Studies in Sulphur Heterocycles. Part 7 [1]. Tricyclic Compounds Related to 5,6,7,8-Tetrahydro-4*H*-cyclohepta[*b*]thiophene

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Synthesis of a number of tricyclic compounds with a fused thiophene ring starting from 5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophen-4-one and benzosuberone is described. Biological testing of these compounds for their antiparasitic activities has been carried out.

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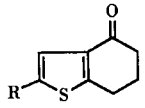
Most of the biologically interesting polynuclear compounds incorporating a fused thiophene ring, *viz.* thiasteroids [3], isosters or analogues of indole alkaloids [4], carcinogenic compounds [5], *etc.* consist of six-membered rings annelated to thiophene, presumably because of their facile synthesis from easily available starting materials. We have already reported [6] [7] a wide variety of such tricyclic compounds from the readily available [6] [8] 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one **1** (R = H) and its various 2-substituted derivatives.



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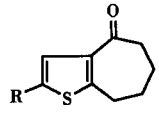

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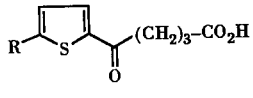
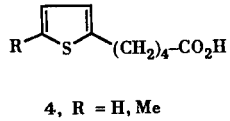
Difficultly accessible 5,6,7,8-tetrahydro-4*H*-cyclohepta-[*b*]thiophen-4-one **2** (R = H), has seldom been used as a starting material for multi-step synthesis. Probably, as a consequence, polycondensed systems, incorporating a seven-membered ring fused to thiophene are sparse. Reported herein are a number of such compounds which were synthesized in connection with our ongoing interest in polycondensed sulphur heterocycles.

Results and Discussion.

The key intermediate **2** (R = H) in these syntheses is obtainable [9] from thiophene by a standard sequence of reactions.

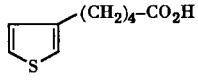


3, R = H, Me



4, R = H, Me

The literature procedure [9] of the use of nitrobenzene as a solvent in glutaroylation resulted in a substantial amount of uncharacterizable polymeric side product, presumably formed by the attack of the acylating agent on the free α-position of thiophene. Double condensation of glutaric anhydride with hydrocarbons [10] is not unknown. Use of dichloromethane and high dilution resulted in a cleaner and improved glutaroylation (75% *vis a vis* 54% as previously reported). The keto acid **3** (R = H) was smoothly reduced under Huang-Minlon condition with excellent yield. While the stannic chloride mediated cyclization of the chloride of the acid **4** (R = H) gave [9] a moderate 33% yield of the ketone **2** (R = H), the polyphosphoric acid (PPA) cyclization of **4** (R = H) resulted only in intractable material from which only a small amount of the starting material could be recovered. Using toluene as the medium and employing high dilution resulted in a modest improvement (11% conversion). The problem is presumably due to the greater difficulty of the formation of the seven-membered ring compared to the six-membered ketone, **1** (R = H). The competing side-reaction of the attack by the acid to the free α-position of another thiophene ring could only be partially off-set by high dilution. This contention receives indirect support from the smooth cyclization [11] of the acid **5** to the ketone **6**, where the attack is to take place in the α-position itself. We, ourselves



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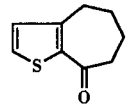

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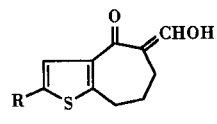
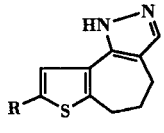
found that blocking the α-position of thiophene with a methyl group removed the difficulties. Thus the methylated acid **4** (R = Me), obtained from 2-methylthiophene in excellent yield, was uneventfully cyclized to the ketone **2** (R = Me) with PPA in very good yield.

There are several reports [12-16] of antibacterial activities of fused pyrazoles and in one case [17] annelation of a

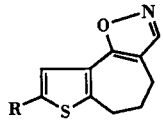
pyrazole moiety to the A ring of a steroid had increased its anti-inflammatory activity. This prompted us to synthesize a number of tricyclic compounds incorporating a pyrazole moiety fused to 5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene. The importance of such tricyclic compounds also arise out of hormonal or antihormonal activities shown by steroidal compounds lacking the A or the D ring [18-21]. The ketones **2** (R = H, Me) were formylated with ethyl formate in the presence of sodium ethoxide and the products **7** (R = H, Me) exist principally as hydroxymethylene tautomers, as is evident from the spectroscopic data. Pyrazolo fused products **8** were obtained when **7** (R = H, Me) reacted with hydrazine hydrate in dry ethanol. Treating the solution of the α-hydroxymethylene ketones in a minimum amount of rectified spirit with hydroxylamine hydrochloride in a very small amount of water and heating to reflux furnished the fused isoxazoles **9** (R = H, Me). Such reactions are usually carried out in glacial acetic acid [22] but its use in this case resulted in considerable difficulty in the isolation of products.



7, R = H, Me

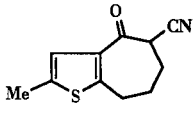


8, R = H, Me



9, R = H, Me

The β-ketonitrile **10** obtained from **9** (X = O, R = Me) with sodium methoxide in methanol reacted smoothly with methyl iodide in the presence of sodium methoxide in methanol to give the dimethyl compound **11**. Methanolysis of **10** and **11** by bubbling dry hydrogen chloride in their methanolic solution till saturation furnished the β-ketoesters **12** and **13**. The tricyclic compounds **14** (R = H, Me) consisting of a pyrazolone ring fused to 5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene moiety were obtained when the β-ketoesters were heated with hydrazine hydrate.



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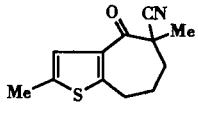

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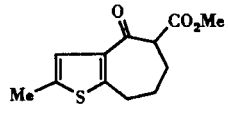

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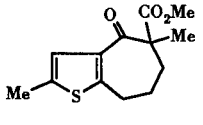

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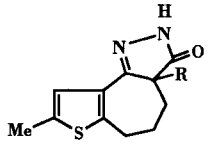
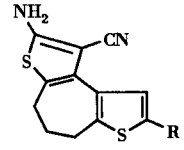
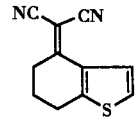


14, R = H, Me

Thienobenzothiophenes of the type **15** (R = H, Me, Br) were obtained [7] from the corresponding dicyanovinyl precursors **16** by treatment with sulphur and morpholine [23]. Compounds of the type **15** could also be fully aromatized and both the dihydro, as well as the fully aromatic compounds were used in the synthesis of polynuclear compounds of biological interest [24]. Attempts to condense **2** (R = H, Me) with malononitrile, however, resulted in gummy products which could not be crystallized. Treating these with sulphur and morpholine resulted only in intractable materials.



15, R = H, Me, Br



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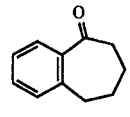
Better success was achieved in synthesizing tricyclic compounds with a benzene ring angularly fused to 5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene. The starting material benzosuberone **17**, unlike its thieno analogue was condensed with malononitrile under standard Knoevenegal conditions to afford the ylidene malononitrile **18** in 82% yield, which reacted with sulphur and morpholine in the usual way to furnish 2-amino-1-cyano-5,6-dihydro-4*H*-benzo[3,4]cycloheptа[1,2-*b*]thiophene **19**, though the yield



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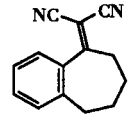

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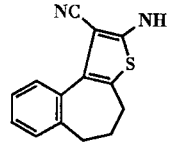

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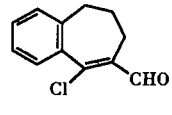

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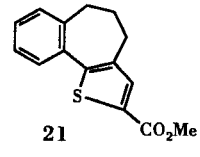

21

was mediocre. Benzosuborone also reacted with phosphorus oxychloride and dimethyl formamide to give the chloroformyl derivative **20**, which reacted further with methyl thioglycolate in the presence of sodium methoxide in methanol, resulting in the tricyclic compound **21** in excellent yield.

The synthesized compounds were tested for their antiparasitic activities against *Entamoeba histolytica, Trichomonus vaginalis* and two nematodes *Ancylostoma ceylanicum* and *Nematospiroides dubius*. Among the compounds subjected to the screening **8** and **9** (R = Me) showed activity against *T. vaginalis* at concentration of 100 μg/ml.

EXPERIMENTAL

General.

Commercially available solvents were distilled and purified by recommended methods prior to use. The ^{1}H nmr were recorded on Varian XL-200, JEOL FX-100 or Varian EM-360 NMR Spectrometer in deuteriochloroform unless otherwise stated. Chemical shifts are expressed in terms of ppm using tetramethylsilane as internal standard. The infra red spectra of solids (potassium bromide) and liquids (neat) were recorded on a Perkin Elmer PE-298 spectrometer. Light petroleum refers to the fraction boiling between 60-80°. Benzosuberone was synthesized from benzaldehyde by literature procedure. Sodium sulphate was used for drying.

General Procedure for Glutaroylation of Thiophene Derivatives.

Finely pulverized anhydrous aluminium chloride (68 g, 0.5 mole) was added portionwise to a vigorously stirred solution of glutaric anhydride (20 g, 0.175 mole) in dry dichloromethane (350 ml) at 0-5° under anhydrous conditions and after thirty minutes thiophene (14.9 g, 0.175 mole) in dry dichloromethane (100 ml) was added over thirty minutes. After stirring for thirty minutes crushed ice (150 g) and concentrated hydrochloric acid (150 ml) were added followed by warming until the suspended materials dissolved. After thorough washing with water the organic layer was extracted with sodium hydroxide solution (30 g in 250 ml water) and the solid separated upon acidification of the alkali layer was crystallized from water.

5-(2-Thienyl)-4-oxopentanoic Acid **3** (R = H).

This compound was obtained in 75% yield, mp 84-85° (lit [9] mp 84-86°).

5-(5-Methyl-2-thienyl)-4-oxopentanoic Acid **3** (R = Me).

This was obtained in 80% yield, mp 117-118° (lit [9] mp 120°).

5-(2-Thienyl)pentanoic Acid **4** (R = H).

This compound was obtained as an oil in 90% yield by Huang-Minlon reduction of **3** (R = H) as described in the literature [10], bp 120-122°/0.3 mm; ir: ν CO 1700 cm^{-1}; pmr: 1.75 (m, 4H, 3- and 4-CH_2), 2.4 (m, 2H, 5-CH_2), 2.9 (t, 2H, 2-CH_2), 6.86 (m, 1H, 3'- or 4'-H), 7.0 (m, 1H, 3'- or 4'-H), 7.2 (m, 1H, 5'-H).

5-(5-Methyl-2-thienyl)pentanoic Acid **4** (R = Me).

This compound was obtained as an oil (which later solidified) by similarly reducing **3** (R = Me) in 90% yield, bp 138-140°/0.3 mm (mp 59°), (lit [9] bp 135°/0.2 mm); ir: ν CO 1705 cm^{-1}.

Cyclization of Thienyl Pentanoic Acids.

To a vigorously stirred polyphosphoric acid (40 g) at 90° in a three-necked flask was added the acid (50 mmoles) in dry toluene (60 ml) keeping the moisture out. After thirty minutes crushed ice was added to the cooled reaction mixture. After extraction with benzene, washing the organic layer with 5% sodium hydroxide solution (3 x 50 ml) and water (3 x 100 ml) and drying, the cyclized product was obtained upon removal of solvent and distillation *in vacuo*.

5,6,7,8-Tetrahydro-4*H*-cyclohepta[*b*]thiophen-4-one **2** (R = H).

This was obtained as an oil in 11% yield, bp 90-95°/0.3 mm (lit [10] bp 92°/0.1 mm); ir: ν CO 1665 cm^{-1}; pmr: 1.7-2.2 (m, 4H, 6- and 7-CH_2), 2.7 (t, 2H, 8-CH_2), 3.1 (t, 2H, 5-CH_2), 6.9 (d, 1H, 2-H), 7.32 (d, 1H, 3-H).

2-Methyl-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophen-4-one **2** (R = Me).

This compound was obtained in 75% yield as an oil, bp 120-123°/0.3 mm (lit [10] bp 135°/0.2 mm); ir: ν CO 1675 cm^{-1}; pmr (carbon tetrachloride): 1.64 (m, 4H, 6-CH_2 and 7-CH_2), 2.50 (t, 2H, 8-CH_2), 2.56 (s, 3H, CH_3), 2.98 (t, 2H, 5-CH_2), 6.98 (s, 1H, 3-H).

Formylation of 5,6,7,8-Tetrahydro-4*H*-cyclohepta[*b*]thiophen-4-one and its 2-Methyl Derivative.

Ethyl formate (0.8 g, 10 mmoles) in dry benzene (15 ml) was added under nitrogen to sodium ethoxide prepared from oil-free sodium hydride (20 mmoles). Under external cooling, the ketone (5 mmoles) in dry benzene (10 ml) was added over 10 minutes and the reaction mixture was stirred at 0° for five hours at the end of which ice-water was added. The organic phase was washed successively with water (2 x 25 ml), and 5% sodium hydroxide solution (3 x 10 ml). Acidification of the combined aqueous phase, extraction with ether, removal of solvent after drying and distillation of the residue *in vacuo* afforded the hydroxymethylene compound which was used for the next step without further purification.

5-Hydroxymethylene-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophen-4-one **7** (R = H).

This compound was obtained in 72% yield, bp 120-123°/0.5 mm; ir: ν OH 3400, CO 1620 cm^{-1}; pmr: 1.72 (m, 2H, 7-CH_2), 2.59 (t, 2H, 8-CH_2), 3.26 (t, 2H, 5-CH_2), 6.90 (d, 1H, 2-H), 7.36 (d, 1H, 3-H), 8.30 (s, 1H, =C*H*OH).

5-Hydroxymethylene-2-methyl-5,6,7,8-tetrahydro-4*H*-cyclohepta-[*b*]thiophen-4-one **7** (R = Me).

This compound was obtained in 76% yield, bp 98-100°/0.3 mm; ir: ν OH 3400, CO 1620 cm^{-1}; pmr: 2.18 (m, 2H, 7-CH_2), 2.6 (s, 3H, CH_3), 2.59 (t, 2H, 8-CH_2), 3.22 (t, 2H, 5-CH_2), 7.36 (s, 1H, 3-H), 8.56 (s, 1H, =C*H*OH).

Preparation of Compounds **8**.

The appropriate hydroxymethylene compound **7** was treated with an equimolar amount of hydrazine hydrate in a minimum quantity of dry ethanol and refluxed for forty minutes. After cooling and addition of water, the precipitated solid was collected and crystallized from ethanol.

1,4,5,6-Tetrahydrothieno[1',2':6,7]cyclohepta[1,2-*c*]pyrazole **8** (R = H).

This compound was obtained in 90% yield, mp 56-58°; ir: ν NH 3400 cm^{-1}; pmr: 2.06 (m, 2H, 5-CH_2), 2.80 (t, 2H, 4-CH_2), 3.09 (t, 2H, 6-CH_2), 7.12 (d, 1H, 9H, J = 6 Hz), 7.48 (d, 1H, 8-H, J = 6 Hz), 8.06 (s, 1H, 3H).

Anal. Calcd. for $C_{10}H_{10}N_2S$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.05; H, 5.13; N, 14.70.

8-Methyl-1,4,5,6-tetrahydrothieno[1',2':6,7]cyclohepta[1,2-*c*]pyrazole **8** (R = Me).

This compound was obtained in 76% yield, mp 134-136°; ir: ν NH 3400 cm^{-1}; pmr: 1.94 (m, 2H, 5-CH_2), 2.32 (s, 3H, CH_3), 2.79 (t, 2H, 4-CH_2), 2.98 (t, 2H, 6-CH_2), 6.98 (s, 1H, 9-H), 7.25 (s, 1H, 3-H).

Anal. Calcd. for $C_{11}H_{12}N_2S$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.58; H, 5.88; N, 13.68.

Preparation of Compounds **9**.

The appropriate hydroxymethylene compound **7** (14 mmoles)

in ethanol (10 ml) was treated with an aqueous solution (5 ml) of an equimolar amount of hydroxylamine hydrochloride and refluxed for thirty minutes. Water was added after cooling and the organic phase was extracted with chloroform. Evaporation of the solvent after drying and crystallization of the residue from ethanol afforded the desired compounds.

5,6-Dihydro-4*H*-thieno[1',2':6,7]cyclohepta[2,1-*d*]isoxazole **9** (R = H).

This compound was obtained in 75% yield, mp 57-59°; pmr: 1.76 (m, 2H, 5-CH_2), 2.54 (t, 2H, 4-CH_2), 3.06 (t, 2H, 6-CH_2), 6.92 (d, 1H, 9-H), 7.32 (d, 1H, 8-H), 8.08 (s, 1H, 3-H).

Anal. Calcd. for $C_{10}H_9ONS$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.78; H, 4.72; N, 7.21.

8-Methyl-5,6-dihydro-4*H*-thieno[1',2':6,7]cyclohepta[2,1-*d*]isoxazole **9** (R = Me).

This compound was obtained in 94% yield, mp 68-69°; pmr: 2.06 (m, 2H, 5-CH_2), 2.46 (s, 3H, CH_3), 2.80 (t, 2H, 4-CH_2), 3.08 (t, 2H, 6-CH_2), 7.16 (s, 1H, 9-H), 8.08 (s, 1H, 3-H).

Anal. Calcd. for $C_{11}H_{11}ONS$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.31; H, 5.35; N, 6.81.

5-Cyano-2-methyl-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophen-4-one (**10**).

The isoxazole **9** (R = Me) (4.5 g, 21 mmoles) in dry tetrahydrofuran (12 ml) was added dropwise under nitrogen to an ice-cold solution of sodium ethoxide (prepared from 1.1 g of sodium) in ethanol (30 ml) and stirred for 2 hours. Water was then added and extracted with 5% sodium hydroxide solution. After removal of the neutral part with ether the aqueous phase was acidified and the liberated oil was extracted with ether. Drying, evaporation of the solvent and sublimation of the residue at 110-112°/0.3 mm afforded **10** in 93% yield; ir: ν CN 2250, CO 1665 cm^{-1}; pmr: 2.06 (m, 2H, 7-CH_2), 2.33 (s, 3H, CH_3), 2.97-3.06 (m, 2H, 8-CH_2), 3.72-3.97 (m, 2H, 6-CH_2), 7.16 (s, 1H, 3-H), 8.08 (s, 1H, 5-H).

Anal. Calcd. for $C_{11}H_{11}ONS$: C, 64.36; H, 5.40; N, 6.82. Found: C, 64.08; H, 5.31; N, 6.52.

5-Cyano-2,5-dimethyl-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophen-4-one **11**.

A solution of the ketonitrile **10** (0.76 g, 3.7 mmoles) in benzene (20 ml) was added under nitrogen to a stirred ice-cold solution of sodium ethoxide (prepared from 0.2 g sodium) in ethanol (10 ml) followed by methyl iodide (10 ml). After stirring at room temperature for one hour and refluxing for two and half hours, usual work up afforded crude **11** which was chromatographed over silica gel (eluant light petrol) sublimed at 120°/0.3 mm, yield 88%; ir: ν CN 2230, CO 1670 cm^{-1}; pmr: 1.86-2.01 (m, 2H, 7-CH_2), 2.3 (s, 3H, 2-CH_3), 2.88-3.0 (m, 4H, 6-CH_2 and 8-CH_2), 3.66 (s, 3H, 5-CH_3), 7.0 (s, 1H, 3-H).

Anal. Calcd. for $C_{12}H_{13}NOS$: C, 65.72; H, 5.98; N, 6.39. Found: C, 65.61; H, 5.76; N, 6.20.

Methanolysis of the Ketonitriles **10** and **11**.

An ice-cold solution of the ketonitrile was saturated with dry hydrogen chloride. After sixteen hours at -10° and two hours at room temperature, the reaction mixture was saturated with sodium chloride and extracted with ether. Evaporation of the solvent after drying, chromatography over silica gel and sublimation afforded the keto esters **12** and **13**.

Methyl 2-Methyl-4-oxo-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]thiophene-5-carboxylate **12**.

This compound was obtained in 82% yield, bp 128°/0.3 mm; ir: ν CO 1660, CO_2Me 1745 cm^{-1}; pmr: 1.86-2.01 (m, 2H, 7-CH_2), 2.3 (s, 3H, 2-CH_3), 2.88-3.0 (m, 4H, 6-CH_2 and 8-CH_2), 3.66 (s, 3H, CO_2CH_3), 7.0 (s, 1H, 3-H).

Anal. Calcd. for $C_{12}H_{14}O_3S$: C, 60.48; H, 5.92. Found: C, 60.42; H, 5.96.

Methyl 2,5-Dimethyl-4-oxo-5,6,7,8-tetrahydro-4*H*-cyclohepta[*b*]-thiophene-5-carboxylate **13**.

This compound was obtained in 75% yield, bp 130°/0.4 mm; ir: ν CO 1660, CO_2Me 1740 cm^{-1}; pmr: 1.60 (s, 6H, 2- and 5-CH_3), 2.03-2.28 (m, 4H, 6- and 7-CH_2), 2.33 (s, 3H, CO_2CH_3), 3.06-3.18 (m, 2H, 8-CH_2), 6.8 (s, 1H, 2-H).

Anal. Calcd. for $C_{13}H_{16}O_3S$: C, 61.88; H, 6.39. Found: C, 61.86; H, 6.37.

Treatment of the Ketoesters **12** and **13** with Hydrazine Hydrate.

Upon heating the ketoester (2 mmoles) and hydrazine hydrate (1 ml) in a silicone oil bath a brisk reaction was observed and a solid residue was left when it had subsided to afford **14** and **15** on crystallization from ethanol.

8-Methyl-3a,4,5,6-tetrahydrothieno[1',2':6,7]cyclohepta[1,2-*c*]pyrazol-3(2*H*)-one **14** (R = H).

This compound was obtained in 81% yield, mp 280° dec; ir: ν NH 3350, CO 1620 cm^{-1}; pmr (DMSO-d_6): 1.98 (m, 2H, 5-CH_2), 2.04 (s, 3H, CH_3), 2.06 (m, 2H, 4-CH_2), 2.09 (m, 2H, 6-CH_2), 7.01 (s, 1H, 9-H), 10.04 (bs, 1H, NH).

Anal. Calcd. for $C_{11}H_{12}N_2OS$: C, 59.97; H, 5.49; N, 12.72. Found: C, 59.59; H, 5.38; N, 12.63.

3a,8-Dimethyl-3a,4,5,6-tetrahydrothieno[1',2':6,7]cyclohepta[1,2-*c*]pyrazol-3(2*H*)-one **14** (R = Me).

This compound was obtained in 72% yield, mp 284° dec; ir: ν NH 3260, CO 1650 cm^{-1}; pmr (DMSO-d_6): 1.96-2.02 (m, 4H, 4-CH_2 and 5-CH_2), 2.36 (s, 3H, 3a-CH_3), 2.52 (s, 3H, CH_3), 2.8-3.0 (m, 2H, 6-CH_2), 7.8 (s, 1H, 9-H), 8.28 (bs, 1H, NH).

Anal. Calcd. for $C_{12}H_{14}N_2OS$: C, 61.51; H, 6.02; N, 11.96. Found: C, 61.22; H, 5.99; N, 11.76.

5-Dicyanomethylene-6,7,8,9-tetrahydro-5*H*-benzocyclohepten-5-one **18**.

Equimolar quantities of benzosuberone and malononitrile dissolved in a minimum quantity of dry ethanol were refluxed for one hour with a catalytic amount of triethylamine. The brown solid which separated upon cooling was crystallized from ethanol, yield 82%, mp 52-54°; ir: ν CN 2215 cm^{-1}; pmr (carbon tetrachloride): 1.6-2.0 (m, 4H, 3-CH_2 and 4-CH_2), 2.6-3.0 (m, 4H, 2-CH_2 and 5-CH_2), 7.32 (m, 4H, aromatic protons).

Anal. Calcd. for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81; N, 13.46. Found: C, 80.70; H, 5.82; N, 13.42.

2-Amino-1-cyano-5,6-dihydro-4*H*-benzo[3,4]cyclohepta[1,2-*b*]thiophene **19**.

Compound **18** (10.8 mmoles), sulphur (0.37 g) and morpholine (5 drops) were refluxed for one hour in dry ethanol (20 ml). The yellow solid which separated on cooling was chromatographed over neutral alumina together with the residue left after evaporation of the mother liquor to afford **19** (eluant ethyl acetate:light

petrol 3:7), yield 10%, mp 109-110° (ethanol); ir: ν NH 3310, CN 2200 cm^{-1}; pmr: 2.28 (t, 2H, 9-CH_2), 2.48 (t, 2H, 8-CH_2), 2.64 (t, 2H, 10-CH_2), 4.78 (bs, 2H, NH_2), 7.28-7.44 (m, 3H, 5- and 7-H), 7.58 (dd, 1H, 4-H).

Anal. Calcd. for $C_{14}H_{12}N_2S$: C, 70.00; H, 5.00; N, 11.66. Found: C, 70.06; H, 5.02; N, 11.77.

5-Chloro-8,9-dihydro-7*H*-benzocycloheptene-6-carbaldehyde **20**.

Freshly distilled phosphorus oxychloride (3.85 g, 25 mmoles) was added at 0° to stirred dimethylformamide (50 ml) followed by benzosuberone (4 g, 25 mmoles). After thirty minutes at 0° and ninety minutes at 80°, the cooled reaction mixture was poured into crushed ice and neutralized with sodium acetate. Extraction with ether, drying and removal of solvent afforded **20** (4.8 g) as an orange oil which was used for the next step without further purification; ir: ν CO 1660 cm^{-1}; pmr (carbon tetrachloride): 2.00-2.33 (m, 4H, 4-CH_2 and 5-CH_2), 2.46-3.0 (m, 2H, 3-CH_2), 7.02-7.73 (m, 4H, aromatic protons), 10.26 (s, 1H, CHO).

Methyl 5,6-Dihydro-4*H*-benzo[6,7]cyclohepta[1,2-*b*]thiophene-2-carboxylate **21**.

Methyl thioglycolate (1.5 g, 14 mmoles) was added dropwise to a stirred solution of sodium (0.4 g) in dry methanol (20 ml) followed by the chloroaldehyde **20** (3 g, 14 mmoles) after five minutes. After allowing to attain room temperature and stirring overnight, ice water was added and extracted with ether. Drying, removal of solvent and distillation of the residue *in vacuo* afforded **21** in 95% yield, bp 148-150°/0.05 mm; ir: ν CO 1710 cm^{-1}; pmr: 1.6-1.8 (m, 2H, 5-CH_2), 2.1-2.2 (m, 4H, 4-CH_2 and 6-CH_2), 3.4 (s, 3H, CH_3), 6.8-7.2 (m, 5H, aromatic protons).

Anal. Calcd. for $C_{15}H_{14}O_2S$: C, 69.76; H, 5.42. Found: C, 69.54; H, 5.53.

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