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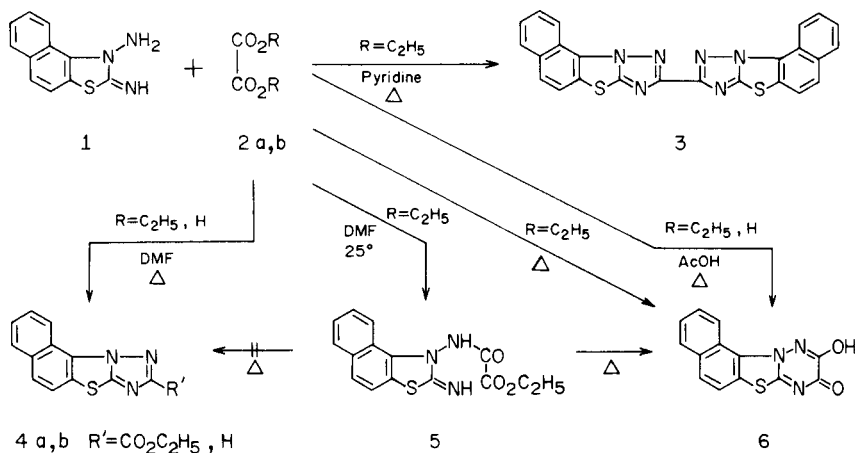
Refluxing 3-amino-2-iminonaphtho[1,2-*d*]thiazole (**1**) with diethyl oxalate (**2a**) in a 2:1 molar ratio in dry pyridine provided 2,2'-binaphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazole (**3**). On the other hand, when **1** was treated with excess amount of **2a** in dimethylformamide, it afforded ethyl naphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazole-2-carboxylate (**4a**) on heating and ethyl *N*-(2-iminonaphtho[1,2-*d*]thiazol-3-yl)oxamate (**5**) by stirring at room temperature. Cyclization of **5** upon fusion led to the formation of 3-hydroxy-2*H*-naphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazin-2-one (**6**). Compound **6** could also be prepared directly from **1** by refluxing either with **2a** neatly, in glacial acetic acid or with oxalic acid (**2b**) in the same medium. The acid form of **4a** might be obtained from **1** and **2b** on heating in dimethylformamide, but it was decarboxylated to naphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazole (**4b**) during the reaction.

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As a progressive continuation of our study on the biological activity of compounds in the condensed naphtho[1,2-*d*]thiazole series [1-3], we have reported in a previous communication [4] the synthesis of a number of 2-substituted naphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazoles. The synthetic experiments were performed starting from 2-aminonaphtho[1,2-*d*]thiazole by selective *N*-amination with *O*-mesitylenesulfonylhydroxylamine to give 3-amino-2-iminonaphtho[1,2-*d*]thiazole (**1**), which was then cyclocondensed with the appropriate carboxylic acid derivatives or their precursor under suitable conditions. Compound **1**, owing to the presence of a 1,4-dinucleophilic center in the molecule, might also undergo cyclocondensation with various 1,2-dielectrophiles to generate a new heterocyclic component fused to this ring system.

In the present paper, we wish to describe the cyclocondensation of **1** with representative 1,2-difunctional acid derivatives, diethyl oxalate (**2a**) and oxalic acid (**2b**). The reactions of some allied 1,4-dinucleophilic heterocycles with oxalic acid derivatives have been investigated by

many research groups [5-15] and also in our laboratory [16]. Consequently, the ring closure was found to be unaccessible in some cases [9], or otherwise different reaction pathways were encountered, which led to forming products of ambiguous structures [5-8,10]. We carried out the reaction at first by treating an excess amount of **1** with **2a** in dry pyridine. After heating at reflux temperature for 2 hours, it gave a red orange crystalline compound, mp >300°, accompanied by trace amounts of by-products, which could be detected only on the thin-layer plate. The ir spectrum of this compound showed the C=N/C=C, C-N and C-S stretching bands at 1548, 1525, 1335 and 670 cm⁻¹ as expected, but surprisingly no N-H, C=O and C-O absorption could be found. It thus revealed that the skeleton of **1** remained unaffected, while the functional groups in **1** or **2a** were all involved in the above reaction and then eliminated. The mass spectrum displayed the molecular ion peak at *m/z* 448, and the elemental analysis established the molecular formula as C₂₄H₁₂N₆S₂ corresponding to a dicondensation product, 2,2'-binaphtho-



[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazole (**3**). The further cleavage pattern supported this assignment, where the characteristic homologous fragments, $C_{12}H_6N_3S$, $C_{11}H_6N_2S$, $C_{10}H_6NS$, $C_{10}H_6S$ and $C_{10}H_6N$ were observed at m/z 224, 198, 172, 158 and 140, respectively. This pathway was in agreement with our previous results obtained from some related derivatives in this series [4,17]. A similar di-condensation involving **2a** and 2-hydrazinopyridine was demonstrated in the literature [6], however, the isolated open-chain intermediate required more drastic conditions for ring closure.

When compound **1** was treated with an excess amount of **2a** in dimethylformamide, it afforded a dark yellow crystalline product with the mp 284-285°, after refluxing for 6 hours, and a crystalline product of light yellow needles with mp ~ 180° dec by stirring at room temperature for 24 hours. These two compounds showed general carbonyl absorption bands at 1665 and 1735 cm^{-1} , and the signals of ethoxyl protons as triplets and quartets at δ 1.44, 4.48 and 1.28, 4.26 ppm in the ir and 1H -nmr spectra, respectively. It suggested that both compounds were generated by incorporation of only one of the two ester functions from **2a** in the ring formation, if any. However, there was no N-H stretching band in the ir spectrum of the former product, but it appeared in moderate intensity at 3356 cm^{-1} and as a broad singlet at δ 6.70 ppm in the ir and 1H -nmr spectra of the latter compound respectively. The mass fragmentation and elemental analysis revealed that the high-melting compound should be a cyclocondensed product, ethyl

naphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazole-2-carboxylate (**4a**) and the low-melting compound, the acylated intermediate, ethyl *N*-(2-iminonaphtho[1,2-*d*]thiazol-3-yl)-oxamate (**5**). It seemed very likely that the above reaction proceeded *via* acylation of the amino group of **1** to form **5**, which was then cyclodehydrated on heating to produce **4a**. In order to ascertain the effective cyclization of **5**, this compound was then heated neatly to melting at about 180°. It changed color from light yellow to brown red at first and solidified soon to an opaque mass, which after recrystallized from dimethylformamide showed its melting point to be higher than 300°. The ir spectrum contained no N-H absorption, and instead of this a broad shallow O-H band at 3105 cm^{-1} was recognized. The signal of the hydroxyl proton was also visualized as a broad singlet at δ 8.70 ppm in the 1H -nmr spectrum, while no ethoxyl protons could be seen in the highfield region. The molecular ion peak appeared at m/z 269 in the mass spectrum corresponding to an acylative cyclization product rather than a cyclodehydrated one. Further mass fragmentation proceeded by the occurrence of $C_{23}H_6N_3OS$, $C_{11}H_6N_2S$, $C_{10}H_6NS$, $C_{10}H_6N_2$ and $C_{10}H_6N$ homologous ion peaks at m/z 226, 198, 172, 154 and 140, respectively. Together with the analytical data, it is reasonable to assign this com-

pound as 3-hydroxy-2*H*-naphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazin-2-one (**6**) instead of **4a**. The compounds obtained from acylative cyclization of allied heterocycles and oxalic acid ester were often claimed to exist in the *ortho* dione form [8,10,14,15]. However, on the basis of spectral analysis, we assigned compound **6** in the α -keto enol form. The strong shift of the OH absorption peak to lower frequency region and lower magnetic field in the ir and 1H -nmr spectra was apparently caused by the intramolecular hydrogen bonding between the two functions. In order to confirm this conversion, compound **1** was also brought into reaction by heating with excess amount of **2a** at 180° or at reflux in glacial acetic acid. In both cases compound **6** was produced, even in more better yields (82 and 80%) and with consistent spectral and analytical data.

In considering that the structure **6** might also be built up using oxalic acid (**2b**) in place of the diethyl ester **2a**, compound **1** was then allowed to react with suitable amount of **2b** in glacial acetic acid and in dimethylformamide. After heating at reflux temperature for 12 hours, compound **6** was obtained as expected, although in a relatively lower yield (45%) in the first case, however, a new product as dark brown needle crystals, mp 205-206° was isolated in the second case. The elemental analysis showed that its molecule contained no oxygen, and there was also no N-H absorption in the ir and 1H -nmr spectra. Further spectral analysis revealed that this compound is identical in all respects with naphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazole (**4b**), a compound we synthesized recently from the mesitylenesulfonate salt of **1** and formic acid by heating in pyridine [4]. In the present experiment a monocyclization of **1** and **2b** seemed to proceed *via* the same route, but the corresponding carboxylic acid formed originally, was soon decarboxylated to compound **4b**. An example reported by Potts and Lovelette [7] involving the *s*-triazolo[3,4-*a*]phthalazine system gave similar results.

So far from these experimental results, a conclusion concerning the reaction pathway might be drawn as follows: The reaction of 3-amino-2-iminonaphtho[1,2-*d*]thiazole (**1**) with diethyl oxalate (**2a**) and oxalic acid (**2b**) might proceed *via* different routes to give dicondensation product, 2,2'-binaphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazole (**3**), or monocondensation product, ethyl naphtho[1',2':4,5]thiazolo[3,2-*b*]triazole-2-carboxylate (**4a**), or acylative cyclization product, 3-hydroxy-2*H*-naphtho[1',2':4,5]thiazolo[3,2-*b*][1,2,4]triazin-2-one (**6**) each depending on the reaction conditions. An acylated intermediate, ethyl *N*-(2-iminonaphtho[1,2-*d*]thiazol-3-yl)oxamate (**5**) could be obtained from the reaction at ambient temperature. The conversion of **5** into **6** proved accessible under different conditions. The carboxylic acid formed from the cyclocondensation of **1** and **2b** could not be isolated but its decarboxylated products, naphtho[1',2':4,5]thiazolo[3,2-*b*]-

[1,2,4]triazole (**4b**) was obtained.

The reactions of **1** with other 1,2-difunctional carboxylic acid derivatives, for example α -keto esters take a different course under similar conditions [18]. The results will be described elsewhere subsequently.

EXPERIMENTAL

All melting points were determined with Tottoli apparatus and are uncorrected. The ultraviolet and infrared spectra were measured with Perkin-Elmer M555 and Perkin Elmer 983G spectrophotometer, respectively. The ¹H-nuclear magnetic resonance and mass spectra were recorded on JEOL FX 100 and JEOL JMS 400 spectrometer, respectively. The elemental analyses were performed in Chungshan Institute of Science and Technology, Taoyuan, Taiwan, China.

3-Amino-2-iminonaphtho[1,2-d]thiazole (**1**).

Compound **1** was prepared from 20.1 g (0.1 mole) 2-aminonaphtho[1,2-d]thiazole by *N*-amination with *O*-mesitylenesulfonylhydroxylamine in dichloromethane according to a procedure described previously [4], yield, 17.4 g (81%), mp 190-191°.

2,2'-Binaphtho[1',2':4,5]thiazolo[3,2-b][1,2,4]triazole (**3**).

A solution of 4.4 g (0.02 mole) of **1** and 1.5 g (0.01 mole) of **2a** in 10 ml of dry pyridine was heated under reflux for 2 hours. The reaction mixture was then allowed to stand at room temperature overnight and the solid substance formed was collected on a filter and recrystallized from dimethylformamide to give 3.1 g (35%) of red orange needle crystals, mp >300°, Rf 0.06, silica gel G, ethyl acetate/*n*-hexane (9:1); ir (potassium bromide): 3010 (=C-H), 1548, 1525 (C=N/C=C), 1335 (C-N), 670 (C-S) cm⁻¹; ms: (70 eV) *m/z* 448 (M⁺, 100), 224 (M⁺/2, 76), 198 (8), 172 (10), 158 (22), 140 (25).

Anal. Calcd. for C₂₂H₁₂N₄S₂: C, 64.27; H, 2.70; N, 18.74; S, 14.29. Found: C, 64.15; H, 2.70; N, 18.71; S, 14.24.

Ethyl Naphtho[1',2':4,5]thiazolo[3,2-b][1,2,4]triazole-2-carboxylate (**4a**).

A solution of 2.2 g (0.01 mole) of **1** and 3.0 g (0.02 mole) of **2a** in 10 ml of dimethylformamide was heated under reflux for 6 hours. After standing at 4° for 2 hours, the precipitate formed was collected on a filter and recrystallized from dimethylformamide to yield 1.2 g (40%) of dark yellow crystals, mp 284-285°, Rf 0.57, silica gel G, ethyl acetate/*n*-hexane (9:1); uv (methanol): λ max (log ϵ) 235 (4.69), 302 (4.13), 315 (4.25), 340 (4.22) nm; λ min (log ϵ) 274 (3.92), 307 (4.09), 323 (4.10) nm; ir (potassium bromide): 3010 (=C-H), 1665 (C=O), 1575, 1500 (C=N/C=C), 1330 (C-N), 1235 (C-O), 670 (C-S) cm⁻¹; ¹H-nmr (pyridine-d₅): δ (ppm) 1.44 (t, 3H, CH₃, J = 7.0 Hz), 4.48 (q, 2H, CH₂, J = 7.0 Hz), 7.68-8.80 (m, 6H, ArH); ms: (70 eV): *m/z* 297 (M⁺, 65), 282 (M-CH₃, 40), 268 (M-C₂H₅, 12), 252 (M-C₂H₅O, 9), 224 (100), 198 (16), 172 (8), 158 (17), 140 (12).

Anal. Calcd. for C₁₅H₁₁N₃O₂S: C, 60.59; H, 3.73; N, 14.13; S, 10.78. Found: C, 60.36; H, 3.59; N, 14.18; S, 10.66.

Ethyl *N*-(2-iminonaphtho[1,2-d]thiazol-3-yl)oxamate (**5**).

A solution of 2.2 g (0.01 mole) of **1** and 3.0 g (0.02 mole) of **2a** in 20 ml of dimethylformamide was stirred at room temperature for 24 hours. The solid substance formed was collected on a filter, washed with a small amount of ethanol and recrystallized from a mixture of dimethylformamide and ethanol to produce 1.9 g (62%) of light yellow needle crystals, mp ~180° dec, Rf 0.93, silica gel G, ethyl acetate/*n*-hexane (9:1); uv (methanol): λ max (log ϵ) 239 (4.63), 346 (3.68), 352 (4.24) nm; λ min (log ϵ) 287 (3.62), 322 (3.67) nm; ir (potassium bromide): 3350 (N-H), 3010 (=C-H), 1735 (C=O), 1610, 1495 (C=N/C=C), 1350 (C-N), 1250 (C-O), 680 (C-S) cm⁻¹; ¹H-nmr (DMSO-d₆): δ (ppm) 1.28 (t, 3H, CH₃, J = 7.0 Hz), 4.26 (q, 2H, CH₂, J = 7.0 Hz), 6.70 (s, br, 1H, NH), 7.56-8.12 (m, 7H, ArH, NH); ms (70 eV): *m/z* 315 (M⁺, 10), 297 (M-H₂O, 65), 224 (100), 198 (30), 172 (14), 154 (15), 140 (12).

Anal. Calcd. for C₁₃H₁₁N₃O₂S: C, 57.13; H, 4.16; N, 13.33; S, 10.17.

Found: C, 56.79; H, 3.95; N, 13.28; S, 10.24.

3-Hydroxy-2*H*-naphtho[1',2':4,5]thiazolo[3,2-b][1,2,4]triazin-2-one (**6**).

Compound **4a** (2.97 g, 0.01 mole) was heated neat in a flask to melting and it soon congealed to a brown red opaque mass. This was then suspended in 20 ml of hot ethanol and filtered. The solid product was recrystallized from dimethylformamide to give 2.1 g (78%) of dark yellow crystals, mp >300°. Rf 0.05, silica gel G, ethyl acetate/*n*-hexane (9:1); uv (methanol): λ max (log ϵ) 241 (4.32), 346 (3.96) nm; λ min (log ϵ) 288 (3.52) nm; ir (potassium bromide): 3105 (O-H), 3010 (=C-H), 1630 (C=O), 1490, 1435 (C=N/C=C), 1340 (C-N), 1290 (C-O), 685 (C-S) cm⁻¹; ¹H-nmr (pyridine-d₅): δ (ppm) 7.70-7.96 (m, 6H, ArH), 8.70 (s, 1H, OH); ms (70 eV): *m/z* 269 (M⁺, 100), 226 (M-CNOH, 72), 198 (23), 172 (10), 154 (25), 140 (18).

Anal. Calcd. for C₁₂H₈N₂O₂S: C, 57.99; H, 2.62; N, 15.60; S, 11.91. Found: C, 58.01; H, 2.60; N, 15.61; S, 11.69.

A mixture of 2.2 g (0.01 mole) of **1** and 55 ml (58.5 g, 0.5 mole) of **2a** was heated under reflux for 2 hours and filtered while hot. The solid substance was washed with hot ethanol and recrystallized from dimethylformamide to yield 2.2 g (82%) of dark yellow crystals, mp >300°. This product gave the same spectral and analytical data as shown above.

A mixture of 2.2 g (0.01 mole) of **1** and 3.0 g (0.02 mole) of **2a** in 20 ml of glacial acetic acid was heated under reflux for 12 hours. After cooling, the mixture was filtered and the residue was recrystallized from dimethylformamide to produce 2.15 g (80%) of dark yellow crystals, mp >300°. This product gave also the same spectral and analytical data as shown above.

A solution of 2.2 g (0.01 mole) of **1** and 2.6 g (0.02 mole) of **2b** as dihydrate in 25 ml of glacial acetic acid was heated under reflux for 12 hours. After cooling, the solid substance was collected and recrystallized from dimethylformamide to afford 1.2 g (45%) of dark yellow crystals, mp >300°. This product gave also the same spectral and analytical data as shown above.

Naphtho[1',2':4,5]thiazolo[3,2-b][1,2,4]triazole (**4b**).

A solution of 2.2 g (0.01 mole) of **1** and 2.6 g (0.02 mole) of **2b** as the dihydrate in 10 ml of dimethylformamide was heated at 120° for 12 hours. After cooling, the precipitate was collected and recrystallized from benzene to give 1.6 g (71%) of dark brown needle crystals, mp 205-206°, Rf 0.07, silica gel G, ethyl acetate/*n*-hexane (9:1); uv (methanol): λ max (log ϵ) 244 (4.63), 295 (3.98), 330 (3.10) nm; λ min (log ϵ) 270 (3.72), 325 (2.82) nm; ir (potassium bromide): 3105 (=C-H), 1620, 1590 (C=N/C=C), 1350 (C-N), 650 (C-S) cm⁻¹; ¹H-nmr (DMSO-d₆): δ (ppm) 7.78-8.28 (m, 6H, ArH), 8.65 (s, 1H, H-2); ms: (70 eV) *m/z* 225 (M⁺, 100), 198 (41), 172 (10), 154 (21), 140 (12).

Anal. Calcd. for C₁₂H₈N₂S: C, 63.98; H, 3.13; N, 18.65; S, 14.23. Found: C, 63.68; H, 3.28; N, 18.54; S, 14.09.

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