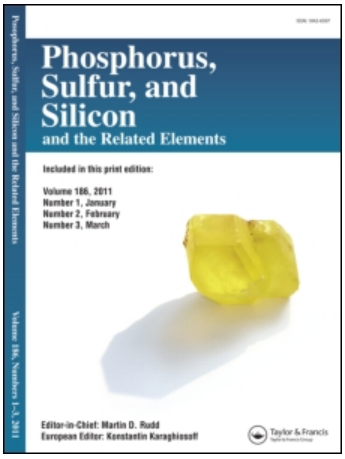

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SYNTHESIS AND REACTIONS OF 11-NITRO-DIBENZO[2,3:6,7]-1,4-THIAZEPINO [5,4-b]THIAZOLIDINE-3(H)-ONE

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Communication

SYNTHESIS AND REACTIONS OF 11-NITRO-DIBENZO[2,3:6,7]-1,4-THIAZEPINO [5,4-b]THIAZOLIDINE-3(H)-ONE

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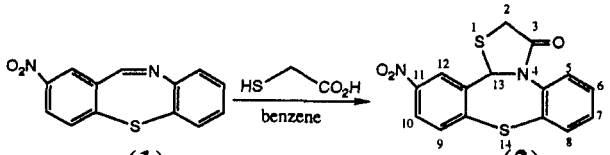
The reaction of 2-nitro-dibenzo[b,f]-1,4-thiazepine 1 with 2-mercaptoacetic acid has been investigated. The yet unreported 11-nitro-dibenzo[2,3:6,7]-1,4thiazepino[5,4-b]thiazolidin-3(H)-one 2 has been synthesized and characterized by chemical reactions and spectral data.

Key words: Fused dibenzo[2,3:6,7]thiazepine, oxidation, aldehydes condensation.

In connection with our previous work on new approaches for synthesis of heterocycles utilizing readily obtainable starting materials[1–4] we report here the synthesis of some new heterocycles using the recently synthesized dibenzo[b,f]-1,4-thiazepine 1. 1 was achieved by condensation of 2-chloro-5-nitrobenzaldehyde with 2-aminothiophenol in the presence of NaOH.[5] The ring system 2 was obtained in a one-pot reaction by cyclofunctionalization of 1 with mercaptoacetic acid. The reaction was performed by adding two equivalents mercaptoacetic acid to a solution of 1 in benzene (see Experimental). The structure of the cycloadduct 2 has been assigned on the basis of elemental analysis, IR, and ^{1}H NMR spectroscopy.



(1) (2)

The mass spectrum of 2, besides the corresponding molecular ion [$M^{+\cdot}$ = 330], show the diagnostic fragmentation pathway described in Scheme I.

The C—S bond cleavage of the molecular ion, followed by a rearrangement through 1,4-hydrogen shift leads to the loss of the ·SCH=C=O radical and to the formation of ion M-73 which is the base peak.

Compound 2 was condensed with aromatic aldehydes such as p-anisaldehyde and/or p-chlorobenzaldehyde in the presence of a catalytic amount of piperidine and afforded 2-arylidene-11-nitro-dibenzo[2,3:6,7]-1,4-thiazepino[5,4-b]thiazolidin-3(H)-one 3 a,b.

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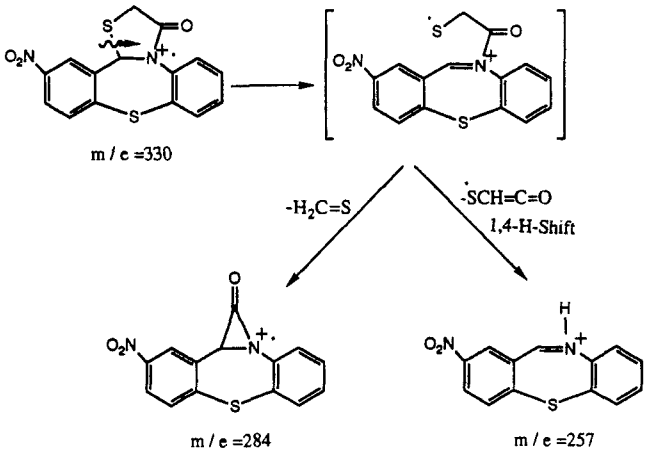
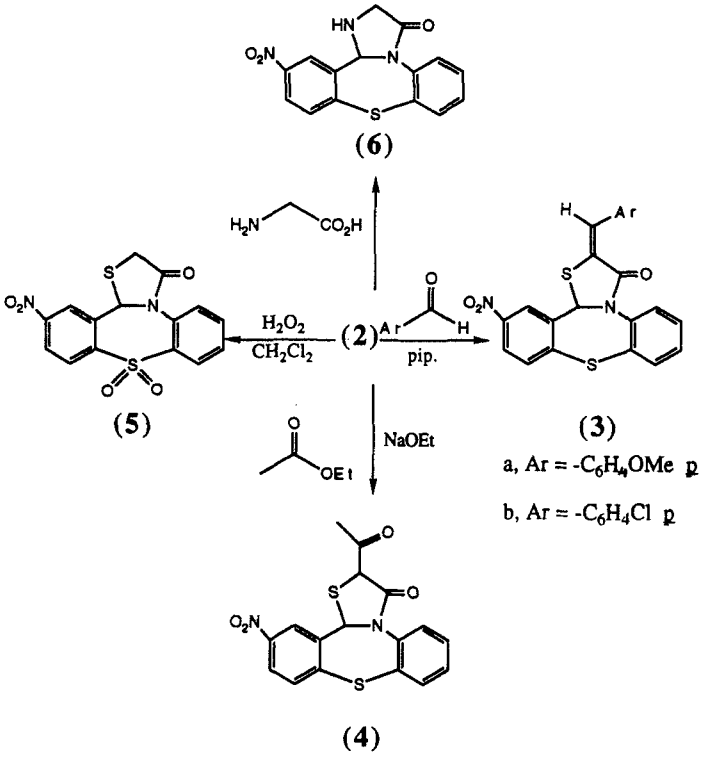


SCHEME I

2-Acetyl-11-nitro-dibenzo[2,3:6,7]-1,4-thiazepino[5,4-b]thiazolidin-3(H)-one 4 was prepared via treatment of 2 with freshly distilled ethyl acetate in the presence of NaOEt in about 20% yield. Furthermore, the reaction of 2 with hydrogen peroxide in a mixed solvent of dichloromethane and formic acid at room temperature[6] led to the sulphone 5.



The dibenzo[b,f]thiazepine 1 was refluxed with glycine in pyridine/H_2O mixture (2:1) for 10 hours and furnished 11-nitro-dibenzo[2,3:6,7]-1,4-thiazepino[5,4-b]-imidazolin-3(H)-one 6.

Our pharmacological findings will be reported elsewhere.

EXPERIMENTAL

Melting points were determined with a Büchi 510 capillary melting apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer M-377 spectrophotometer. The ^{1}H NMR spectra were recorded on a Hitachi Perkin-Elmer R 600 F.T. using TMS as an internal standard. TLC on silica gel plates (Merck, 60, F_{254}) was used to control the purity of the products. Silica gel 60 (Merck, 70-230 mesh) was used for column chromatography. Mass spectra were recorded on Hitachi Perkin-Elmer RMV-6L mass spectrophotometer. Elemental analysis were carried out in the unit of microanalysis in Ain Shams University and Cairo University. Compound 1 was prepared by a previously reported procedure.[5]

2-Chloro-5-nitrobenzaldehyde (1.15 g, 0.006 mole) in ethanol-water (4:1) 10 ml. was slowly added to a solution of 2-aminothiophenol (1 g, 0.008 mole) in NaOH (0.5 g, 0.013 mole) in the same solvent (10 ml.). The mixture was stirred at room temperature for one hour. The orange colored precipitate was collected and washed with acetic acid, water, dried and recrystallized from ethanol (30 ml) to give the title compound 1 as pale yellow needles. (yield 82%). m.p. 176°C (lit.[5] m.p. 178°). IR (KBr) 1636 cm^{-1} (C=N), 3050 (CH, arom.), 1605, 770, 762 cm^{-1} (C=C arom.); ^{1}H NMR ($CDCl_3$): δ (ppm) 9.05 (S, 1H, —CH=N), 8.52 (d, 1H, J = 2.3, C_1—H), 8.3 (d, d, 2H, J = 2.88, C_3—H, C_4—H) and 7.5–7.3 (m, 4H, arom.-H). MS m/e 256 [$M^{+\cdot}$, 9.3%], 229 [M^+—HCN, 70.3%], 210, 165, 139, 91, 76, 65, 46, 32, and 27 (100%). *Anal.* calcd. for $C_{13}H_8N_2O_2S$: C, 60.93; H, 3.13; N, 10.94; S, 12.5. Found: C, 60.61; H, 2.92; N 10.51; S, 12.02.

11-Nitro-dibenzo[2,3:6,7]-1,4-thiazepino[5,4-b]thiazolidin-3(H)-one. 2

To a solution of 2-nitro-dibenzo[b,f]-1,4-thiazepine 1 (2.5 g, 0.01 mole) in dry benzene (80 ml), mercaptoacetic acid (1.39 ml, 0.02 mole) was added and the mixture was refluxed for 45 hrs. After removal of the solvent in vacuo, the obtained oily residue was neutralized with 2% Na_2CO_3 solution and chromatographed on a silica gel column, using light petroleum-diethyl ether 7:3 V/V as eluent, to give a yellow compound 2.05 g, yield 62%, m.p. 232–4°C (from benzene). IR (KBr) 2890–2935 cm^{-1} (CH aliph.), 3059 cm^{-1} (CH arom.), 1682 cm^{-1} (C=O), 1605, 780, 760 cm^{-1} (C=C arom.). H^1 NMR ($CDCl_3$): δ 8.15 (d, 1H, J = 3.1, C_{12}—H), 8.0 (d, d, 2H, J = 4.1, C_9—H, C_{10}—H), 7.7–7.35 (m, 4H, arom. H's), 6.2 (S, 1H, methine proton) and 3.85 (d, 2H, J = 5.1, CH_2). MS m/e = 330 [$M^{+\cdot}$, 32.7%], 288 (31%), 284 (9.1%), 257 (96.2%), 256 (18.3%), 210 (33%), 197, 165, 139, 91, 76, 65, 46, 32, 27. *Anal.* Calcd. for $C_{15}H_{10}N_2O_3S_2$: C, 54.54; H, 3.03; N, 8.48; S, 19.39. Found: C, 54.09; H, 3.0; N, 8.21; S, 19.10.

Condensation of 2 *with aromatic aldehydes. Formation of* 3 *a,b.*

A solution of 2 (3.3 g, 0.01 mole), the appropriate aromatic aldehyde (0.01 mole) in abs. ethanol (50 ml) was refluxed for 4 hrs. The reaction mixture was concentrated and the precipitate formed after cooling was filtered off, washed with ethanol, dried and recrystallized from a proper solvent to give 3 a,b.

3a: recrystallized from benzene as pale yellow crystals (yield 32%). m.p. 205°C. IR (KBr) 3052 cm^{-1} (CH arom.), 1665 cm^{-1} (C=O), 1609 (C=C), 1602, 780–751 cm^{-1} (C=C arom.). H^1 NMR ($CDCl_3$) showed signals characteristic for a —OCH_3 group and an olefinic proton at δ 3.45 and 6.3, respectively. *Anal.* Calcd. for $C_{23}H_{16}N_2O_4S_2$: C, 61.61; H, 3.57; N, 6.25; S, 14.28. Found: C, 61.63; H, 4.0; N, 6.7; S, 13.91.

3b: recrystallized from ethanol as yellow crystals (yield, 36%). m.p. 190–2°C. IR (KBr) 3050 cm^{-1} (CH arom.), 1672 cm^{-1} (C=O), 1612 (C=C), 1604, 780, 746 cm^{-1} (C=C arom.). H^1 NMR ($CDCl_3$): δ 8.1 (d, 1H, J = 3.2 H_z, C_{12}—H), 7.93 (d, d, 2H, J = 4.3, C_9—H, C_{10}—H), 7.26–7.11 (m, 8H, arom. H), 6.25 (S, 1H, olefinic proton) 4.9 (br.s, 1H, methine proton). *Anal.* Calcd. for $C_{22}H_{13}N_2O_3S_2Cl$: C, 58.3; H, 2.87; N, 6.19; S, 14.1. Found: C, 58.12; H, 3.0; N, 6.45; S, 13.82.

2-Acetyl-11-nitro-dibenzo[2,3:6,7]-1,4-thiazepino[5,4-b]thiazolidin-3(H)-one 4.

A mixture of compound 2 (0.01 mole), freshly distilled ethyl acetate (0.02 mole) and NaOEt (0.25 mole) in abs. ethanol (30 ml) was refluxed on an oil-bath at 130–140°C for 3 hrs. The reaction mixture was allowed to stand overnight at r.t., then poured into 10% HCl and extracted with ether. The ether layer was washed with water, dried over $MgSO_4$ and evaporated. The oil thus obtained was treated with ethanol to give a solid which was recrystallized from dil. AcOH to give colorless crystals (yield 20%) m.p. 135–7°C. IR (KBr): 2872–2935 cm^{-1} (CH aliph.), 3046 (CH arom.), 1694 cm^{-1} (C=O Ketone), 1674 (C=O), 1618, 810, 760 cm^{-1} (C=C arom.). H^1 NMR ($CDCl_3$): showed singlet for 3H at δ 2.3 characteristic for CH_3CO. *Anal.* Calcd. for $C_{17}H_{12}N_2O_4S_2$: C, 54.83; H, 3.22; N, 7.53; S, 17.2. Found: C, 54.36; H, 3.1; N, 7.09; S, 17.36.

Oxidation of 2

Compound 2 (10 m mole) was dissolved in CH_2Cl_2 (150 ml), 30% H_2O_2 (12 m moles) and formic acid (40 m moles) were added to the solution. The reaction mixture was stirred for 7 hrs at r.t. The solvent was then evaporated in vacuo and the residue was crystallized from benzene to give 5 as white crystals (yield 52%), m.p. 204°C. IR (KBr) 1046–1073 cm^{-1} characteristic for $\upsilon_{S=O}$. *Anal.* Calcd. for $C_{15}H_{10}N_2O_5S_2$: S, 17.68. Found: S, 17.36.

Formation of 6

A mixture of 1 (0.01 mole) and glycine (0.02 mole) in pyridine/H_2O (2:1) was heated for 6 hrs on an oil-bath at 150°C. The filtrate was concentrated to one third of the initial volume. The residue was poured into chilled 10% HCl, and the resulting semisolid was extracted with ether. The ether layer was washed with 10% $NaHCO_3$ solution, H_2O, dried over $MgSO_4$, and evaporated. The residue was recrystallized from a mixture of benzene-ethanol to give 6 as yellow crystals (yield 11%) m.p. 148–9°C. IR (KBr): 3300 cm^{-1} (NH), 2878–2932 cm^{-1} (CH aliph.), 3052 cm^{-1} (CH arom.), 1686 cm^{-1} (C=O), 1600, 786, 750 cm^{-1} (C=C arom.). H^1 NMR ($CDCl_3$): δ 8.6 (S, 1H, NH), 8.1 (d, 1H, J = 4.5, C_{12}—H), 7.81–7.83 (d, d, 2H, J = 5.1, C_9—C_{10}—H) 7.7–7.26 (m, 4H, arom. H's), 6.0 (S, 1H, methine proton) and 3.8 (d, 2H, J = 5.4, CH2). *Anal.* Calcd. for $C_{15}H_{11}N_3O_3S$: C, 57.5; H, 3.5; N, 13.4; S, 10.2. Found: C, 57.4; H, 3.2; N, 12.96; S, 9.61.

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