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Reaction of 3-amino-2-benzoylbenzo[*b*]furan with bromoacetyl bromide followed by cyclization in methanolic ammonia gave 5-phenyl-1,3-dihydrobenzo[*d'*]furo[3,2-*e*][1,4]diazepin-2-one, a representative of a new ring-system. The corresponding chloro substituted diazepin-2-one was similarly prepared from 3-amino-2-(4-chlorobenzoyl)benzo[*b*]furan. Some alkylation and thionation reactions of these diazepines have been investigated.

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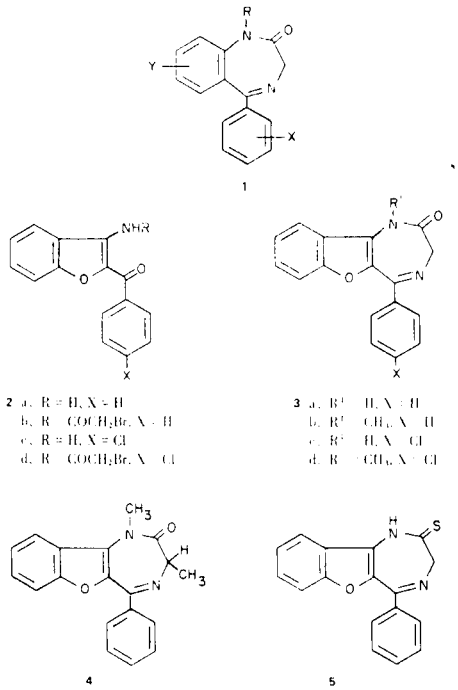
The synthesis and potent antianxiety properties of certain benzo[1,4]diazepines of type (1) are well documented (3,4). The synthesis and properties of several fused 1,4-diazepines in which the benzomoiety of (1) is replaced by, for example, thieno (5) or pyrazolo (6) moities has also been reported. The recently described preparation of 3-amino-2-benzoylbenzo[*b*]furan from *o*-cyanophenol (7) enabled us to undertake the synthesis of several benzo[*b*]furo fused analogs of **1** as described below. The synthetic procedure was essentially that of Sternbach (3). Reaction of 2-benzoyl-3-aminobenzo[*b*]-furan (**2a**) with bromoacetyl bromide gave 2-benzoyl-3-(2-bromoacetamido)benzo[*b*]furan (**2b**) which was cyclized with methanolic ammonia to give the benzo[d^1]furo-[3,2-*e*][1,4]diazepine (**3a**). Alkylation of **3a** with sodium hydride-DMF-methyl iodide gave the corresponding 1-methyl compound (**3b**) whilst the use of an excess of sodium hydride-methyl iodide resulted in formation of the expected 1,3-dimethyl compound (**4**). The *p*-chlorobenzoyl compound 3-amino-2-(4-chlorobenzoyl)benzo[*b*]furan (**2c**) was prepared as Gewald (7) had prepared **2a** except that α-bromo-*p*-chloroacetophenone was used in place of phenacyl bromide. The procedures described above for the preparation of **3a** and **3b** were used to convert **2c** into the diazepines **3c** and **3d**.



Reaction of **3a** with phosphorus pentasulfide-pyridine (8) gave 5-phenyl-1,3-dihydrobenzo[d^1]furo[3,2-*e*][1,4]-diazepine-2-thione (**5**). The ^{1}H nmr spectrum of this compound did not show a singlet CH_2 resonance at δ 4.5 as its precursor **3a** had, which is probably due to *ene-thione* tautomerism between C-2 and C-3 in **5**. Two broad peaks were observed at δ 5.8 and 3.5 which could be associated with the CH and SH resonances of the *ene* form of **5**.

EXPERIMENTAL

Nmr spectra were determined on a Varian HA100 spectrometer, with TMS as internal standard and mass spectra on either an AE1 MS12 or MS9 spectrometer. The drying agent used was magnesium sulfate.

2-Benzoyl-3-(2-bromoacetamido)benzo[*b*]furan (**2b**).

To a solution of (**2a**) (7) (1.18 g., 0.005 mole) in a mixture of toluene (50 ml.) and pyridine (0.87 g., 0.011 mole) at 80° was added bromoacetylbromide (2.0 g., 0.01 mole) when a precipitate formed immediately. The mixture was heated on the steam bath for 45 minutes, cooled and added to water. The toluene layer was separated and the aqueous layer extracted with toluene. The combined extracts were washed with 2N sodium hydroxide solution, water and dried. Evaporation of the solvent gave the crude product which was crystallized from ethanol (carbon) yielding the product **2b** as a colourless solid (1.4 g., 70%), m.p. 130°; ^{1}H nmr (deuteriochloroform): δ 4.12 (s, CH_2), 7.6-8.4 (m, aromatics).

Anal. Calcd. for $C_{17}H_{12}BrO_3N$: C, 57.0; H, 3.4; N, 3.9; M^+ 357. Found: C, 57.0; H, 3.4; N, 3.9; M^+ 357.

5-Phenyl-1,3-dihydrobenzo[d^1]furo[3,2-*e*][1,4]diazepine-2-one (**3a**).

To a 13% (w/v) solution of ammonia in absolute ethanol (5 ml.) was added a solution of **2b** (0.89 g., 0.0025 mole) in dry ether (80 ml.) and the mixture kept at room temperature for 24 hours. Evaporation of the solution gave a solid which was washed with water and crystallized from ethanol to give the product **3a** (0.4 g., 59%), m.p. 264-266°; ^{1}H nmr (DMSO d_6): δ 4.5 (s, CH_2), 7.5 and 7.8 (m, aromatics).

Anal. Calcd. for $C_{17}H_{12}O_2N_2$: C, 73.9; H, 4.3; N, 10.1; M^+ 276. Found: C, 73.8; H, 4.5; N, 10.1; M^+ 276.

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1-Methyl-5-phenyl-1,3-dihydrobenzo[d^1]furo[3,2-*e*][1,4]diazepin-2-one (**3b**).

To a stirred solution of **3a** (3.9 g., 0.015 mole) in dry DMF (50 ml.) was added sodium hydride (80% in oil, 0.465 g., 0.0165 mole) and the mixture stirred at room temperature for 15 minutes. Methyl iodide (4.26 g., 0.03 mole) was then added and the stirring continued for a further 30 minutes when the mixture was added to water at 0° (600 ml.). The resulting aqueous mixture was extracted with ethyl acetate (2 x 500 ml.) and the combined extracts washed with water and dried. Evaporation of the solvent gave a solid which was crystallized from ethanol to give the product **3b** as yellow needles (2.2 g., 50%), m.p.192-194°; ^{1}H nmr (deuteriochloroform): δ 3.7 (s, N-CH_3), 4.6 (s, CH_2) and 7.5-7.9 (m, aromatics).

Anal. Calcd. for $C_{18}H_{14}O_2N_2$: C, 74.4; H, 4.8; N, 9.7; M^+ 290. Found: C, 74.3; H, 5.0; N, 9.4; M^+ 290.

1,3-Dimethyl-5-phenyl-1,3-dihydrobenzo[d^1]furo[3,2-*e*][1,4]diazepin-2-one (**4**).

To a solution of **3a** (3.12 g., 0.0113 mole) in dry DMF (40 ml.) was added sodium hydride (80% in oil; 2.0 g., 0.064 mole) and the mixture stirred at room temperature for 15 minutes when methyl iodide (1.43 ml., 0.023 moles) was added and the stirring continued for a further 30 minutes. Treatment of the reaction solution as described above for compound **3b** gave the product **4** (1,2 g., 36%), m.p. 152-154°; ^{1}H nmr (deuteriochloroform): δ 1.8 (d, J = 6 Hz, C-3 CH_3), 3.6 (s, N-CH_3), 3.95 (q, J = 6 Hz, C-3 H) and 7.5-7.9 (m, aromatics).

Anal. Calcd. for $C_{19}H_{16}O_2N_2$: C, 75.0; H, 5.3; N, 9.2; M^+ 304. Found: C, 74.8; H, 5.3; N, 9.2; M^+ 304.

5-Phenyl-1,3-dihydrobenzo[d^1]furo[3,2-*e*][1,4]diazepine-2-thione (**5**).

Phosphorus pentasulphide (0.88 g., 0.004 mole) was added to a stirred solution of **3a** (1.0 g., 0.004 mole) in anhydrous pyridine (7.3 ml., 0.009 mole) and the mixture refluxed for 45 minutes when it was cooled and added to a saturated aqueous sodium chloride solution (25 ml.) at 0°. The crude product was filtered, washed with water and stirred in boiling ethanol to remove impurities. Filtration gave the pure product **5** (0.4 g., 34%), m.p. 280-282°; ^{1}H nmr (DMSO d_6): δ 3.5 and 5.8 (broad humps CH and SH), 7.6 and 8.2 (m, 8H and 1H respectively, aromatics).

Anal. Calcd. for $C_{17}H_{12}ON_2S$: C, 69.2; H, 4.1; N, 9.6; M^+ 292. Found: C, 69.1; H, 4.1; N, 9.3; M^+ 292.

3-Amino-2-(4-chlorobenzoyl)benzo[*b*]furan (**2c**).

A solution of sodium hydroxide (3.0 g., 0.075 mole) in water (30 ml.) was added to a mixture of 2-cyanophenol (9.0 g., 0.075 mole) and α-bromo-*p*-chloroacetophenone (17.6 g., 0.075 mole) in 2-ethoxyethanol (60 ml.) and the mixture refluxed for 10 minutes. Upon cooling, the precipitated *o*-cyanophenyl-(*p*-chlorophenacyl) ether was filtered and recrystallized from ethanol (11.3 g., 55%), m.p. 140-142°; ^{1}H nmr (deuteriochloroform-DMSO-d_6): δ 5.65 (s, CH_2), 7.0-8.2 (m, aromatics and NH_2); ms: m/e 271 (M^+).

Anal. Calcd. for $C_{15}H_{10}ClO_2N.3/4H_2O$: C, 63.0; H, 3.9; N, 4.9. Found: C, 63.2; H, 3.7; N, 4.8.

This solid (11.1 g. 0.041 mole) was added with stirring to a solution of sodium (0.23 g. 0.01 mole) in absolute ethanol (100 ml.) and the mixture stirred at room temperature for 10 minutes when water (150 ml.) was added and the crude product filtered and crystallized from ethanol (7.8 g., 70%), m.p.196-198°; ^{1}H nmr (DMSO-d_6): δ 7.6-8.1 (m, aromatics).

Anal. Calcd. for $C_{15}H_{10}ClO_2N$: C, 66.3; H, 3.6; N, 5.2; M^+ 271. Found: C, 66.7; H, 3.6; N, 4.9; M^+ 271.

Upon repeating this reaction we several times isolated the final product 2c after the first condensation, in the same overall yield (38%).

3-(2-Bromoacetamido)-2-(4-chlorobenzoyl)benzo[*b*]furan (**2d**).

This compound was prepared from **2c** as described for the preparation of **2b** (0.005 mole scale) (36%), m.p. 178-180° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 4.1 (s, CH_2), 7.6 and 8.3 (m, 6H and 2H respectively, aromatics).

Anal. Calcd. for $C_{17}H_{11}BrClNO_3$: C, 52.6; H, 2.8; N, 3.5. Found: C, 52.3; H, 2.8; N, 3.6.

5-(4-Chlorophenyl)-1,3-dihydrobenzo[d^1]furo[3,2-*e*][1,4]diazepin-2-one (**3c**).

This compound was prepared from **2d** as described for the preparation of **3a** (0.005 mole scale) (32%), m.p. 278-280° (from ethanol); ^{1}H nmr (deuteriochloroform/DMSO-d_6): δ 4.5 (s, CH_2) and 7.7 (m, aromatics).

Anal. Calcd. for $C_{17}H_{11}ClN_2O_2$: C, 65.7; H, 3.5; N, 9.0. M^+ 310. Found: C, 65.3; H, 3.5; N, 8.8; M^+ 310.

5-(4-Chlorophenyl)-1-methyl-1,3-dihydrobenzo[d^1]furo[3,2-*e*]-[1,4]diazepine-2-one (**3d**).

This compound was prepared from **3c** as described for the preparation of **3b** (0.003 mole scale) (47%), m.p. 214-216° (from ethanol); ^{1}H nmr (deuteriochloroform): δ 3.6 (s, N-CH_3), 4.5 (s, CH_2), 7.5 (m, 5H), 7.7 (m, 2H) and 7.9 (m, 1H), aromatics.

Anal. Calcd. for $C_{18}H_{13}ClO_2N_2$: C, 66.5; H, 4.0; N, 8.6; M^+ 324. Found: C, 66.1; H, 4.1; N, 8.2; M^+ 324.

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