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By application of the Friedlander synthesis on 2,3-dihydro-1-benzothiepin-4(5*H*)one (**4**), the corresponding [4,5-*b*]quinoline derivatives **5a** and **5b** were obtained. Starting from the ketone (**4**) and by application of the Fischer indole synthesis, 1-benzothiepino[4,5-*b*]indole (**6**) and 1-benzothiepino[4,5-*b*]benzo[*g*]indole (**7**) were obtained. When β-naphthylhydrazine was used in the indolisation reaction, a mixture of 1-benzothiepino[4,5-*b*]benzo[*e*]indole (**8**) and 1-benzothiepino[4,3-*b*]benzo[e]indole (**9**) was obtained.

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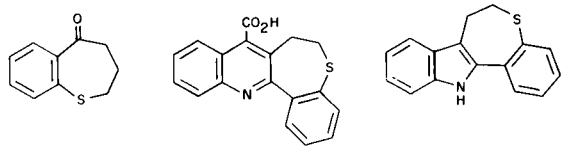
A great deal of effort has been spent in recent years in the preparation of benzo[1]thiepin derivatives of potential pharmacological interest (1). In this connection, a number of indole and quinoline derivatives have been prepared.

Cagniant and Deluzarche (2) first reported the preparation of the benzothiepino[5,4-*b*]quinolinecarboxylic acid (**2**) and of additional quinoline derivatives *via* the Pfitzinger and Friedlander syntheses starting from 3,4-dihydro-1-benzothiepin-5(2*H*)one (**1**). The preparation of additional 4-substituted benzothiepino[5,4-*b*]quinoline derivatives and preliminary results of their pharmacological properties was subsequently reported by Dudykina and Zagorevskii (3).

By application of the Fischer indole synthesis, Aksanova, Kucherova and Zagorevskii (4) have reported the preparation of 12*H*-6,7-dihydro-1-benzothiepino[5,4-*b*]indole (**3**) and of a large number of derivatives. More recently, the preparation and pharmacological activity of the *S*-oxide derivative of **3** has been described in a U. S. Patent (5).



1 2 3

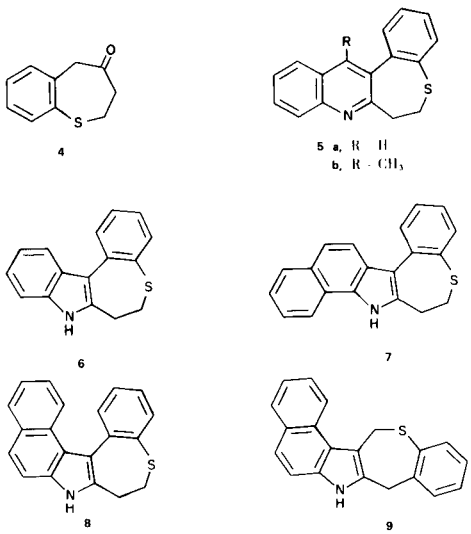
In all the above reported syntheses, the ketone (**1**) has been used as starting material. In a recent paper (6) two of us have described the preparation of the 2,3-dihydro-1-benzothiepin-4(5*H*)one (**4**) by decarboxylation of ethyl 2,3-dihydro-4-hydroxy-1-benzothiepin-5-carboxylate, obtained by a two-step addition-ring expansion of thiochroman-4-one with ethyl diazo (lithio) acetate. Since **4** appeared to be an excellent precursor for the preparation of benzothiepino indole and quinoline derivatives isomeric with those above reported, and in connection with previous work in this area (7), the synthesis of a variety of quinoline and indole derivatives was undertaken.

6,7-Dihydro-1-benzothiepino[4,5-*b*]quinoline (**5a**) was obtained by treatment of the ketone (**4**) with *o*-amino benzaldehyde under alkaline conditions; a similar reaction in which *o*-amino benzaldehyde was replaced by *o*-amino acetophenone afforded 13-methyl-6,7-dihydro-1-benzothiepino[4,5-*b*]quinoline (**5b**).

The ketone (**4**) and phenylhydrazine in ethanolic acetic acid gave after refluxing with acetic acid saturated with hydrogen chloride (65%), 6,7-dihydro-1-benzothiepino[4,5-*b*]indole (**6**).

Similarly, the ketone (**4**) was readily converted *via* α-naphthylhydrazone into the corresponding 6,7-dihydro-1-benzothiepino[4,5-*b*]benzo[*g*]indole (**7**).

Finally, when **4** was treated under similar conditions with β-naphthylhydrazine, a mixture of two compounds, identified as the isomeric 6,7-dihydro-1-benzothiepino-[4,5-*b*]benzo[*e*]indole (**8**) and 6,7-dihydro-1-benzothiepino[4,3-*b*]benzo[*e*]indole (**9**), was obtained.



4 5 a, R = H; b, R = CH_3 6 7 8 9

Nmr data for compounds **5-9** are given in the Table.

EXPERIMENTAL

Melting points were determined with a Kofler micro hot stage apparatus. Nmr spectra were recorded with a JEOL INM-C-60 HL spectrometer (TMS standard), and ir spectra with a Perkin-Elmer 257 spectrophotometer. Column chromatography was performed with Merck silica gel (0.063-0.200 mm).

Table

Compound	δ	Solvent
5a	3.0-3.7 (4H, m), 7.0-8.2 (9H, m)	Deuteriochloroform
5b	2.56 (3H, s), 2.8-3.7 (4H, m), 7.0-8.2 (9H, m)	Deuteriochloroform
6	3.0-3.7 (4H, m), 6.9-8.5 (9H, m)	DMSO-d_6
7	3.2-3.7 (4H, m), 7.0-8.6 (11H, m)	DMSO-d_6
8	2.4-3.7 (4H, m), 7.1-8.4 (11H, m)	Deuteriochloroform
9	3.94 (1H, s), 4.71 (2H, s), 7.0-8.4 (11H, m)	Acetone-d_6

6,7-Dihydro-1-benzothiepino[4,5-*b*]quinoline (**5a**).

2,3-Dihydro-1-benzothiepin-4(5*H*)one (1 g.) and *o*-aminobenzaldehyde hydrochloride (0.885 g.) were heated at 140° for 30 minutes (8). Ice water was then added and the resulting mixture was basified with dilute ammonium hydroxide and extracted with portions of chloroform. The combined extracts were washed with 1*N* sodium hydroxide and water, dried and evaporated. A methanolic solution of the foregoing residue and picric acid was heated under reflux for 1 hour; the solvent was then distilled off and the amorphous picrate thus obtained suspended in hot benzene and decomposed with aqueous ammonia. The organic phase was washed with water, dried and evaporated. The residue (0.66 g., 45% yield) afforded benzothiepino[4,5-*b*]quinoline (**5a**) as needles (from cyclohexane), m.p. 90-92°.

Anal. Calcd. for $C_{17}H_{13}NS$: C, 77.55; H, 4.98; N, 5.32. Found: C, 77.20; H, 5.16; N, 5.11.

13-Methyl-6,7-dihydro-1-benzothiepino[4,5-*b*]quinoline (**5b**).

Similarly, treatment of 2,3-dihydro-1-benzothiepin-4(5*H*)one (1 g.) with *o*-amino acetophenone (0.96 g.) afforded 13-methylbenzothiepino[4,5-*b*]quinoline (**5b**) as needles (1 g., 65% yield) (from aqueous methanol), m.p. 133°.

Anal. Calcd. for $C_{18}H_{15}NS$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.70; H, 5.64; N, 4.95.

6,7-Dihydro-1-benzothiepino[4,5-*b*]indole (**6**).

The indolisation of 2,3-dihydro-1-benzothiepinphenylhydrazone (not isolated), prepared from the ketone **4** (1.78 g.) with phenylhydrazine (1.3 g.) was effected by boiling it in acetic acid saturated with hydrogen chloride; dilution with water precipitated benzothiepino[4,5-*b*]indole (**6**) as needles (1.63 g., 65% yield), m.p. 204-205° (from ethanol).

Anal. Calcd. for $C_{16}H_{13}NS$: C, 76.46; H, 5.21; N, 5.57. Found: C, 76.27; H, 5.44; N, 5.47.

6,7-Dihydro-1-benzothiepino[4,5-*b*]benzo[*g*]indole (**7**).

Indolisation as above of 2,3-dihydro-1-benzothiepin-4(5*H*)one α-naphthylhydrazone (not isolated) prepared from the ketone **4** with α-naphthylhydrazine in methanol afforded this indole (**7**) (50% yield) as white needles, m.p. 242-243° (from acetic acid).

Anal. Calcd. for $C_{20}H_{15}NS$: C, 79.71; H, 5.02; N, 4.65. Found: C, 79.54; H, 4.98; N, 4.53.

6,7-Dihydro-1-benzothiepino[4,5-*b*]benzo[*e*]indole (**8**) and 6,7-Dihydro-1-benzothiepino[4,3-*b*]benzo[*e*]indole (**9**).

Indolisation as above of 2,3-dihydro-1-benzothiepin-4(5*H*)one β-naphthylhydrazone (not isolated), prepared from the ketone **4** with β-naphthylhydrazine gave a residue constituted of two products (tlc analysis). Chromatography of this residue on a silica gel column and elution with benzene-hexane 1:1 gave benzothiepino[4,5-*b*]benzo[*e*]indole (**8**) (25% yield), m.p. 85-87° (from cyclohexane).

Anal. Calcd. for $C_{20}H_{15}NS$: C, 79.71; H, 5.02; N, 4.65. Found: C, 79.18; H, 4.95; N, 4.40.

Further elution with the same solvents yielded benzothiepino-[4,3-*b*]benzo[*e*]indole (**9**) (10% yield), m.p. 183-185° (from cyclohexane).

Anal. Calcd. for $C_{20}H_{15}NS$: C, 79.71; H, 5.02; N, 4.65. Found: C, 79.98; H, 5.08; N, 4.28.

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