra of substituted 2,1-benzisothiazoles, and τ values are listed in Table I. Uv maxima (in 95% EtOH) were at 203 nm (ϵ 14,300), 221 (16,400), 288 sh (7600), 298 (9100), and 315 sh (4000).

Experimental Section

All melting points are uncorrected and were obtained with the Büchi apparatus. Nmr spectra were recorded with a Varian A60-D spectrometer system. Analyses were by the Australian Microanalytical Service, Melbourne.

Chemicals.—Reagents prepared by methods in the literature included 2-amino-4-nitrotoluene,[15] 2-amino-5-nitrotoluene,[16] and 2-amino-4-bromotoluene.[17] Other reagents were obtained from Koch-Light Laboratories Ltd., Colnbrook, England.

2-Amino-5-bromobenzyl Alcohol.—This was prepared in quantitative yield by $LiAlH_4$ reduction of an ether solution of 2-amino-5-bromobenzoic acid.[18] It formed colorless needles (from MeOH), mp 112°.

Anal. Calcd for C_7H_8BrNO: C, 41.6; H, 4.0; Br, 39.6; N, 6.9. Found: C, 41.9; H, 4.1; Br, 39.7; N, 6.8.

6-Bromo-2-thio-4H-3,1-benzothiazine.—This was prepared (85% yield) from 2-amino-5-bromobenzyl alcohol by Kitamura's method.[19] It formed pale yellow needles (from EtOH), mp 235–236°.

Anal. Calcd for $C_8H_6BrNS_2$: C, 36.9; H, 2.3; N, 5.3; S, 24.6. Found: C, 36.6; H, 2.3; N, 5.1; S, 24.0.

6-Bromo-2-oxo-4H-3,1-benzothiazine.—The corresponding thio compound (above) was oxidized in alkaline solution with hydrogen peroxide.[20] The product (80% yield) formed colorless needles (from 50% ethanolic DMF), mp 176°.

Anal. Calcd for C_8H_6BrNOS: C, 39.3; H, 2.5; N, 5.7; S, 13.1. Found: C, 39.0; H, 2.5; N, 5.6; S, 13.0.

2-Amino-5-bromotoluene-α-thiol.—This was prepared from 6-bromo-2-oxo-4H-3,1-benzothiazine by alkaline hydrolysis under nitrogen.[19] The product (85% yield) formed colorless fluffy needles (from aqueous EtOH), mp 133°.

Anal. Calcd for C_7H_8BrNS: C, 38.6; H, 3.7; N, 6.4; S, 14.8. Found: C, 38.9; H, 3.7; N, 6.2; S, 15.1.

5-Bromo-2,1-benzisothiazole.—Iodine oxidation of an alkaline solution of 2-amino-5-bromotoluene-α-thiol by the method of Goerdeler and Kandler[2] afforded in low yield (less than 10%) 5-bromo-2,1-benzisothiazole, identical with that prepared from 2-amino-5-bromotoluene by the general procedure A below. Analyses for this and other 2,1-benzisothiazoles are given in Table I.

Reaction between 2-Aminotoluene and Thionyl Chloride in DMF.—Two grams (19 mmol) of 2-aminotoluene was mixed with 10 ml of DMF and 4 ml (55 mmol) of thionyl chloride was added. An exothermic reaction occurred and the mixture solidified. The mixture was left for 2 hr, water was added, and the solution was neutralized ($NaHCO_3$) and extracted with carbon tetrachloride. Evaporation of the dried extract afforded a pale yellow oil (2.4 g) which contained no 2,1-benzisothiazole (vpc). Infrared and nmr spectra indicated that the principal component of this mixture was 2,N,N-trimethylphenylformamidine (**2**).

Reaction of 2-Aminotoluenes with Thionyl Chloride. General Procedure. A. 6-Bromo-2,1-benzisothiazole.—To a solution of 5.8 g (31 mmol) of 2-amino-4-bromotoluene[17] in 15 ml of xylene (bp 141–144°) was added slowly 8 ml (100 mmol) of thionyl chloride. A vigorous reaction occurred and a yellow crystalline mass separated. The mixture was heated under gentle reflux for 24 hr, a further 8 ml of thionyl chloride was added, and heating was continued for another 24 hr. The mixture was cooled and 50 ml of concentrated hydrochloric acid was added. Sulfur dioxide, from the hydrolysis of the N-sulfinylamine,[13] was evolved. After standing for 30 min, with occasional stirring, the pasty mass was filtered through a coarse fritted filter. The aqueous layer was separated, washed with petroleum ether (bp 40–60°), and diluted with water to 250 ml. The resulting crystalline precipitate was recrystallized from aqueous methanol, affording almost colorless long needles of 6-bromo-2,1-benzisothiazole (2.7 g, 42%), mp 81°. The solid on the fritted filter was extracted with boiling water and yielded, after treatment with activated charcoal, colorless crystals (2.6 g, 39%) of the hydrochloride of 2-amino-4-bromotoluene, mp 246° subl, identified by direct comparison.

General Procedure. B. 4-Methyl-2,1-benzisothiazole.—The procedure A, using 6.1 g (50 mmol) of 2,3-dimethylaniline, was followed, but after dilution of the hydrochloric acid solution an emulsion of the 4-methyl-2,1-benzisothiazole was formed. This was extracted with chloroform, the extracts were dried and evaporated, and the residue was dissolved in 70 ml of a saturated solution of picric acid in methanol. The copious yellow precipitate was recrystallized from methanol, affording yellow needles (5.2 g, 28%) of the picrate of 4-methyl-2,1-benzisothiazole, mp 135°. Decomposition of the picrate salt with dilute sodium hydroxide solution yielded an oil, which was distilled, giving the pure free base, a very pale yellow oil, bp 116° (2 mm).

A list of the 2,1-benzisothiazoles and their picrate salts prepared by procedures A and B is given in Tables I and II. 2-Amino-5-nitrotoluene failed to yield a 2,1-benzisothiazole.

2-Methyl-N-sulfinylaniline (**5**).—This was prepared by the

(15) F. Ullman and E. Grether, *Chem. Ber.*, **35**, 337 (1902).
(16) H. J. Page and B. R. Heasman, *J. Chem. Soc.*, 3238 (1923).
(17) N. W. Janney, *Ann.* **398**, 359 (1913).
(18) A. S. Wheeler and W. M. Oates, *J. Amer. Chem. Soc.*, **32**, 770 (1910).
(19) R. Kitamura, *J. Pharm. Soc. Jap.*, **57**, 54 (1937); *Chem. Abstr.*, **36**, 3804[7] (1942).
(20) R. Kitamura, *J Pharm. Soc. Jap.*, **54**, 1 (1934); *Chem. Abstr.*, **30**, 3434[2] (1936).

procedure given by Kresze;[13] it was a pale yellow oil, bp 73° (0.5 mm) [lit.[21] 184° (100 mm)].

Reactions of 2-Methyl-N-sulfinylaniline (5).—The heating of this compound on its own, or in solution, at temperatures between 100 and 200°, failed to yield any 2,1-benzisothiazole. If, however, thionyl chloride was added to a solution of **5** in xylene, or other inert solvent with a boiling point of between about 140 and 170°, and the mixture was heated to reflux, then 2,1-benzisothiazole could be detected in the reaction mixture by vpc within a few minutes. Formation of 2,1-benzisothiazole paralleled the disappearance of thionyl chloride; it ceased when the latter was exhausted, and could be reestablished by further addition of thionyl chloride. In this way, using 3 or more equiv of thionyl chloride, yields of up to 80% (by vpc) of 2,1-benzisothiazole could be produced. However, the increasing viscosity and darkening of the reaction mixture led to difficulties in isolation of the product. 2-Amino-5-chlorotoluene (as its N-sulfinyl derivative) and 5-chloro-2,1-benzisothiazole were also formed in this reaction in yields of a few percent. Doubtless the chlorine came from the thermal decomposition of the thionyl chloride.

(21) A. Michaelis, *Ann.*, **274**, 226 (1893).

Reaction of 2-Amino-3-methylpyridine with Thionyl Chloride.—A mixture of 5.4 g (50 mmol) of 2-amino-3-methylpyridine was treated with thionyl chloride and xylene as in general procedure A. Neutralization of the final dilute hydrochloric acid solution with ammonia solution afforded a yellow oil which crystallized slowly. On recrystallization from hot water, it afforded colorless leaflets (0.8 g, 11%) of 2-amino-5-chloro-3-methylpyridine, mp 66°.

Anal. Calcd for $C_6H_7ClN_2$: C, 50.5; H, 4.9; Cl, 24.9; N, 19.6. Found: C, 50.4; H, 4.8; Cl, 24.9; N, 19.6.

Registry No.—2-Amino-5-bromobenzyl alcohol, 20712-12-3; 6-bromo-2-thio-4H-3,1-benzothiazine, 20712-13-4; 6-bromo-2-oxo-4H-3,1-benzothiazine, 20712-14-5; 2-amino-5-bromotoluene-α-thiol, 20712-15-6; 2-amino-5-chloro-3-methylpyridine, 20712-16-7.

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2-Alkylidene-2H-indole Intermediates. The Thermolysis of 2-Hydroxydiphenylmethylindole[1,2]

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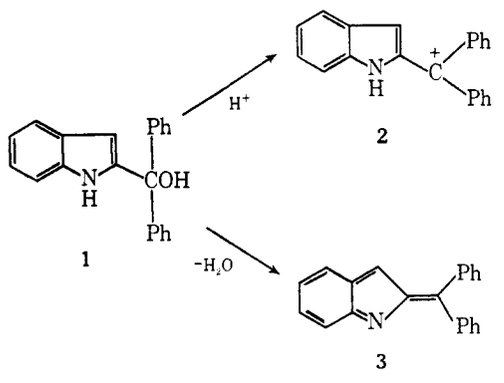
The solution thermolysis of 2-hydroxydiphenylmethylindole (**1**) has been studied and, unlike 1-hydroxytetrahydrocarbazole, does not yield a simple "head-to-tail" dimer but affords a mixture of 2 monomers and 3 dimers: 2-diphenylmethylindole (**5**), 11-phenyl-10-H-indolo[1,2-*a*]indole (**7**), 11,11′,10,10′-biindolo[1,2-*a*]indole (**9**), 11-phenyl-10-[3-(2-diphenylmethyl)indolyl]indolo[1,2-*a*]indole (**8**), and 11,11′-diphenyl-10,10′-biindolo[1,2-*a*]-indolylidene (**10**). Monomer **7** appears to have formed from the 2-alkylidene-2H-indole **3**. The composition of the product mixture is concentration dependent. The structures of the monomers were determined by their uv and nmr spectra, and those of the dimers were determined by their uv and mass spectra and chemical transformations. Compound **5** was synthesized by the zinc–acetic acid reduction of carbinol **1** and by the lithium aluminum hydride hydrogenolysis of 2-methoxydiphenylmethylindole (**4**). Dimer **10** was obtained when **7** was treated with N-bromosuccinimide followed by exposure to base.

A number of transformations of substituted indoles can be rationalized by 2-alkylidene-2H-indole intermediates or their conjugate acids. The hydrogenolysis of 2-indolecarbinols by lithium aluminum hydride has been suggested to proceed *via* a 2-alkylidene-2H-indole intermediate[4] and the dimerization of 1-hydroxytetrahydrocarbazole undoubtedly involves such a species or its conjugate acid.[5] Moreover, these intermediates are obviously implicated in the biosynthesis and synthesis of the dimeric *Vocanga* and *Vinca* alkaloids.[5,6]

It was the purpose of the present study to examine the stability and transformations of such species. An attractive compound for such a study appeared to be 2-hydroxydiphenylindole (**1**) since the stability of the derived triarylcarbonium ion (**2**) could be examined directly and the corresponding 2-alkylidene-2H-indole intermediate (**3**) would be expected to be exceptionally stable.



Carbinol **1** was obtained in 78% yield from the reaction of 2-carbethoxyindole with phenylmagnesium bromide. The carbinol affords a highly stable carbonium ion (**2**) ($pK_R{}^+$ [7] = −1.50) in aqueous sulfuric acid solution.[8] The solvolysis of **1** in acidic methanol gave 2-methoxydiphenylmethylindole (**4**) in high yield.

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(2) Taken from the Doctoral Thesis of P. D. Lord, University of Oregon, Dec 1967.

(3) Alfred P. Sloan Fellow, 1965–1967.

(4) L. J. Dolby and S. Sakni, *J. Amer. Chem. Soc.*, **86**, 1890 (1964); L. J. Dolby and D. L. Booth, *J. Org. Chem.*, **30**, 1550 (1965).

(5) G. Büchi, R. E. Manning, and S. A. Monti, *J. Amer. Chem. Soc.*, **86**, 4631 (1964).

(6) J. P. Kutney, J. Beck, F. Bylsma, and W. J. Cretney, *ibid.*, **90**, 4504 (1968).

(7) N. C. Deno, J. Jaruzelski, and A. Schriesheim, *ibid.*, **77**, 3044 (1955). The $pK_R{}^+$ of 4,4′-dimethoxytriphenylmethyl cation is −1.24 compared with −6.65 for triphenylmethyl cation.

(8) K. Hafner and K. Pfeiffer have recently [*Tetrahedron Lett.*, 4311 (1968)] synthesized **1** from 2-benzoylindole and phenylmagnesium bromide which is reported to have a melting point of 155–156°, some 20° higher than that which we have found. These authors have isolated the carbonium ion **6** as the fluoroborate which shows a visible spectrum similar to that which we observed. They also report the ultraviolet spectrum of **3**.