# Reaction of Benzazole Derivatives with Dimethyl Acetylenedicarboxylate. Crystal and Molecular Structures of [1,4]Thiazino[4,3-*a*]benzimidazole Derivatives

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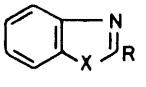
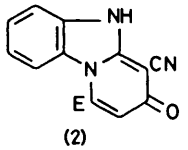
The reaction of (1*H*-benzimidazol-2-ylthio)acetonitrile with dimethyl acetylenedicarboxylate (DMAD) has been studied. In benzene, THF or DMF the major product is a [1,3]thiazolo[3,2-*a*]benzimidazole derivative (5a) but in ethanol the major product is either a [1,3]thiazino[3,2-*a*]benzimidazole or a [1,3]thiazepino[3,2-*a*]benzimidazole derivative. (1-Methyl-1*H*-benzimidazol-2-ylthio)acetonitrile reacted with DMAD in DMF to give three products in very low yield; two of these compounds were shown to be [1,4]thiazino[4,3-*a*]benzimidazoles by *X*-ray crystallographic analysis. The analogous (benzo-1,3-thiazol-2-ylthio)acetonitrile reacts with DMAD in aqueous methanol to give a complex product, one compound of which is a pyrido[1,2-*b*][1,3]benzothiazole derivative. The mechanisms of these novel annelation processes are discussed.

THE value of activated acetylenes (*e.g.* dimethyl acetylenedicarboxylate, DMAD) in heterocyclic synthesis is well established.[1] An interesting elaboration is the approach using alkyl [2] or substituted-alkyl [3] groups as side-chains in the heterocyclic substrate. In this manner the site of nucleophilic reactivity is removed from the initial DMAD-derived intermediate to the side-chain, and ensuing cyclisations provide facile syntheses of condensed heterocycles [*e.g.*[3] (1a) ⟶ (2) + (3) + (4)]. A logical extension of reactions of this type [2,3] would involve the use of more complex side-chains. With the intention of synthesising sulphur-containing tricyclic compounds we have investigated reactions of (benzimidazol-2-ylthio)acetonitrile derivatives (1b and c) and the (1,3-benzothiazol-2-ylthio)acetonitrile (1d) with DMAD.



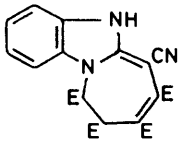
(1)

| | X | R |
|---|---|---|
| a; | NH | $CH_2CN$ |
| b; | NH | $SCH_2CN$ |
| c; | NMe | $SCH_2CN$ |
| d; | S | $SCH_2CN$ |
| e; | NH | $SCH(CO_2Et)_2$ |



(2)

E = $CO_2Me$



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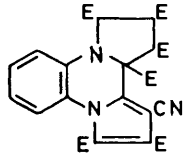
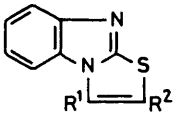


(4)

RESULTS AND DISCUSSION

(1*H*-Benzimidazol-2-ylthio)acetonitrile (1b) reacted with DMAD in benzene, tetrahydrofuran (THF), or dimethylformamide (DMF) to give a product containing three compounds. In each case the major product (9—17%) was the thiazolo[3,2-*a*]benzimidazole derivative (5a) as evidenced by analytical and spectroscopic data (see Experimental section). This compound was



(5)

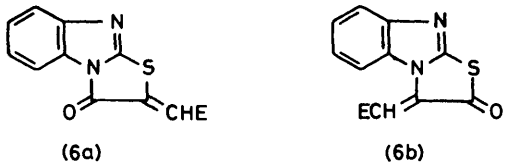
| | $R^1$ | $R^2$ |
|---|---|---|
| a; | $CO_2Me$ | $CO_2Me$ |
| b; | $CO_2Me$ | H |
| c; | H | $CO_2Me$ |
| d; | $CO_2H$ | $CO_2H$ |
| e; | H | H |

converted into a monoester by treatment with ethanolic potassium hydroxide at room temperature, but n.m.r. data could not be used to differentiate between the two possible structures (5b or c).† The diester was successfully hydrolysed to the diacid (5d) by treatment with potassium hydroxide in aqueous dioxan and the diacid (5d) rapidly decarboxylated when it was heated to 220 °C in admixture with sand; the product, thiazolo-[3,2-*a*]benzimidazole (5e) was spectroscopically (n.m.r.) identical to material prepared independently [4,5] by a different route.

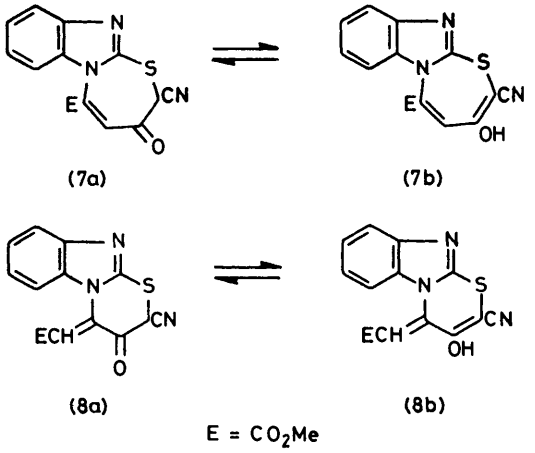
The mechanism of formation of the diester (5a) is unclear. One possible route could involve an intramolecular nucleophilic substitution at sulphur although it should be noted that whilst nucleophilic displacements at divalent sulphur have been observed,[6] we know of no previous examples of substitution at divalent sulphur by a carbanion and involving a carbanion leaving group; this suggestion is thus tentative. Evidently the cyanomethyl moiety of (1b) can be replaced by the good leaving group diethylmalonyl: the diester (1e) reacted with DMAD in DMF to give the thiazolo[3,2-*a*]benzimidazole derivative (5a) in 16% yield.

† We cannot offer an explanation for this unusual selective hydrolysis–decarboxylation process.

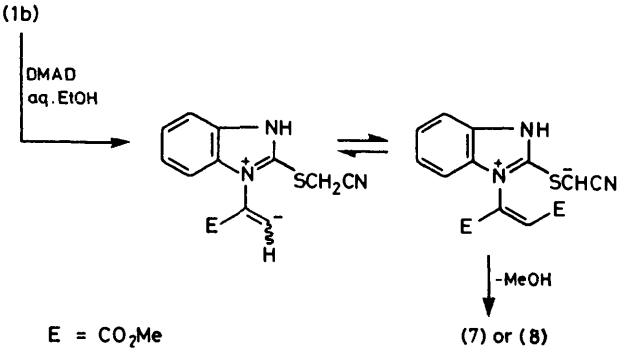
Of the two other compounds (A and B) * formed in the initial DMAD reaction with (1*H*-benzimidazol-2-ylthio)acetonitrile, the first (A) was formed in trace quantities (0.5%) in benzene and THF and in higher yield (16%) in dry ethanol. This compound is identical to the material prepared [7] by treating benzimidazoline-2-thione with DMAD in glacial acetic acid and formulated [7] as the thiazolo[3,2-*a*]benzimidazole derivative (6a). The structure (6a) is only one of four possible formulations (6a—d) that can be envisaged from the reaction of benzimidazoline-2-thione with DMAD. The validity of structure (6a) was confirmed in the present work by an *X*-ray crystallographic study.[8] Presumably in the present work compound (6a) is formed *via* benzimidazoline-2-thione which arises by decomposition of the thioacetonitrile derivative (1a).




Compounds A (6a) and B are also formed in 12 and 3% yields, respectively, when the nitrile (1b) is treated with DMAD under reflux in aqueous ethanol, but the major product (23% yield) is an insoluble pale yellow compound ($C_{14}H_9N_3O_3S$). The i.r. spectrum indicates strong hydrogen bonding (3 200—2 200 $cm^{-1}$) which would obscure nitrile group absorption, and showed two



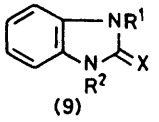

peaks in the carbonyl region (1 740 and 1 720 $cm^{-1}$). These data, together with information from the $^1H$ n.m.r. spectrum (four aromatic, three methoxy, one alkene, and one other proton) can be accommodated



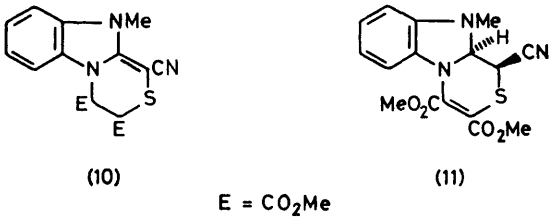

SCHEME 1

either within the thiazepino[3,2-*a*]benzimidazole (7) or the [1,3]thiazino[3,2-*a*]benzimidazole (8) structures.† An intramolecular cyclization of the type depicted in Scheme 1 can be envisaged for this reaction [(1b)—(7) or (8)] [*cf.* the mechanism suggested for the conversion (1a)→(2) [3]].

Extensive tar formation occurred when (1-methyl-1*H*-benzimidazol-2-ylthio)acetonitrile was allowed to react with DMAD in hot DMF, and three compounds were isolated with difficulty and in very low yield [D (2%), E (<2%), and F (<0.5%)]. Compound (D)




| | $R^1$ | $R^2$ | X |
|---|---|---|---|
| a; | Me | $MeO_2CC{=}CHCO_2Me$ | S |
| b; | $(CH_2)_2CN$ | $(CH_2)_2CN$ | S |
| c; | $(CH_2)_2CN$ | $(CH_2)_2CN$ | O |



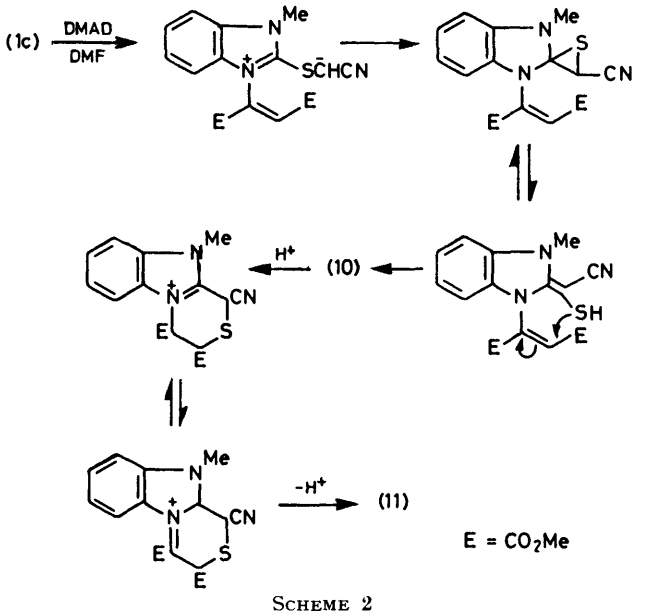

was easily identified from analytical and spectroscopic data as the benzimidazoline-2-thione derivative (9a); the characteristic [9] $^{13}C$ n.m.r. resonance of the thione carbon was apparent.

The i.r. spectrum of compound E ($C_{26}H_{25}N_3O_4S$) indicated the presence of two carbonyl groups (1 715 and 1 735 $cm^{-1}$) and a nitrile group. The n.m.r. spectrum showed the presence of four aromatic protons, three methyl groups (NMe + 2MeO), and two other

* The structure of compound B ($C_{24}H_{16}N_4O_6S_2$) has not been elucidated.

† It proved impossible to obtain material suitable for *X*-ray crystallographic analysis and the structure has not been fully elucidated.

coupled protons ($J$ 2 Hz).* These data together with $^{13}C$ n.m.r. spectral data (see Experimental section) led




SCHEME 2

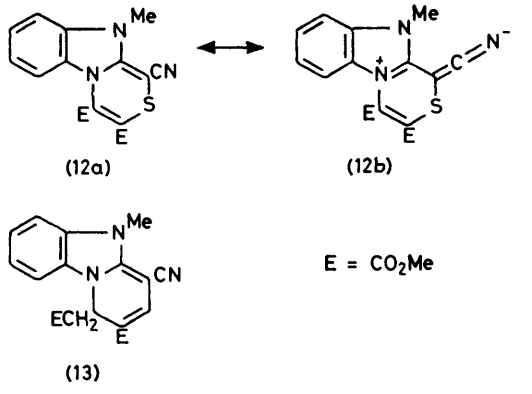
us to believe that compound (E) was the [1,4]thiazino-[4,3-*a*]benzimidazole derivative (10). A subsequent *X*-ray crystallographic study showed that compound (E) is the isomer (11).† A possible mechanism for this transformation is shown in Scheme 2 in which ring-opening of an intermediate spirothiiran is proposed; isomerisation of (10) to (11) *via* a [1,4]thiazino[4,3-*a*]-benzimidazolium intermediate can be envisaged.

In the context of the spirothiiran intermediate, the reaction is analogous to the behaviour of 3-methyl-2-phenacylthiobenzothiazolium bromide in the presence of triethylamine.[11]

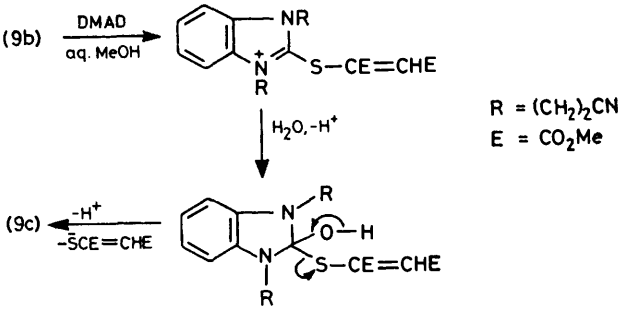
Compound F ($C_{16}H_{13}N_3O_4S$), a red crystalline material, is closely related to compound (E) in terms of molecular formula and i.r. spectrum although the C≡N stretching frequency of the former (2 180 $cm^{-1}$) is unusually intense and at a lower frequency than the latter (2 240 $cm^{-1}$). It was considered that compound (F) could arise by oxidation of compound (E) and it was thus tentatively assigned the [1,4]thiazino[4,3-*a*]benzimidazole structure (12). This formulation was confirmed by *X*-ray crystallographic analysis, and the reason for i.r. C≡N stretching differences between (11) and (12) is apparent. In compound (12), in addition to normal conjugation, a nitrile group resonance interaction is possible [*cf.* (12a) ⟷ (12b)] which would be expected to lower the C≡N stretching frequency {*cf.* the abnormally low value (2 190 $cm^{-1}$) exhibited by the analogous 1,5-dihydropyrido[1,2-*a*]benzimidazole derivative (13) compared to normal values (2 218—2 232 $cm^{-1}$) for conjugated nitriles [12] }.

* Coupling constants of this magnitude (1.3—2.2 Hz) have been noted by Acheson *et al.*[10] for *cis* and *trans* hydrogens of the type CHECHE in carbazole derivatives.

One reaction was carried out with a benzimidazoline-2-thione derivative (9b). It reacted with DMAD in hot aqueous methanol and was converted almost quantitatively into the benzimidazolinone analogue (9c). The involvement of DMAD in this hydrolytic process was confirmed by blank experiments in which no reaction of

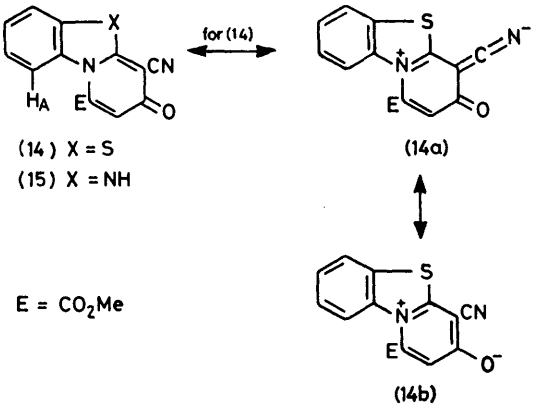



the benzimidazole-2-thione (9b) occurred; a simple mechanism for this process is outlined in Scheme 3.




SCHEME 3

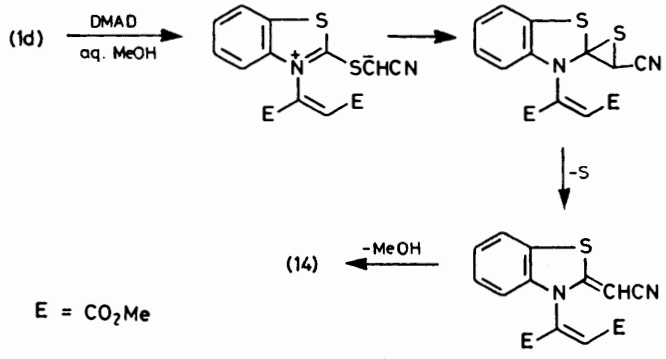
No reaction occurred when (1,3-benzothiazol-2-ylthio)acetonitrile (1d) was treated with DMAD in THF,




aqueous THF, acetonitrile, benzene, or methanol, but in aqueous methanol a complex mixture of compounds was

† It is interesting to note that the CN group adopts the axial position in the thiazine ring (see Figure 2).

formed from which one compound (G) was isolated in poor yield (8%). The molecular formula ($C_{14}H_8N_2O_3S$) indicated the involvement of one DMAD moiety with concomitant extrusion of sulphur and methoxide. From i.r. (CN, $CO_2Me$, and CO groups) and n.m.r. data (aromatic, alkenyl, and ester hydrogens) we believe that compound (G) is the pyrido[2,1-*b*]benzothiazole derivative (14); we assign the low-field aromatic proton (δ 9.12) as $H_A$ and attribute this deshielding effect to the influence of the thiazolium character of the five-membered ring {*cf.* (14) ⟷ (14a) ⟷ (14b), and a similar effect observed for a closely related pyrido[1,2-*a*]benzimidazole derivative (15) [3]}. A mechanism involving an intermediate spirothiiran can again be envisaged for this reaction (see Scheme 4) but a desulphurisation step must be involved (*cf.* analogous processes in the chemistry of benzothiazolium [11] and oxazolium [13] compounds).




SCHEME 4

## EXPERIMENTAL

Routine spectral data on all compounds described in this paper are listed in Supplementary Publication No. SUP 22408 (40 pp.).*

(1*H*-Benzimidazol-2-ylthio)acetonitrile (1b) was prepared by a reported [14] method. 2-(Methoxycarbonyl)methylidene-3-oxo[1,3]thiazolo[3,2-*a*]benzimidazole (6a) was prepared by the method of Grinblat and Postovskii.[7] The sample for *X*-ray crystallographic study was obtained as yellow clusters (from benzene–hexane), m.p. 192—193 °C (lit.,[7] 190—192 °C).

*Reaction of* (1H-*benzimidazol-2-ylthio*)*acetonitrile* (1b) *with Dimethyl Acetylenedicarboxylate* (*DMAD*).—(*a*) *In benzene.* (1*H*-Benzimidazol-2-ylthio)acetonitrile (3.0 g, 16 mmol) and DMAD (2.5 g, 18 mmol) were heated under reflux in dry benzene (800 ml) for 30 h. The benzene solution was evaporated under reduced pressure to afford a yellow oil which was dissolved in acetone (30 ml) and set aside overnight. The yellow precipitate (520 mg, 11%) was recrystallised to give *dimethyl* [1,3]*thiazolo*[3,2-a]*benzimidazole-2,3-dicarboxylate* as pale yellow needles (from benzene–hexane), m.p. 166—167 °C. The solution was evaporated under reduced pressure to yield a yellow oil which was dissolved in toluene and chromatographed on silica gel (150 g). Elution with light petroleum–ethyl acetate (8 : 1 v/v) gave, on recrystallisation, the [1,3]thiazolo[3,2-*a*]benzimidazole derivative (6a) (5 mg; 0.1%) as yellow plates (from benzene–hexane), m.p. 192—193 °C (lit.,[7] 190—192 °C). Further elution with light petroleum–ethyl acetate (8 : 1 v/v) gave an unidentified compound (30 mg, 0.3%) as intense yellow needles (from benzene–hexane), m.p. 174—175 °C (accurate mass measurement at *m/e* 520; Found: $M^+$, 520.050 1. $C_{24}H_{16}N_4S_2O_6$ requires *M*, 520.051 2) (Found: C, 55.10; H, 3.45; N, 10.20; S, 12.80. $C_{24}H_{16}N_4O_6S_2$ requires C, 55.38; H, 3.08; N, 10.77; S, 12.31%).

(*b*) *In THF, DMF, and ethanol.* The above reaction was repeated in these solvents with the following results [mmol of compound (1b) and DMAD, temperature, time (h), % yields of (5a) and (6a) given]: THF (16, 18, reflux, 30, 9, trace); DMF (5.3, 5.4, 100, 0.5, 17, trace); anhydrous EtOH (1.3, 3.9, reflux, 4, 0, 16).

(*c*) *In aqueous ethanol.* The nitrile (1b) (250 mg, 1.3 mmol) and DMAD (560 mg, 3.9 mmol) were heated together under reflux in aqueous ethanol (20 ml, 50%) for 4 h. A pale yellow solid (91 mg, 23%) was filtered off. The solid was only appreciably soluble in hot dimethyl sulphoxide, but was recrystallised by using a large volume of hot methanol to give a compound believed to be (7) or (8), m.p. 350 °C (decomp.); $\nu_{max.}$ (KBr) 3 200—2 200, 1 740, 1 720, 1 600, 1 570, 1 480, 1 450, 1 330, 1 300, 1 260, 1 220, 1 190, 1 160, 1 060, 780, 760, and 750 $cm^{-1}$; δ[$(CD_3)_2SO$, 140 °C, 100 MHz] 8.44 (1 H, m, Ar-H), 7.80 (1 H, m, Ar-H), 7.45 (2 H, m, Ar-H), 7.2 (1 H, s, alkene-H), 4.08 (*ca.* 3 H, s, OMe), and 3.30 (*ca.* 2 H, s, unassigned). Addition of $D_2O$ caused the sample to precipitate; *m/e* 299 (100%), 284 (8), 270 (13), 267 (10), 240 (20), and 212 (20) (accurate mass measurement at *m/e* 299; Found: $M^+$, 299.035 946. $C_{14}H_9N_3O_3S$ requires *M*, 299.036 459) (Found: C, 56.50; H, 3.20; N, 14.30; S, 10.75. $C_{14}H_9N_3O_3S$ requires C, 56.18; H, 3.01; N, 14.05; S, 10.70%).

The filtrate was evaporated *in vacuo* to give a dark oil (450 mg) which was chromatographed on silica gel (4 g) to give compound (6a) (40 mg, 12%), the material of molecular weight 520 described above (20 mg, 3%), and the starting material [90 mg, 36%].

*Hydrolysis of Dimethyl* [1,3]*Thiazolo*[3,2-a]*benzimidazole-2,3-dicarboxylate* (5a).—(*a*) *Ethanolic potassium hydroxide.* Dimethyl [1,3]thiazolo[3,2-*a*]benzimidazole-2,3-dicarboxylate (5a) (200 mg, 0.69 mmol) in ethanol (20 ml) was treated with ethanolic potassium hydroxide (1 ml, 10% w/v) at room temperature for 5 min. The solution was acidified (dilute hydrochloric acid) and evaporated to dryness, and the residual solid was heated in xylene (50 ml) under reflux for 10 h. The mixture was filtered and the xylene solution was evaporated under reduced pressure to give a powder (100 mg) which was dissolved in toluene and chromatographed on silica gel (10 g). Elution with light petroleum–ethyl acetate (10 : 1 v/v) gave a major product (37 mg) which was recrystallised to afford *ethyl* [1,3]*thiazolo*[3,2-a]*benzimidazole-*(2 *or* 3)*-carboxylate* (5b or c) (26 mg, 15%) as colourless plates (from hexane), m.p. 150—151 °C.

(*b*) *Aqueous* 1,4-*dioxan* (*and subsequent decarboxylation*). Dimethyl [1,3]thiazolo[3,2-*a*]benzimidazole-2,3-dicarboxylate (5a) (1.0 g, 3.45 mmol) was stirred in aqueous 1,4-dioxan (50 ml, 80% v/v) with potassium hydroxide (400 mg, 7.1 mmol) for 10 min at room temperature. The mixture was extracted with chloroform (2 × 100 ml). The aqueous layer was acidified (dilute hydrochloric acid) and the white precipitate was separated by centrifuge. The solid was washed twice with water to give [1,3]*thiazolo*[3,2-a]*benzimidazole-2,3-dicarboxylic acid* (5d) (568 mg, 63%) as a white powder, m.p. 211 °C (decomp.). This material (5d)

* For details see Notice to Authors No. 7 in *J.S.C. Perkin I*, 1978, Index issue.

[568 mg, 2.17 mmol] was mixed with acid-washed sand (50 g) and was heated at 220 °C for 10 min. The sand was extracted with ether (3 × 100 ml) and the combined extracts were evaporated under reduced pressure to give a solid which was recrystallised to yield [1,3]*thiazolo*[3,2-a]-*benzimidazole* (5e) [330 mg, 91%] as colourless rods (from chloroform–hexane), m.p. 142—142.5 °C (lit., 135.5—136.5,[4] 140 °C [5]). This material was spectroscopically (n.m.r.) identical to the compound prepared by Alper and Taurins [4] by a different route.

*Preparation of Diethyl* (1H-*Benzimidazol-2-ylthio*)*propanedioate* (1e).—Diethyl bromomalonate (15.77 g, 66 mmol) was added with stirring to a solution of 1,3-dihydro-2*H*-benzimidazole-2-thione (10 g, 66 mmol) in aqueous sodium hydroxide (2.66 g, 66.5 mmol, 150 ml). The mixture was stirred at room temperature for 3 h. Water (250 ml) was added and the mixture was extracted with chloroform (4 × 100 ml). The combined chloroform extracts were dried ($MgSO_4$) and evaporated under reduced pressure to give an oil which quickly solidified. The oil was recrystallised twice to give the title compound (1e) (7.8 g, 38%) as a white powder (from ether–hexane), m.p. 141—142 °C.

*Reaction of Diethyl* (1H-*Benzimidazol-2-ylthio*)*propanedioate* (1e) *with DMAD*.—Diethyl (1*H*-benzimidazol-2-ylthio)propanedioate (1e) (2.27 g, 7.4 mmol) and DMAD (3.14 g, 22 mmol) were stirred together in dry DMF (15 ml) for 24 h. The solvent was evaporated off under reduced pressure and the dark oil (6.6 g) was chromatographed on silica gel (32 g). Elution with light petroleum–ethyl acetate (5 : 1 v/v) gave a yellow solid (1.4 g) which was chromatographed [light petroleum–ethyl acetate (20 : 1 v/v)] to give the diester (5a) (350 mg, 16%), as yellow needles (from benzene–hexane), m.p. 165—166 °C.

*Preparation of* 1,3-*Dihydro*-1,3-*bis*(2-*cyanoethyl*)-2H-*benzimidazole*-2-*thione* (9b).—1,3-Dihydro-2*H*-benzimidazole-2-thione (3.0 g, 20 mmol), acrylonitrile (30 ml), and sodium methoxide (50 mg) were stirred together at room temperature for 60 h. The pale yellow residue was evaporated under reduced pressure and extracted (Soxhlet) with chloroform for 30 min. The chloroform was evaporated off under reduced pressure to give a white powder which was recrystallised to yield the title compound (9b) (2.0 g, 40%) as colourless plates (from methanol–THF), m.p. 217—218 °C (lit.,[15] 219—220 °C).

*Reaction of* 1,3-*Dihydro*-1,3-*bis*(2-*cyanoethyl*)-2H-*benzimidazole*-2-*thione* (9b) *with DMAD*.—1,3-Dihydro-1,3-bis(2-cyanoethyl)-2*H*-benzimidazole-2-thione (9b) (512 mg, 2 mmol) and DMAD (470 mg, 3.3 mmol) were heated together under reflux in aqueous methanol (50 ml, 75% v/v) for 6 h. The solution was evaporated under reduced pressure and the residue was recrystallised to yield 1,3-*dihydro*-1,3-*bis*-(2-*cyanoethyl*)-2H-*benzimidazol*-2-*one* (9c) [470 mg, 97%] as colourless plates (from ethyl acetate), m.p. 169—170 °C (lit.,[15] m.p. 165—168 °C).

*Reaction of* [(1-*Methyl*-1H-*benzimidazol*-2-*yl*)*thio*]*acetonitrile* (1c) *with DMAD*.—[(1-Methyl-1*H*-benzimidazole-2-yl)thio]acetonitrile (1c) (7.0 g, 34.5 mmol) and DMAD (9.8 g, 69 mmol) were heated in dry DMF (150 ml) at 100 °C for 3 h. The solvent was evaporated under reduced pressure and the residual viscous black oil (15 g) was chromatographed on silica gel (100 g). Elution with light petroleum–ethyl acetate (5 : 1 v/v) gave a dark red tar (10 g) which was rechromatographed on silica gel [100 g, light petroleum–ethyl acetate (10 : 1—1 : 2 v/v)], to give (*a*) 1,3-*dihydro*-1-[1,2-*bis*(*methoxycarbonyl*)*vinyl*]-3-*methyl*-2H-*benzimidazole*-2-*thione* (9a) (180 mg, 1%) as intense yellow crystals (from benzene–hexane), m.p. 154—155 °C; (*b*) the [1,4]thiazino[4,3-*a*]benzimidazole derivative (12) (7 mg) as red prisms, m.p. 199—200 °C (from ethyl acetate–light petroleum); (*c*) the [1,4]thiazino[4,3-*a*]benzimidazole derivative (11) (126 mg, 1%) as pale yellow prisms (from ether), m.p. 165—167 °C; and (*d*) an unidentified compound (67 mg, 0.6%); $\nu_{max.}$ (KBr) 2 980, 2 220, 1 750, 1 700, 1 630, 1 610, 1 540, 1 390, 1 310, 1 230, 1 200, 1 160, 1 090, and 750 $cm^{-1}$; δ ($CDCl_3$, 100 MHz) 8.4 (1 H, m), 7.2 (3 H, m), 3.90 (3 H, s), 3.85 (3 H, s), and 3.82 (3 H, s). Starting material (820 mg, 11.7%) was also recovered.

*Preparation of* (*Benzo*-1,3-*thiazol*-2-*ylthio*)*acetonitrile* (1d).—2-Mercaptobenzo-1,3-thiazole (2.0 g, 9.7 mmol), chloroacetonitrile (1.5 g, 19.8 mmol), and triethylamine (2.5 g, 24.7 mmol) were stirred in dry THF (30 ml) for 90 min. The solvent was evaporated under reduced pressure, and the residue recrystallised to afford the title compound (1d) (2.0 g, 78%) as colourless needles (from cyclohexane), m.p. 75—76 °C (lit.,[16] 76—79 °C).

*Reaction of* (1,3-*Benzothiazol*-2-*ylthio*)*acetonitrile* (1d) *with DMAD*.—The nitrile (1d) (9.0 g, 43.7 mmol) and DMAD (6.8 g, 47.9 mmol) were heated under reflux in aqueous methanol (250 ml, 50% v/v) for 24 h. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (120 g). Elution with light petroleum–ethyl acetate (8 : 1 v/v) gave one major product, the pyrido[1,2-*b*][1,3]benzothiazole derivative (14) (1.0 g, 8%), yellow rods (from acetone), m.p. 210 °C. Further elution gave the starting material (6.0 g, 67%).

X-*Ray Crystallographic Analyses of the* [1,4]*Thiazino*-[4,3-a]*benzimidazole Derivatives* (11) *and* (12).—Crystal data are as follows. *Compound* (11). $C_{16}H_{15}N_3O_4S$, $M$ = 345.3. Monoclinic, $a$ = 8.929(3), $b$ = 15.612(4), $c$ = 5.813(2) Å, β = 93.05(10)°, $U$ = 809.2 $Å^3$, $D_c$ = 1.417 g $cm^{-3}$, $Z$ = 2, $D_m$ = 1.39 g $cm^{-3}$, $F(000)$ = 360. Space group $P2_1$, Mo-$K_\alpha$ radiation (graphite monochromator), λ = 0.710 69 Å, μ = 2.27 $cm^{-1}$.

TABLE 1

Fractional co-ordinates (× $10^4$) with standard deviations in parentheses for compound 11

| Atom | *x/a* | *y/b* | *z/c* |
|---|---|---|---|
| C(1) | −4 809(9) | 8 588(7) | −3 027(15) |
| C(2) | −6 229(10) | 8 292(7) | −3 811(16) |
| C(3) | −6 863(8) | 7 587(7) | −2 838(15) |
| C(4) | −6 107(8) | 7 133(6) | −1 114(12) |
| C(5) | −4 681(7) | 7 411(5) | −383(10) |
| C(6) | −4 059(7) | 8 132(5) | −1 300(11) |
| N(7) | −3 687(6) | 7 038(4) | 1 238(9) |
| C(8) | −2 419(7) | 7 595(5) | 1 615(11) |
| C(9) | −912(7) | 7 137(4) | 1 220(10) |
| S(10) | 602(2) | 7 871 | 1 959(3) |
| C(11) | −98(8) | 8 755(4) | 347(10) |
| C(12) | −1 529(7) | 8 825(4) | −536(10) |
| N(13) | −2 662(6) | 8 274(4) | −86(9) |
| C(14) | −882(7) | 6 868(5) | −1 171(2) |
| N(15) | −880(9) | 6 707(5) | −3 072(11) |
| C(16) | 992(8) | 9 438(4) | 48(12) |
| O(17) | 765(7) | 10 088(4) | −1 018(11) |
| O(18) | 2 279(6) | 9 283(4) | 1 264(11) |
| C(19) | 3 433(10) | 9 915(7) | 1 179(21) |
| C(20) | −1 987(7) | 9 603(4) | −1 951(10) |
| O(21) | −2 697(7) | 10 177(4) | −1 204(9) |
| O(22) | −1 613(5) | 9 536(4) | −4 106(7) |
| C(23) | −1 921(12) | 10 291(7) | −5 528(13) |
| C(24) | −4 175(10) | 6 547(6) | 3 182(14) |

*Compound* (12). $C_{16}H_{13}N_3O_4S$, $M = 343.3$. Triclinic, $a = 7.651(2)$, $b = 10.452(3)$, $c = 12.823(3)$ Å, $\alpha = 126.8(1)$,

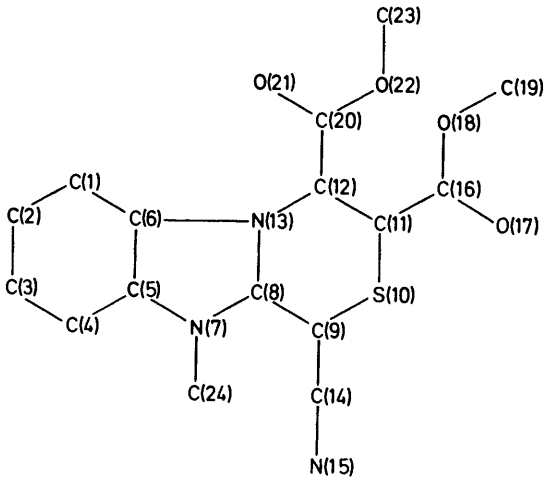



FIGURE 1 Crystallographic numbering scheme for (11) and (12)

$\beta = 92.6(1)$, $\gamma = 104.5(1)°$, $U = 769.1$ Å$^3$, $D_c = 1.48$ g cm$^{-3}$, $Z = 2$, $D_m = 1.47$ g cm$^{-3}$, $F(000) = 356$. Space group

TABLE 2

Bond lengths in Å (standard deviations in parentheses) for compounds (11) and (12)

| | Compound (11) | Compound (12) |
|---|---|---|
| C(1)–C(2) | 1.403(11) | 1.392(7) |
| C(1)–C(6) | 1.375(10) | 1.382(6) |
| C(2)–C(3) | 1.372(14) | 1.387(7) |
| C(3)–C(4) | 1.375(12) | 1.387(7) |
| C(4)–C(5) | 1.390(9) | 1.389(7) |
| C(5)–C(6) | 1.375(10) | 1.386(6) |
| C(5)–N(7) | 1.388(9) | 1.388(6) |
| N(7)–C(8) | 1.436(9) | 1.348(6) |
| N(7)–C(24) | 1.451(9) | 1.461(6) |
| C(8)–C(9) | 1.552(8) | 1.364(6) |
| C(8)–N(13) | 1.458(8) | 1.411(5) |
| C(9)–S(10) | 1.807(6) | 1.777(5) |
| C(9)–C(14) | 1.453(9) | 1.407(7) |
| S(10)–C(11) | 1.763(7) | 1.760(5) |
| C(11)–C(12) | 1.355(9) | 1.341(6) |
| C(11)–C(16) | 1.460(10) | 1.489(7) |
| C(12)–N(13) | 1.364(8) | 1.405(6) |
| C(12)–C(20) | 1.511(9) | 1.496(6) |
| N(13)–C(6) | 1.418(8) | 1.415(6) |
| C(16)–O(17) | 1.201(9) | 1.183(6) |
| C(16)–O(18) | 1.338(9) | 1.336(6) |
| O(18)–C(19) | 1.430(10) | 1.441(7) |
| C(20)–O(21) | 1.192(8) | 1.193(5) |
| C(20)–O(22) | 1.315(7) | 1.326(5) |
| O(22)–C(23) | 1.456(10) | 1.452(6) |
| C(14)–N(15) | 1.133(9) | 1.148(6) |

$P\bar{1}$ from $E$-statistics, Mo-$K_\alpha$ radiation (graphite monochromator), $\lambda = 0.710\,69$ Å, $\mu = 2.27$ cm$^{-1}$.

The cell parameters were initially found from oscillation and Weissenberg photographs, and then refined by least squares from the setting angles of 21 reflections on a Hilger and Watt four-circle diffractometer. Reflections were scanned ($\omega$—$2\theta$ mode) for $\theta \geqslant 27.5°$. For compound (11) 1 511 reflections had a net count $I \geqslant 3\sigma(I)$ and were deemed observed and used in the refinement. For compound (12) 2 707 reflections were available in this range and 1 751 of these had a net count $I \geqslant 3\sigma(I)$ and were used in the refinement. Lorentz and polarisation but not absorption corrections were applied.

TABLE 3

Bond angles (°) with standard deviations in parentheses, for compounds (11) and (12)

| | Compound (11) | Compound (12) |
|---|---|---|
| C(2)–C(1)–C(6) | 117.6(8) | 117.7(5) |
| C(1)–C(2)–C(3) | 121.0(8) | 120.3(5) |
| C(2)–C(3)–C(4) | 121.2(7) | 122.4(5) |
| C(3)–C(4)–C(5) | 117.8(8) | 116.6(5) |
| C(4)–C(5)–C(6) | 121.3(7) | 121.5(4) |
| C(4)–C(5)–N(7) | 128.2(7) | 130.4(4) |
| C(6)–C(5)–N(7) | 110.5(6) | 108.1(4) |
| C(1)–C(6)–C(5) | 121.1(7) | 121.5(4) |
| C(1)–C(6)–N(13) | 131.6(7) | 131.8(4) |
| C(5)–C(6)–N(13) | 107.3(6) | 106.7(4) |
| C(5)–N(7)–C(8) | 108.7(6) | 110.0(4) |
| C(5)–N(17)–C(24) | 122.9(6) | 125.0(4) |
| C(8)–N(7)–C(24) | 117.9(5) | 124.2(4) |
| N(7)–C(8)–C(9) | 112.4(5) | 131.9(4) |
| N(7)–C(8)–N(13) | 104.4(5) | 107.5(4) |
| C(9)–C(8)–N(13) | 109.5(5) | 121.6(4) |
| C(8)–C(9)–S(10) | 108.4(4) | 116.9(4) |
| C(8)–C(9)–C(14) | 109.6(5) | 125.3(4) |
| S(10)–C(9)–C(14) | 111.0(5) | 117.7(4) |
| C(9)–S(10)–C(11) | 97.5(3) | 97.0(2) |
| S(10)–C(11)–C(12) | 124.4(5) | 119.2(4) |
| S(10)–C(11)–C(16) | 114.5(5) | 120.2(3) |
| C(12)–C(11)–C(16) | 121.1(6) | 120.5(4) |
| C(11)–C(12)–N(13) | 124.8(6) | 120.7(4) |
| C(11)–C(12)–C(20) | 119.6(6) | 122.9(4) |
| N(13)–C(12)–C(20) | 115.4(5) | 115.9(4) |
| C(6)–N(13)–C(8) | 108.6(5) | 107.7(3) |
| C(6)–N(13)–C(12) | 130.2(5) | 125.4(4) |
| C(8)–N(13)–C(12) | 120.2(5) | 120.0(4) |
| C(9)–C(14)–N(15) | 176.0(8) | 176.8(6) |
| C(11)–C(16)–O(17) | 125.7(7) | 124.2(4) |
| C(11)–C(16)–O(18) | 111.4(6) | 110.4(4) |
| O(17)–C(16)–O(18) | 122.8(7) | 125.3(5) |
| C(16)–O(18)–C(19) | 117.2(7) | 114.9(4) |
| C(12)–C(20)–O(21) | 122.7(6) | 122.8(4) |
| C(12)–C(20)–O(22) | 112.4(6) | 111.5(4) |
| O(21)–C(20)–O(22) | 124.7(6) | 125.7(4) |
| C(20)–O(22)–C(23) | 115.4(6) | 115.0(4) |

For compound (11) the structure was solved using MULTAN [17] although with some difficulty, over 256 sets of phases being calculated before one was found which gave an $E$-map containing 16 atoms in chemically sensible positions.

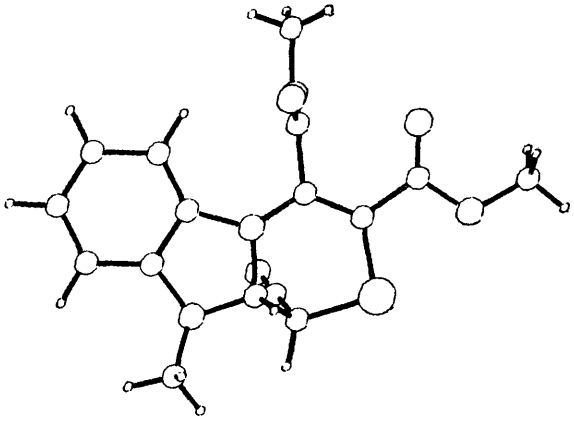


FIGURE 2 Perspective view of compound (11)

The remaining 8 atoms were readily found from a difference map phased on the first 16 atoms and thereafter refinement

proceeded by full-matrix least-squares methods. Initially the structure was refined isotropically nearly to convergence and then anisotropically; after two cycles of anisotropic refinement a difference map showed all the expected hydrogen atoms and for subsequent refinement hydrogen was included in calculated positions but was not refined. Finally a weighting scheme of the form $w = 1/\{1 + [(F_0 - P_2)/P_1]^2\}$ with $P_1 = 14$ and $P_2 = 16$ was applied. At convergence the maximum shift/standard deviation was 0.09 and $R$ was 7.3%.

TABLE 4

Fractional co-ordinates, with standard deviation in parentheses for compound (12)

| Atom | $x/a$ | $y/b$ | $z/c$ |
|---|---|---|---|
| C(1) | 0.456 8(7) | 0.832 2(6) | 0.188 0(5) |
| C(2) | 0.424 0(7) | 0.978 3(7) | 0.226 6(6) |
| C(3) | 0.339 7(8) | 1.059 8(6) | 0.331 1(6) |
| C(4) | 0.280 1(7) | 0.998 7(6) | 0.398 8(5) |
| C(5) | 0.312 4(6) | 0.852 0(6) | 0.358 5(5) |
| C(6) | 0.403 5(7) | 0.773 6(6) | 0.257 9(5) |
| N(7) | 0.265 2(5) | 0.757 8(5) | 0.402 5(4) |
| C(8) | 0.322 5(6) | 0.622 7(6) | 0.333 4(4) |
| C(9) | 0.309 4(7) | 0.495 5(6) | 0.340 2(5) |
| S(10) | 0.351 9(2) | 0.313 5(2) | 0.203 6(1) |
| C(11) | 0.552 8(7) | 0.424 1(6) | 0.190 4(5) |
| C(12) | 0.558 9(7) | 0.564 0(6) | 0.205 8(4) |
| N(13) | 0.414 4(5) | 0.630 8(5) | 0.243 5(4) |
| C(14) | 0.274 8(7) | 0.500 7(7) | 0.449 4(5) |
| N(15) | 0.245 7(7) | 0.497 1(7) | 0.534 8(5) |
| C(16) | 0.718 2(7) | 0.368 8(6) | 0.170 8(5) |
| O(17) | 0.867 0(5) | 0.450 2(4) | 0.181 8(4) |
| O(18) | 0.671 7(5) | 0.212 4(4) | 0.133 6(4) |
| C(19) | 0.825 4(9) | 0.152 5(8) | 0.123 3(8) |
| C(20) | 0.727 1(7) | 0.670 6(6) | 0.202 (95) |
| O(21) | 0.829 0(5) | 0.805 5(4) | 0.302 0(3) |
| O(22) | 0.741 8(5) | 0.599 2(4) | 0.078 0(3) |
| C(23) | 0.908 8(8) | 0.688 5(8) | 0.066 8(6) |
| C(24) | 0.144 2(8) | 0.783 6(7) | 0.493 5(5) |

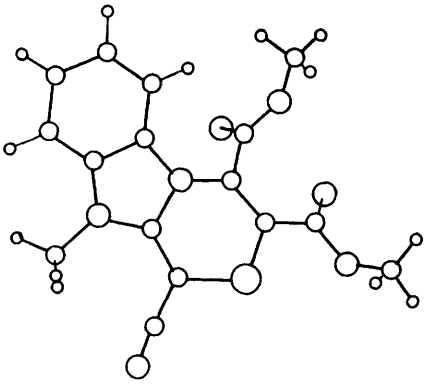


FIGURE 3 Perspective view of compound (12)

Table 1 gives the fractional co-ordinates, and Tables 2 and 3 contain the bond lengths and angles. Figure 1 shows the crystallographic numbering and Figure 2 is a perspective view of the molecule. Apart from MULTAN, crystallographic computations were done using the Oxford CRYSTALS package.[18] The drawing was prepared using PLUTO.[19] The thermal parameters for these non-hydrogen atoms, and a list of observed and calculated structure factors are available in SUP 22408.

For compound (12) the structure was solved using the centrosymmetric direct-methods routine of SHELX[20] which automatically found all but two of the atoms and these appeared in a difference map calculated using the 22 located atoms. Refinement by full-matrix least-squares methods proceeded normally, first isotropically and then anisotropically. After two cycles of anisotropic refinement a difference map revealed all the hydrogen atoms which were subsequently included in the computations in refined calculated positions. Finally a weighting scheme of the form $w = 1.0/[A(0)\cdot T(0)\cdot X + A(1)\cdot T(1)\cdot X + A(2)\cdot T(2)\cdot X + A(3)\cdot T(3)\cdot X]$ where $A(0)$—$A(3)$ are the coefficients of a Chebyshev series in $T(i),X$ with $X = F_0/F_0(\text{max.})$ was applied. The coefficients used were $A(0) = 42.7$, $A(1) = 53.3$, $A(2) = 10.1$, and $A(3) = -4.6$. At convergence the maximum shift/standard deviation was 0.01 and the final $R$ was 5.9%.

Table 4 gives the fractional co-ordinates for the non-hydrogen atoms. Tables 2 and 3 contain the bond lengths and angles. Figure 1 shows the crystallographic numbering and Figure 3 is a perspective view of the molecule.

Apart from SHELX, crystallographic computation was done using the Oxford CRYSTALS package[18] and the drawing was prepared by PLUTO.[19] The thermal parameters for the non-hydrogen atoms and a list of observed and calculated structural factors are available in SUP 22408.

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