2,1-Benzisothiazoles. XIII [1]. Intermediates and Products in the Sulfur Extrusion Reaction of 2,1-Benzisothiazolin-3(1*H*)-one. A New Synthesis of 11*H*-Pyrido[2,1-*b*]quinazolin-11-one ("Pyracridone")

Michael Davis*, Robert J. Hook and Wen Yang Wu

Department of Organic Chemistry, La Trobe University, Bundoora, Victoria, Australia, 3083

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Triethyl phosphite abstracts sulfur from 2,1-benzisothiazolin-3(1*H*)-one (**1**); a reaction intermediate is the spirocyclic compound **11**, and products include the benzoxazine **6** and polyanthraniloyl compounds. In the presence of pyridine, pyracridone (**13**) is formed. The ketene-imine **9** is probably not an intermediate in these reactions. The reactions of other nucleophiles with **1** and with its *N*-methyl derivative **15**, have been examined.

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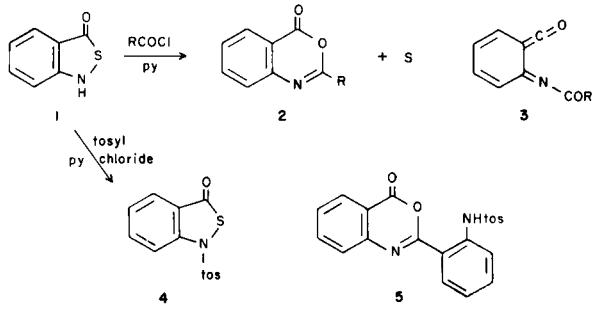
In 1977 we reported [2] that acylation of 2,1-benzisothiazolin-3(1*H*)-one (**1**) in pyridine brings about a sulfur-extrusion reaction with formation of benzoxazinones **2**. It

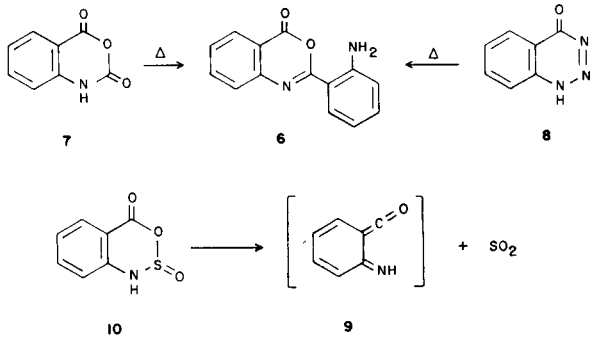


seemed possible that an *N*-acyl ketene-imine **3** might be a reaction intermediate. However, Perronnet and Taliani [3] in 1980 showed that the treatment of **1** with isocyanates, which causes a similar sulfur-extrusion reaction, yields products that seem to exclude the participation of **3**.

Addition of **1** to a solution of tosyl chloride in pyridine affords the highly crystalline *N*-tosyl derivative **4**, mp 124-125°. This compound is more stable to sulfur extrusion than the acyl derivatives. If, however, the order of addition was reversed, *i.e.*, if tosyl chloride was added to a solution of **1** in pyridine, then a second product was obtained; this was the benzoxazinone **5**, suggesting that **1**, perhaps as its anion, could react with the *N*-tosyl derivative **4** and bring about sulfur extrusion. Indeed, when equimolar quantities of **1** and **4** were dissolved in pyridine and set aside for two days, a quantitative yield of **5** was obtained.

The sulfur-extrusion resulting from acylation of **1** in the presence of pyridine, is autocatalytic [4], the catalyst being low-molecular-weight sulfur. This low-molecular-weight sulfur, such as S_6, is a reasonably good sulfur scavenger, but not as efficient as triethyl phosphite. We found that reaction between **1** and **4**, in pyridine, is greatly accelerated by addition of triethyl phosphite; the product **5** crystallises from the mixture within a couple of minutes.

The efficiency of triethyl phosphite in this, and similar, reactions suggested that it might remove sulfur from 2,1-benzisothiazolin-3(1*H*)-one (**1**) itself. This was found to be so; addition of triethyl phosphite to a solution of **1** in pyridine produced a bright yellow solution from which the benzoxazinone **6** could be isolated. This benzoxazinone **6** has been made previously from thermolysis of isatoic anhydride (**7**) or of the benzotriazinone **8** [5,6], and the possible intermediacy of the ketene-imine **9** in these reactions

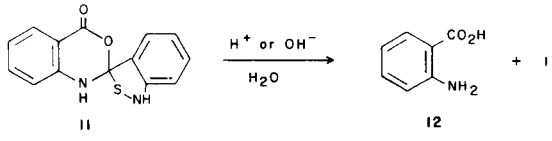


has been proposed. Kametani and his coworkers, in their elegant synthesis of a number of alkaloids, suggested [7] that the same intermediate **9** may be formed by the decomposition of the cyclic sulfinamide **10**, a key compound in their work.

It thus seemed possible that despite the results of Perronnet and Taliani, the reaction of **1** with triethyl phosphite might be a room-temperature source of the ketene-imine **9** and, as such, it merited further study.

Reaction between a pyridine solution of **1**, and triethyl phosphite, produced a mixture which after workup contained at least seven compounds. These were designated **E**, **A**, $\mathbf{B_1}$, $\mathbf{B_2}$, **C**, **X** and **D** in order of increasing Rf. The components were separated and, as far as possible, identified. Component **D**, the major proportion of the mixture, was the yellow benzoxazinone **6** mentioned before; $\mathbf{B_1}$ was starting material **1**; $\mathbf{B_2}$ (trace only) was not examined fur-

ther. Component **C** has a strong carbonyl band at 1770 cm^{-1}, typical of benzoxazinones, and an amide band at 1650 cm^{-1} which, with the nmr spectra, indicated that **C** was probably an *N*-dianthraniloyl derivative of the benzoxazinone **6**. Microanalysis supports this assignment. Component **X** was of interest; the carbonyl frequency in this compound was much lower at 1705 cm^{-1}, and the mass spectrum and nmr indicated that it was the spirocyclic compound **11**; it probably is the key intermediate in the formation of other compounds. Further reaction of **11** with pyridine and triethyl phosphite produced the components **E, A, C** and **D**. Hydrolysis of **11** by aqueous base or acid afforded a mixture of anthranilic acid (**12**) and the starting 2,1-benzisothiazolin-3(1*H*)-one (**1**).



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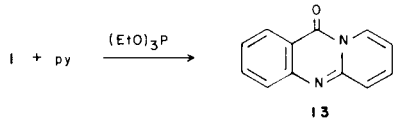
The component **E**, which did not move on tlc, possessed an ir spectrum which was very similar to that of component **C**. The band positions were all the same, but the relative intensities differed, especially the carbonyl band at 1770 cm^{-1}, which was much smaller in **E**. The high mp and general insolubility of **E**, together with the ir, nmr and microanalytical evidence suggests that it is poly(anthraniloyl)benzoxazinone.

Component **A** was the most surprising product; it was 11*H*-pyrido[2,1-*b*]quinazolin-11-one ("pyracridone") (**13**). Pyridine is regarded as relatively unreactive, and it was not expected it would take part in the extrusion reaction, other than as a base. As far as we are aware, this is a novel synthesis of pyracridone (**13**), and the only one that makes



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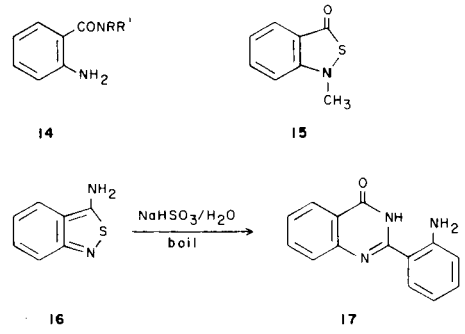
use of the unsubstituted pyridine itself. All other syntheses employ a 2-substituted pyridine (2-amino or 2-chloropyridine, or 2-pyridone) for the preparation of pyracridone. We are investigating the scope of this new reaction. We have found, for example, that pyracridone (**13**) can be produced in about 20% yield by simply boiling a solution of **1** in *aqueous* pyridine for a few hours.

The reaction between **1** and triethyl phosphite in other solvents (ether, tetrahydrofuran, acetonitrile, *etc.*) generally afforded mixtures of **6** and **11**. As **11** is only slightly soluble in diethyl ether, it precipitated out as the major product when the reaction was performed in that solvent; in other inert solvents, **6** was the major product. In acetic acid, *N*-acetylanthranilic acid was formed.

Attempts to form simple anthranilate esters, by reaction between **1** and triethyl phosphite in the presence of alcohols, or phenols, were unsuccessful; if any reaction did occur, then the benzoxazinone **6** was the main product. Even the use of sodium ethoxide failed to produce ethyl anthranilate.

Primary alkylamines, in a mixture of water and dimethylformamide, reacted with **1** in the presence of triethyl phosphite to yield the corresponding anthraniloylamides **14** in low yield; secondary amines reacted similarly even in the absence of triethyl phosphite.



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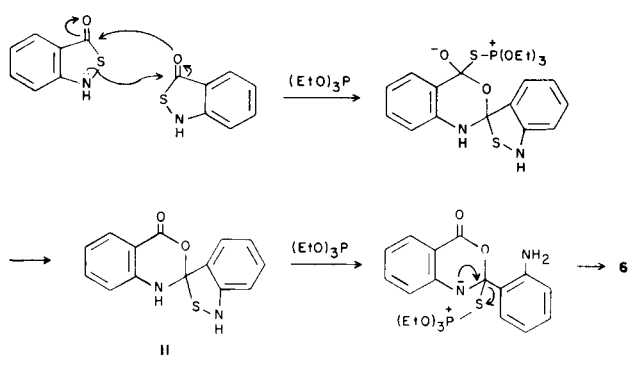
1-Methyl-2,1-benzisothiazolin-3-one (**15**) reacts more readily with sodium ethoxide, or amines, even in the absence of triethyl phosphite or other sulfur scavengers, and high yields of the corresponding *N*-methylanthraniloyl ester, or amides, can be obtained.

Some years ago in this laboratory, the reaction between 3-amino-2,1-benzisothiazole (**16**) and sodium hydrogen sulfite was investigated: the aim was to bring about a Bucherer-type exchange of the amino group for a hydroxy group, thus affording 3-hydroxy-2,1-benzisothiazole which is, of course, the enol form of **1**. Instead, the quinazolinone **17** was formed in 66% yield. It is now obvious that this reaction is analogous to the ones reported above. The sulfite ion, which forms thiosulfate ion with sulfur, plays the part of sulfur scavenger [8].

It seems that the ketene-imine **9** or a related compound is not an intermediate in these sulfur-extrusion reactions of **1**. If it were, then anthranilic acid would have been found in the aqueous solutions, rather than the pyracrid-

SCHEME I



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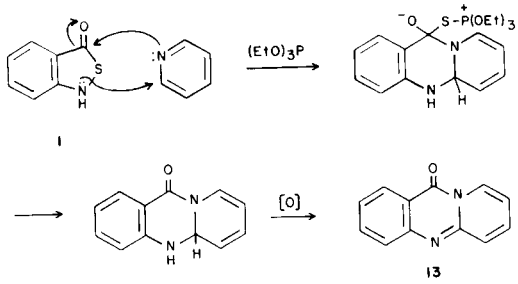
one **13**, and esters would have been produced in the presence of alcohols or phenols. The isolation of the intermediate **11** shows that these reactions are indeed stepwise. All the observed products can be accommodated by a mechanism in which nucleophilic attack of the amine (or anion of **1** *etc.*) occurs at the carbonyl group of **1**. Schemes 1 and 2 show possible sequences.

SCHEME 2



EXPERIMENTAL

The pmr spectra were recorded on a Perkin-Elmer R32 spectrometer with chemical shifts reported in δ values relative to tetramethylsilane. Infrared spectra were recorded on a Perkin-Elmer 257 spectrophotometer. Melting points are uncorrected and were obtained with a microscope hot stage apparatus. Mass spectra were recorded on a Jeol JMS D-100 instrument. The tlc was performed on silica gel 60 F_{254} plates (Merck), and observed under uv light. Microanalyses were performed by the Australian Microanalytical Service, Melbourne.

3-Tosyl-2,1-benzisothiazolin-3(1*H*)-one (**4**).

A solution of 0.320 g (2 mmoles) of **1** in 1 ml of dry pyridine was added dropwise to a solution of 0.4 g (2.1 mmoles) of tosyl chloride in 1 ml of dry pyridine. After 30 minutes the mixture was cooled in ice and 5 ml of ice-water added. After a further 90 minutes the crystals were separated and recrystallised from aqueous acetone giving 0.386 g (63%) of colorless needles, mp 124-125°; ir (potassium bromide): 1680 (C=O), 1580, 1360, 1160 (S=O), 890 cm^{-1}; nmr (deuteriochloroform): δ 2.30 (s, CH_3, 3H), 7.11 (m, aromatic, 3H), 7.56 (m, aromatic, 4H), 8.13 (m, aromatic, 1H).

Anal. Calcd. for $C_{14}H_{11}NO_3S_2$: C, 55.1; H, 3.6; N, 4.6; S, 21.0. Found: C, 55.1; H, 3.9; N, 4.4; S, 20.8.

Reaction Between **1** and Tosyl Chloride With Inverse Addition.

A solution of 0.4 g (2.1 mmoles) of tosyl chloride in 1 ml of dry pyridine was added slowly to a solution of 0.302 g (2 mmoles) of **1** in 1 ml of dry pyridine. After 90 minutes the mixture was diluted with 5 ml of water. The resulting solid was fractionally crystallised from aqueous acetone, affording 0.180 g (30%) of the *N*-tosyl derivative **4**, and 0.250 g (32%) of pale yellow rhombs of 2-(2′-tosylaminophenyl)-3,1-benzoxazin-4-one (**5**), mp 219°, identical with an authentic sample prepared from anthranilic acid and tosyl chloride in pyridine, lit mp 220-221° [10].

Reaction Between **1** and **4** in Pyridine, in the Absence or Presence of Triethyl Phosphite.

A solution of 0.025 g (0.16 mmole) of **1** and 0.051 g (0.16 mmole) of **4** in 0.3 ml of dry pyridine was set aside at room temperature for 2 days. Large pale yellow rhombic crystals, 0.060 g (95%) of **5** had separated, mp and mixed mp 220°. Some lemon yellow octahedral crystals, mp 118° and thus probably of sulfur, were also present in the mixture. This reaction was repeated, but with two drops of triethyl phosphite being added after mixing. The solution crystallised within 2 minutes. After 30 minutes the product was filtered off and recrystallised from a mixture of chloroform and light petroleum, affording 0.051 g (81%) of pale yellow needles of **5**, mp and mixed mp 220°.

Reaction Between **1** and Triethyl Phosphite in Pyridine Solution.

To a stirred solution of 3 g (20 mmoles) of **1** in 25 ml of dry pyridine, 4 g (24 mmoles) of triethyl phosphite was added dropwise at room temperature. The mixture was left to stand at room temperature overnight, and was then evaporated under reduced pressure. The yellow semi-solid residue was triturated with three lots of 50 ml of light petroleum (bp 40-70°), affording 2.1 g of a yellow powder. The tlc of this powder on ethyl acetate:chloroform:cyclohexane (1:3:4) indicated seven compounds designated **E**, Rf 0.0; **A**, Rf 0.11; $\mathbf{B_1}$, Rf 0.18; $\mathbf{B_2}$, Rf 0.24 (trace); **C**, Rf 0.29; **X**, Rf 0.41; **D**, Rf 0.53 (main component). Component $\mathbf{B_1}$, which could be extracted from the mixture by cold dilute sodium hydroxide solution, proved to be starting material **1**. Component $\mathbf{B_2}$ was not further investigated.

Isolation of Component **A**, **13**, From the Reaction Mixture.

One g of the above yellow powder was dissolved in 500 ml of diethyl ether and the solution, after being filtered to remove 0.18 g of insoluble components **C** and **E**, was extracted three times with 100 ml of ice-cold 0.1*M* hydrochloric acid. The light petroleum washings (above) were similarly extracted. The acidic extracts were combined, washed with 50 ml ether, then whilst being kept cold, were carefully basified to *p*H 10 with 10% aqueous sodium hydroxide solution. The solution was extracted with three 100 ml portions of diethyl ether and the extract was washed with water, dried, and evaporated. The residue was recrystallised successively from a mixture of acetone and light petroleum, then methanol, affording 0.080 g (5%) of pale yellow prisms of 11*H*-pyrido[2,1-*b*]quinazolin-11-one ("pyracridone") (**13**), mp 210-211°, identical with an authentic sample prepared from 2-chloropyridine and anthranilic acid, lit mp 210° [11]. A greater yield of **13** (*ca* 10%) is obtained by using a more dilute solution of **1** in pyridine.

Isolation of Components **E** and **C** From the Reaction Mixture.

The 0.18 g of ether-insoluble components **C** and **E** was stirred twice with 50 ml portions of chloroform. The amorphous insoluble residue **E**, 0.12 g, appeared to be of polyanthraniloylbenzoxazinone, mp >325°; ir (potassium bromide): 3460, 3340, 3150, 3100, 3060, 1770, 1650, 1610, 1580, 1520, 1420, 1330, 1300, 1270, 1235, 1170, 1055, 1040, 1010, 980, 920, 780, 640 cm^{-1}; nmr (perdeuteriodimethyl sulfoxide): δ 6.1 (m, NH), 6.5-8.15 (m, aromatic H), 11 (s, CONH or CO_2H).

Anal. Calcd. for $(C_7H_6NO)_x$: C, 70.5; H, 4.2; N, 11.7. Found: C, 70.3; H, 4.4; N, 11.6.

Component **C** was isolated by preparative tlc on silica gel of the above chloroform extract using benzene:ethyl acetate:cyclohexane (2:2:3) followed by elution with tetrahydrofuran. Recrystallisation from chloroform and light petroleum (bp 40-70°) afforded fine needles, mp 190-192°; ir (potassium bromide) identical band positions to those of component **E**, but different relative intensities especially the 1770 cm^{-1} band; nmr (deuteriochloroform): δ 5.8 (br, NH, 2H), 6.72 (m, 2H), 7.1-8.1 (m, aromatic H, 10H), 8.38 (m, 2H), 8.90 (m, 2H), 12.0 (m, 1H), 13.48 (s, 1H).

Anal. Calcd. for $(C_7H_5NO)_x$: C, 70.5; H, 4.2; N, 11.7. Found: C, 70.6; H, 4.0; N, 11.6.

Component **C** appears to be 2-(*N*-anthraniloyl-N′-anthraniloyl-2-aminophenyl)-3,1-benzoxazin-4-one.

Isolation of Component **D**, **6**, From the Reaction Mixture.

The ether solution, from which component **A** had been extracted, was concentrated to about 120 ml and quickly extracted four times with 100 ml of ice-cold 1.75*M* aqueous hydrochloric acid. The extracts were washed with ether, adjusted to *p*H 9 with 10% aqueous sodium hydroxide solution whilst being kept cold, then extracted twice with 150 ml lots of ether. The ether layers were washed, dried, and evaporated, and the residue (0.22 g) sublimed under vacuum at 130°. The light yellow sublimate was recrystallised three times from hexane to afford fine yellow needles of **6**, mp 173-174°, identical with an authentic sample, lit mp 170-172° [5,6].

Isolation of Component **X**, **11**, From the Reaction Mixture in Pyridine.

The ether solution (above) from which component **D** had been extracted was evaporated to dryness and the residue extracted with 100 ml of boiling light petroleum (bp 40-70°). On cooling overnight the light petroleum deposited a pale yellow precipitate, 0.050 g, which was chromatographed on a preparative tlc plate with ethyl acetate:chloroform:cyclohexane (1:3:4), and eluted with tetrahydrofuran. The residue was recrystallised from benzene and formed light yellow prisms of 2,1-benzisothiazoline-3-spiro-2',4'-oxo-4'*H*-3',1'-benzoxazolidine (**11**), mp 152-153°; ir (potassium bromide): 3450, 3300, 3170, 1705, 1630, 1600, 1560, 1490, 1405, 1380, 1295, 1235, 1160, 1140, 1120, 1035, 775, 770 cm^{-1}; nmr (deuteriochloroform): δ 5.89 (br, NH, 2H), 6.89 (m, aromatic H, 2H), 7.06-7.67 (m, aromatic H, 3H), 7.67-8.0 (m, aromatic H, 2H), 8.11 (m, aromatic H, 1H); ms: 270 (M^+), 238 (M-S), 151 (M-C_7H_5NO), 121, 92.

Anal. Calcd. for $C_{14}H_{10}N_2O_2S$: C, 62.2; H, 3.7; N, 10.4; S, 11.9. Found: C, 62.3; H, 3.9; N, 10.3; S, 11.8.

Isolation of **11** and **6** From the Reaction Between **1** and Triethyl Phosphite in Ether Solution.

To a suspension of 1 g (6.6 mmoles) of **1** in 20 ml anhydrous diethyl ether, 1.2 g (7.2 mmoles) of triethyl phosphite was added and the mixture was stirred at room temperature for 8 hours. The precipitate, 0.320 g, was filtered off, washed with small portions of cold ether and light petroleum (bp 40-70°) then dissolved in 200 ml of ether. The ether solution was washed successively with cold 5% aqueous sodium hydroxide solution, and with water, then was dried and evaporated. The residue (0.270 g) was recrystallised from benzene, affording light yellow prisms of **11**, mp 152-153° as before. The best yield of **11** (42%) was obtained by using a smaller proportion of triethyl phosphite, about two-thirds of an equivalent. Washing of the original ether solution with cold 0.1*M* aqueous hydrochloric acid, water, cold 0.1*M* sodium hydroxide solution, and water again, afford a solution from which **6** could be extracted with 1.75*M* aqueous hydrochloric acid, as described above.

Hydrolysis of **11** With Aqueous Alkali or Acid.

To 0.054 g (0.2 mmole) of **11** in 1 ml of tetrahydrofuran, 1 ml of 8% aqueous sodium hydroxide solution was added and the mixture shaken for 10 minutes at room temperature. To this mixture 10 ml of diethyl ether was added and the mixture, cooled in an ice bath, was brought to *p*H 4 by addition of 10% hydrochloric acid. The ether layer was separated, washed with water, and applied to a tlc plate, using ethyl acetate:chloroform:cyclohexane (1:3:4) as eluent. Two spots, Rf 0.063 and 0.188, showed, corresponding to anthranilic acid and 2,1-benzisothiazolin-3(1*H*)-one respectively. A similar result was obtained when 1 ml of concentrated hydrochloric acid was used, in place of the sodium hydroxide solution, and the hydrolysis allowed to proceed for 20 minutes.

Further Reaction of **11** With Triethyl Phosphite and Pyridine.

To a solution of 0.100 g (0.37 mmole) of **11** in 5 ml of anhydrous pyridine was added 0.100 g (0.60 mmole) of triethyl phosphite, and the mixture was set aside overnight. Evaporation of this solution and examination of the residue by tlc, as described above, showed that it contained mainly **6** together with smaller quantities of **11**, **13** and the polyanthraniloyl components **C** and **E**.

Reaction of **1** With Triethyl Phosphite in Acetic Acid.

To a suspension of 0.100 g (0.66 mmole) of **1** in 1 ml of acetic acid, 0.120 g (0.72 mmole) of triethyl phosphite was added, and the mixture left overnight at room temperature. Saturated aqueous sodium hydrogen carbonate solution was then added to bring the *p*H to 6.5-7.0, and after extraction with ether the solution was acidified to *p*H 1.0-1.5 with 10% aqueous hydrochloric acid. The white precipitate, 0.080 g (67%) was recrystallised from ethyl acetate, affording 2-acetamidobenzoic acid (*N*-acetylanthranilic acid), mp and mixed mp 184-185°.

Formation of Pyracridone (**13**) from 2,1-Benzisothiazolin-3(1*H*)-one (**1**) by Boiling With Aqueous Pyridine.

A solution of 0.100 g (0.66 mmole) of **1** in a mixture of 10 ml of pyridine and 10 ml of water was heated under reflux for 6 hours. The mixture was evaporated to dryness under reduced pressure, 100 ml of dry diethyl ether was added, and the mixture heated under reflux for a further 2 hours. The precipitate, indicated as component **E** by tlc, was filtered off, and the ether solution extracted twice with 75 ml portions of 0.1*M* aqueous hydrochloric acid solution. The acid extracts were washed with 10 ml of ether, then basified to *p*H 10 with 10% aqueous sodium hydroxide solution. This alkaline solution was extracted twice with 100 ml portions of ether, and the combined ether extracts washed with water, dried, and evaporated. The residue was recrystallised from methanol, affording 0.025 g (19%) of pale yellow prisms, mp 209-210°, of 11*H*-pyrido[2,1-*d*]-quinazolin-11-one (pyracridone) (**13**).

Reaction Between **1** and Ethanol or Phenol.

Attempts to produce simple esters of anthranilic acid by reaction between **1** and ethanol or phenol, in the presence or absence of triethyl phosphite, or of bases, were unsuccessful. In general, the main product, in those cases where any reaction occurred, was the benzoxazinone **6**; only traces of esters were formed.

Reaction Between **1** and Methylamine.

To a solution of 0.300 g (1.98 mmoles) of **1** in 1 ml of dimethylformamide was added 0.710 g (5.93 mmoles) of 25% aqueous methylamine solution and 0.400 g (2.41 mmoles) of triethyl phosphite. The mixture was left overnight and was then evaporated under reduced pressure. The residue was dissolved in 90 ml of chloroform and extracted three times with 30 ml quantities of 1.5*M* hydrochloric acid. The combined acid layers were neutralised with 10% aqueous sodium hydroxide solution, extracted three times with 30 ml quantities of chloroform, and the extracts dried and evaporated. Chromatography of the residual oil on a short silica gel column using ethanol:chloroform (1:9) as eluent afforded 0.080 g (27%) of a solid identified by ir and nmr as 2-amino-*N*-methylbenzamide (**14**, R = H, R' = Me), mp 52-54°, lit mp 57-58° [12].

Reaction Between **15** and Sodium Ethoxide in Ethanol.

To a solution of 0.020 g (0.87 mmole) of sodium in 1 ml of ethanol was added 0.050 g (0.30 mmole) of 1-methyl-2,1-benzisothiazolin-3-one (**15**) [14] and the mixture set aside overnight at room temperature. The mixture was poured into 10 ml of water and extracted three times with 20 ml quantities of chloroform. Evaporation of the dried chloroform extracts afforded 0.030 g (56%) of a solid identified by ir and nmr as ethyl 2-*N*-methylaminobenzoate, mp 37-38°, lit mp 39° [15].

Reaction Between **15** and Alkylamines in Aqueous Dimethylformamide.

To a mixture of 0.470 g (3.64 mmole) of 24% aqueous methylamine solution and 1 ml of dimethylformamide was added 0.300 g (1.82 mmoles) of **15**, and the mixture was set aside overnight. Work-up, as described above for the reaction between **1** and methylamine, afforded 0.115 g (35%) of a solid identified by ir and nmr as *N*-methyl-2-*N'*-methylaminobenzamide, mp 39-41°, lit mp 43-45° [16]. A similar reaction with dimethylamine afforded a 96% yield of *N,N*-dimethyl-2-*N*-methylaminobenzamide, mp 88-89°, lit mp 90-91° [13].

Reaction Between **16** and Aqueous Sodium Hydrogen Sulfite Solution [8].

To a solution of 55 g of sodium hydrogen sulfite in 200 ml of water was added 7.0 g (47 mmoles) of 3-amino-2,1-benzisothiazole [17] and the mixtue was heated under reflux for 60 hours. The yellow-brown solid that had separated was recrystallised successively from aqueous ethanol and from a mixture of benzene and chloroform, affording 3.63 g (66%) of a yellow compound identified by ms and elemental analysis as 2-(2-aminophenyl)-3*H*-quinazolin-4-one (**17**), mp 238°, lit mp 236-238° [18]. Extraction of the aqueous filtrate five times with 25 ml quantities of ether afforded 0.85 g (15%) of 2-aminobenzonitrile, mp and mixed mp 47°.

REFERENCES AND NOTES

[1] Part XII, M. Davis and M. J. Hudson, *J. Heterocyclic Chem.*,

20, 1707 (1983).

[2] M. Davis and S. P. Pogany, *ibid.*, **14**, 267 (1977).

[3] J. Perronnet and L. Taliani, *ibid.*, **17**, 673 (1980).

[4] M. Davis and K. C. Tonkin, *Aust. J. Chem.*, **34**, 755 (1981).

[5] R. K. Smalley, H. Suschitzky and E. M. Tanner, *Tetrahedron Letters*, 3465 (1966).

[6] H. E. Crabtree, R. K. Smalley and H. Suschitzky, *J. Chem. Soc. (C)*, 2730 (1968).

[7] T. Kametani, C. V. Loc, T. Higa, M. Koizumi, M. Ihara and K. Fukumoto, *J. Am. Chem. Soc.*, **99**, 2306 (1977).

[8] E. Homfeld, Ph.D. thesis, La Trobe University (1975).

[9] A. H. Albert, R. K. Robins and D. E. O'Brien, *J. Heterocyclic Chem.*, **10**, 413 (1973).

[10] All-Union Scientific Research Institute of Chemical Reagents and Pure Substances, French Patent 1,392,448 (1965); *Chem. Abstr.*, **63**, 13277g (1965).

[11] P. K. Boze and D. C. Sen, *J. Chem. Soc.*, 2843 (1931); C. Räth, *Ann. Chem.*, **486**, 284 (1931). The structure proposed by these workers has been shown to be incorrect by E. Späth and F. Kuffner, *Ber.*, **71**, 1657 (1938), and others.

[12] J. Maillard, M. Benard, M. Vincent, V. V. Tri, R. Jolly, R. Morin, C. Menillet and Mrs. Benharkate, *Chim. Ther.*, **2**, 202 (1967); *Chem. Abstr.*, **68**, 12949h (1968).

[13] R. P. Staiger and E. B. Miller, *J. Org. Chem.*, **24**, 1214 (1959).

[14] M. Davis, L. W. Deady, E. Homfeld and S. P. Pogany, *Aust. J. Chem.*, **28**, 129 (1975).

[15] D. Voslander, R. V. Schilling and M. Schrodter, *Ber.* **34**, 1645 (1901).

[16] D. J. Fry, J. D. Kendall and A. J. Morgan, *J. Chem. Soc.*, 5062 (1960).

[17] R. F. Meyer, B. L. Cummings, P. Bass and H. O. J. Collier, *J. Med. Chem.*, **8**, 515 (1965).

[18] K. Butler and M. W. Partridge, *J. Chem. Soc.*, 2396 (1959).