

A New Anti-inflammatory/Analgesic Agent

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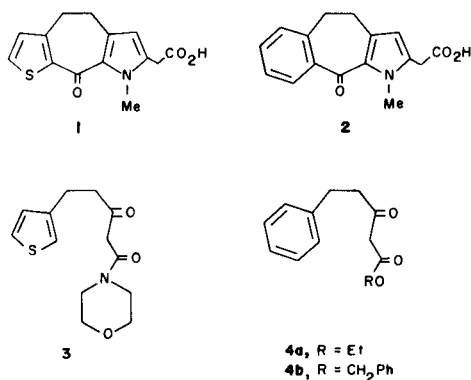
Received December 13, 1982

The synthesis of the thienocyclohepta[1,2-*b*]pyrrole acid **1** from the morpholide **3** is reported. This novel morpholide was prepared by regiospecific alkylation of the dianion of 4-(1,3-dioxobutyl)morpholine with 3-bromomethylthiophene. Subsequent Knorr pyrrole synthesis led to the morpholide **8b** which was converted to the desired tricyclic ring system under Vilsmeier conditions. An alternative route involving Friedel-Crafts cyclisation was used to prepare the related benzocycloheptapyrrole **2**.

J. Heterocyclic Chem., **20**, 1027 (1983).

Our interest in the synthesis of potentially useful anti-inflammatory/analgesic agents has led us to prepare derivatives of thieno[3',2':5,6]cyclohepta[1,2-*b*]pyrrole, a novel heterocyclic ring system. This paper describes the preparation of 4,5,8,9-tetrahydro-8-methyl-9-oxothieno[3',2':5,6]cyclohepta[1,2-*b*]pyrrole-7-acetic acid (**1**) [1]. In addition a recent publication [2] concerning the synthesis of the related tricyclic acid **2** has prompted us to describe our earlier alternative route [3] to this compound.

Our approach to these ring systems utilised a Knorr synthesis [4] in which diethyl acetone-1,3-dicarboxylate was a common synthon for generation of the pyrrole ring. The β -ketoamide **3** and the β -ketoester **4b** were chosen as the other starting components for the synthesis of **1** and **2**, respectively.

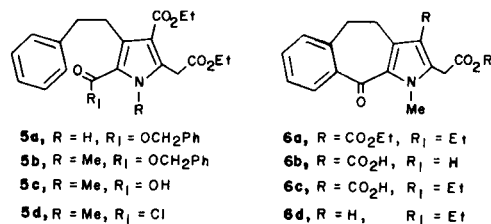


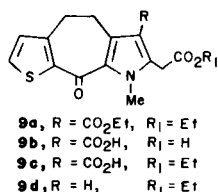
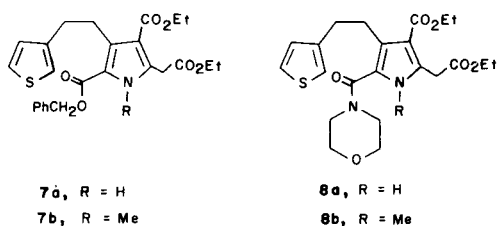
Sequential treatment of ethyl acetoacetate with sodium hydride, butyl lithium and benzyl chloride in tetrahydrofuran afforded the ketoester **4a** [5], which was then transesterified to the benzyl ester **4b**. An attempt to prepare this benzyl ester from benzyl acetoacetate and benzyl chloride with the same bases was unsuccessful, presumably due to the competitive abstraction of a benzylic proton. Oximation of **4b** with sodium nitrite and subsequent reaction with diethyl acetone-1,3-dicarboxylate under the usual Knorr conditions furnished the pyrrole **5a**. Treatment of this pyrrole with dimethyl sulphate followed by

hydrogenolysis of the resulting *N*-methylpyrrole benzyl ester **5b** gave the acid **5c**. This was then converted to the acid chloride **5d** and cyclised with aluminium chloride to the tricyclic benzo[5,6]cyclohepta[1,2-*b*]pyrrole **6a**. Further elaboration to the desired acid **2** was achieved by saponification to **6b**, selective esterification of the acetic acid group to give **6c**, thermal decarboxylation of the remaining carboxylic acid moiety, and finally hydrolysis of the monoester **6d**.

When the same methodology was applied to the synthesis of the thienoacid **1**, benzyl 3-oxo-5-(3-thienyl)pentanoate was readily converted to the corresponding benzyl ester **7a**. Since selective removal of the benzyl group from either this compound or its *N*-methyl derivative **7b** proved difficult to achieve in reasonable yield, we decided to use a Vilsmeier approach [6] for the cyclisation step. Accordingly, 4-(1,3-dioxobutyl)morpholine, prepared by the reaction of morpholine with diketene [7], was converted to its dianion and treated with 3-bromomethylthiophene to give the β -ketoamide **3**. A Knorr synthesis of the latter with diethyl acetone-1,3-dicarboxylate afforded the pyrrole **8a**, which was converted to its *N*-methyl derivative **8b** before being cyclised in phosphoryl chloride to the tricyclic diester **9a**. Sequential transformation of this compound to the desired acid **1** was then accomplished *via* the intermediates **9b**, **9c** and **9d** using the previously described conditions.

Although the thienocycloheptapyrrole **1** possessed anti-inflammatory and analgesic properties, these were not sufficient to warrant progression to the clinic.





EXPERIMENTAL

The melting points were determined using a Kofler block and are uncorrected. The nmr spectra were recorded in deuteriochloroform solution, unless otherwise specified, with a Varian EM360A spectrometer. The chemical shifts are expressed as ppm (δ) from internal tetramethylsilane.

4-[1,3-Dioxo-5-(3-thienyl)pentyl]morpholine (**3**).

To a slurry of sodium hydride (77 g of a 50% dispersion in oil, 1.6 moles) in tetrahydrofuran (800 ml) under nitrogen was added over 30 minutes with stirring a solution of 4-(1,3-dioxobutyl)morpholine (275 g, 1.6 mmoles) in tetrahydrofuran (1.2 l). The resulting suspension was diluted with ether (1 l) and tetrahydrofuran (1 l) and stirred mechanically for 30 minutes at 0° before a solution of *n*-butyl lithium in hexane (1 l, 1.6M) was added dropwise. To the now clear solution was added crude 3-bromomethylthiophene [8] (260 g, purity 75%) in dry tetrahydrofuran (250 ml), again dropwise, and the reaction allowed to warm to room temperature. The reaction was allowed to stand at room temperature overnight before the precipitate was filtered off, the solvents were removed from the filtrate *in vacuo*, and the solid residues combined and acidified carefully with 5*N* hydrochloric acid in the presence of ethyl acetate. The organic layer was separated off and the aqueous layer extracted twice more with ethyl acetate. The combined organic layers were washed with water, dried over magnesium sulphate and the solvent removed *in vacuo* to give an oil. The oil was taken up in dichloromethane and the solution treated with activated charcoal. Ether was then added and the mixture concentrated to give the product as a solid (126 g, 39%), mp 81-84°; nmr: 2.95 (s, 4H), 3.2-3.7 (m, 10H), 7.0 (m, 2H), 7.25 (m, 1H).

Anal. Calcd. for C₁₃H₁₇NO₃S: C, 58.4; H, 6.41; N, 5.24; S, 11.99. Found: C, 58.03; H, 6.22; N, 5.20; S, 11.77.

3-(Ethoxycarbonyl)-4-(2-phenylethyl)-5-[(phenylmethoxy)carbonyl]-1H-pyrrole-2-acetic Acid, Ethyl Ester (**5a**).

Ethyl 3-oxo-5-phenylpentanoate (**4a**) [5] was transesterified to the corresponding benzyl ester **4b** by heating at 190-210° under nitrogen with removal of the ethanol by distillation. This ester was used without further purification in a standard Knorr synthesis.

Benzyl 3-oxo-5-phenylpentanoate (**4b**) (101.6 g, 0.36 mole) in glacial acetic acid (240 ml) was treated with sodium nitrite (33 g, 0.48 mole) in water (50 ml) at 5-7°, stirred for ½ hour at 0°, 2 hours at room temperature and then stored overnight at -20°. On warming to room temperature this solution was added to diethyl acetone-1,3-dicarboxylate (94.3 g) in acetic acid (390 ml) at 70° with concurrent addition of zinc (102 g) and sodium acetate (114 g) keeping the temperature below 100°. The mixture was heated at reflux temperature for 1 hour and then poured into water (6 l). The resulting solid was collected, dried and recrystallised twice

from toluene/petroleum ether (60-80°) to give the required product (81.22 g, 49%), mp 100-103°; nmr: 1.24 (t, 3H, J = 7 Hz), 1.33 (t, 3H, J = 7 Hz), 2.4-3.5 (m, 4H), 4.02 (s, 2H), 4.15 (q, 2H, J = 7 Hz), 4.26 (q, 2H, J = 7 Hz), 5.25 (s, 2H), 7.07 (m, 5H), 7.30 (s, 5H), 10.20 (broad s, 1H).

Anal. Calcd. for C₂₇H₂₉NO₆: C, 69.96; H, 6.31; N, 3.02. Found: C, 69.80; H, 6.29; N, 3.10.

3-(Ethoxycarbonyl)-1-methyl-4-(2-phenylethyl)-5-[(phenylmethoxy)carbonyl]-1H-pyrrole-2-acetic Acid, Ethyl Ester (**5b**).

A solution of the N-H pyrrole **5a** (81 g, 0.175 mole) in isobutyl methyl ketone (800 ml) with dimethyl sulphate (33 ml, 0.35 mole) and anhydrous potassium carbonate (81 g) was heated at reflux temperature overnight. Additional dimethyl sulphate (10 ml) and potassium carbonate (10 g) were added and the mixture heated for a further 5 hours before pouring into water (1 l). The product (70.04 g, 84%) was extracted with ethyl acetate and purified by recrystallisation from toluene/petroleum ether (60-80°) to give a white solid, mp 84-86°; nmr: 1.23 (t, 3H, J = 7 Hz), 1.30 (t, 3H, J = 7 Hz), 2.4-3.6 (m, 4H), 3.79 (s, 3H), 4.08 (s, 2H), 4.17 (q, 2H, J = 7 Hz), 4.25 (q, 2H, J = 7 Hz), 5.28 (s, 2H), 7.06 (m, 5H), 7.31 (s, 5H).

Anal. Calcd. for C₂₈H₃₁NO₆: C, 70.42; H, 6.54; N, 2.93. Found: C, 70.49; H, 6.57; N, 3.01.

5-Carboxy-3-(ethoxycarbonyl)-1-methyl-4-(2-phenylethyl)-1H-pyrrole-2-acetic Acid, Ethyl Ester (**5c**).

The benzyl ester **5b** (68.98 g, 0.145 moles) in ethyl acetate (1 l) with 10% palladium on charcoal (3.5 g) was hydrogenated at atmospheric pressure to give the acid (53 g, 95%) as a white solid, mp 128-130°; nmr: 1.25 (t, 3H, J = 7 Hz), 1.33 (t, 3H, J = 7 Hz), 2.6-3.7 (m, 4H), 3.83 (s, 3H), 4.1 (s, 2H), 4.13 (q, 2H, J = 7 Hz), 4.28 (q, 2H, J = 7 Hz), 7.2 (broad s, 5H), 11.83 (broad s, 1H).

Anal. Calcd. for C₂₁H₂₅NO₆: C, 65.10; H, 6.50; N, 3.61. Found: C, 65.10; H, 6.35; N, 3.70.

3-(Ethoxycarbonyl)-1,4,5,10-tetrahydro-1-methyl-10-oxobenzof[5,6]cyclohepta[1,2-*b*]pyrrole-2-acetic Acid, Ethyl Ester (**6a**).

Oxalyl chloride (26.1 g, 0.206 mole) was added to the acid **5c** (53 g, 0.137 mole) in dry toluene (250 ml) and the mixture heated at reflux temperature for 6 hours to give the corresponding acid chloride (**5d**). After removal of solvent most of the acid chloride (54 g, 0.133 mole) was taken up in dichloromethane (600 ml) and powdered aluminium trichloride (21.3 g, 0.16 mole) added in portions with stirring. The mixture was heated at reflux temperature for 5½ hours and left to stand at room temperature overnight before pouring onto ice (500 ml), separating, and extracting the aqueous layer with dichloromethane (3 × 200 ml). The combined organic layers were washed with water, dried with anhydrous magnesium sulphate and the solvent evaporated *in vacuo*. The resulting viscous red oil was chromatographed on silica gel with ether as eluant to give the product (**6a**) still as a red oil (42.38 g, 86%). A small sample was rechromatographed on silica gel with 1:1 ether/petroleum ether (60-80°) as eluant and recrystallised from petroleum ether (60-80°) to give the pure diester (**6a**) as white needles, mp 71-72°; nmr: 1.22 (t, 3H, J = 7 Hz), 1.32 (t, 3H, J = 7 Hz), 2.8-3.5 (m, 4H), 3.93 (s, 3H), 4.14 (s, 2H), 3.9-4.5 (two overlapping q, 4H, J = 7 Hz), 7.0-7.5 (m, 3H), 7.7-7.9 (m, 1H).

Anal. Calcd. for C₂₁H₂₃NO₆: C, 68.28; H, 6.28; N, 3.79. Found: C, 68.08; H, 6.21; N, 3.64.

3-Carboxy-1,4,5,10-tetrahydro-1-methyl-10-oxobenzof[5,6]cyclohepta[1,2-*b*]pyrrole-2-acetic Acid (**6b**).

The diester **6a** (23.57 g, 0.064 mole) was saponified with 25% aqueous sodium hydroxide by heating at reflux temperature for 3 hours. On cooling the solution was extracted with ether and the aqueous layer acidified with 5*N* hydrochloric acid. The resulting pink solid was collected, washed with water and dried to give the required diacid **6b** (16.65 g, 83%), mp 214-216° (decarboxylation); nmr (perdeuteriomethanol/DMSO-*d*₆): 2.87-3.47 (m, 4H), 3.94 (s, 3H), 4.27 (s, 2H), 7.07-7.57 (m, 3H), 7.67-7.92 (m, 1H).

Anal. Calcd. for C₁₇H₁₅NO₅·½H₂O: C, 63.34; H, 5.00; N, 4.35. Found: C, 63.01; H, 5.02; N, 4.39.

3-Carboxy-1,4,5,10-tetrahydro-1-methyl-10-oxobenzo[5,6]cyclohepta[1,2-*b*]pyrrole-2-acetic Acid, Ethyl Ester (**6c**).

The diacid **6b** (15.65 g, 0.05 mole) was selectively esterified by heating at reflux in 0.5% hydrochloric acid in ethanol (200 ml) for an hour. After cooling the reaction, the resulting solid (14.35 g, 84%) was collected, mp 178-180°; nmr (deuteriochloroform/pyridine-*d*₃): 1.21 (t, 3H, J = 7 Hz), 2.8-3.7 (m, 4H), 3.93 (s, 3H), 4.15 (q, 2H, J = 7 Hz), 4.33 (s, 2H), 7.0-7.5 (m, 3H), 7.7-8.0 (m, 1H).

Anal. Calcd. for C₁₉H₁₉NO₅: C, 66.85; H, 5.61; N, 4.10. Found: C, 66.71; H, 5.66; N, 4.17.

1,4,5,10-Tetrahydro-1-methyl-10-oxobenzo[5,6]cyclohepta[1,2-*b*]pyrrole-2-acetic Acid, Ethyl Ester (**6d**).

The monoester **6c** (14 g, 0.041 mole) was heated under nitrogen in an oil bath at 180-205° for 4 hours. Acidic material was removed by washing an ethyl acetate solution of the reaction mixture with dilute sodium hydroxide. After removal of solvent a brown oil, 8 g, was obtained which was purified by column chromatography on silica gel with 1:1 ether/petroleum ether (60-80°) as eluant to give a pale yellow solid (5.83 g, 48%), mp 69-70°, after recrystallisation from petroleum ether (60-80°); nmr: 1.25 (t, 3H, J = 7 Hz), 2.7-3.2 (m, 4H), 3.6 (s, 2H), 3.89 (s, 3H), 4.15 (q, 2H, J = 7 Hz), 5.9 (s, 1H), 6.9-7.4 (m, 3H), 7.7-8.0 (m, 1H).

Anal. Calcd. for C₁₈H₁₉NO₅: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.54; H, 6.42; N, 4.66.

1,4,5,10-Tetrahydro-1-methyl-10-oxobenzo[5,6]cyclohepta[1,2-*b*]pyrrole-2-acetic Acid (**2**).

The ester **6d** (3.6 g, 0.012 mole) in 1*N* sodium hydroxide (80 ml) and ethanol (70 ml) was heated at reflux for 1½ hours. After cooling the reaction and extraction with ether the solution was acidified with 5*N* hydrochloric acid and the resulting solid collected, washed and dried. After recrystallisation from chloroform/hexane the required acid **2** was obtained as a white crystalline solid (2.07 g, 64%), mp 164-166°. The melting point and spectroscopic properties of **2** agreed with those reported [2].

3-(Ethoxycarbonyl)-5-(4-morpholinylcarbonyl)-4-[2-(3-thienyl)ethyl]-1*H*-pyrrole-2-acetic Acid, Ethyl Ester (**8a**).

In a similar manner to the preparation of the pyrrole **5a**, the morpholine derivative **3** (90.5 g, 0.34 moles) in glacial acetic acid (350 ml) was treated with a solution of sodium nitrite (23.4 g, 0.34 mole) in water (35 ml). Subsequent reaction with diethyl acetone-1,3-dicarboxylate (68.5 g, 0.34 mole), zinc (115 g), and sodium acetate (148 g) gave the required product **8a** (82.25 g, 54%) mp 122-124° after recrystallisation from toluene; nmr: 1.2 (t, 3H, J = 7 Hz), 1.3 (t, 3H, J = 7 Hz), 2.93 (m, 4H), 3.56 (broad s, 8H), 3.98 (s, 2H), 4.14 (q, 2H, J = 7 Hz), 4.25 (q, 2H, J = 7 Hz), 6.83 (m, 2H), 7.1 (m, 1H), 10.1 (broad s, 1H).

Anal. Calcd. for C₂₂H₂₈N₂O₆S: C, 58.91; H, 6.29; N, 6.24. Found: C, 58.87; H, 6.14; N, 6.24.

3-(Ethoxycarbonyl)-1-methyl-5-(4-morpholinylcarbonyl)-4-[2-(3-thienyl)ethyl]-1*H*-pyrrole-2-acetic Acid, Ethyl Ester (**8b**).

Methylation of **8a** (75 g, 0.167 mole) was carried out in an analogous manner to the preparation of compound **5b** but using dry dioxan as solvent. The product was isolated as a viscous oil (72 g, 93%) by column chromatography on silica gel eluting with 1% methanol/chloroform and was used without further purification; nmr: 1.23 (t, 3H, J = 7 Hz), 1.3 (t, 3H, J = 7 Hz), 2.85 (broad s, 4H), 3.45 (s, 3H), 3.67 (broad s, 8H), 4.06 (s, 2H), 4.2 (q, 2H, J = 7 Hz), 4.3 (q, 2H, J = 7 Hz), 6.88 (m, 2H), 7.12 (m, 1H).

3-(Ethoxycarbonyl)-4,5,8,9-tetrahydro-8-methyl-9-oxothieno[3',2':5,6]cyclohepta[1,2-*b*]pyrrole-7-acetic Acid, Ethyl Ester (**9a**).

Cyclisation of the above pyrrole **8b** (72 g, 0.156 mole) was achieved by heating a solution of the compound in phosphoryl chloride (300 ml) at reflux temperature for 3 hours under an atmosphere of nitrogen. The reaction was then cooled and poured carefully onto ice covered with ethyl acetate. The aqueous solution was neutralized by the addition of solid

sodium carbonate, the organic layer was then separated and the aqueous layer was twice further extracted with ethyl acetate. The combined organic layers were washed with a saturated sodium chloride solution, dried over anhydrous magnesium sulphate, filtered and the solvent evaporated *in vacuo* to give a grey solid. Recrystallisation from ethyl acetate/pentane afforded the product (32.8 g, 56%) mp 105-106°. A second recrystallisation from ether/petroleum ether (60-80°) gave fine white needles and raised the melting point to 115-116°; nmr: 1.26 (t, 3H, J = 7 Hz), 1.33 (t, 3H, J = 7 Hz), 2.83-3.13 (m, 2H), 3.23-3.56 (m, 2H), 3.9 (s, 3H), 4.1 (s, 2H), 4.16 (q, 2H, J = 7 Hz), 4.3 (q, 2H, J = 7 Hz), 6.9 (d, 1H, J = 5 Hz), 7.46 (d, 1H, J = 5 Hz).

Anal. Calcd. for C₁₉H₂₁NO₅S: C, 60.78; H, 5.64; N, 3.73. Found: C, 60.53; H, 5.51; N, 3.70.

3-Carboxy-4,5,8,9-tetrahydro-8-methyl-9-oxothieno[3',2':5,6]cyclohepta[1,2-*b*]pyrrole-7-acetic Acid (**9b**).

The diethyl ester **9a** (4.6 g, 12.2 mmoles) was saponified with 25% sodium hydroxide (60 ml) by heating at reflux temperature for 2 hours. The cooled aqueous solution was washed with ether, acidified and the resulting solid filtered off and dried (3.9 g, 100%). Recrystallisation from ethanol/water gave white crystals, mp 230-231° (decarboxylation); nmr (deuteriochloroform/pyridine-*d*₃): 2.73-3.09 (m, 2H), 3.3-3.67 (m, 2H), 3.94 (s, 3H), 4.37 (s, 2H), 6.70 (d, 1H, J = 5 Hz), 7.36 (d, 1H, J = 5 Hz), 8.62 (broad s, 2H).

Anal. Calcd. for C₁₅H₁₃NO₅S·½H₂O: C, 54.87; H, 4.30; N, 4.27. Found: C, 54.68; H, 4.02; N, 4.30.

3-Carboxy-4,5,8,9-tetrahydro-8-methyl-9-oxothieno[3',2':5,6]cyclohepta[1,2-*b*]pyrrole-7-acetic Acid, Ethyl Ester (**9c**).

The diacid **9b** (3.9 g, 12.2 mmoles) was suspended in 0.5% hydrochloric acid in ethanol (86 ml) and heated at reflux temperature for 1 hour to give a clear solution. On cooling the reaction a precipitate appeared which was isolated to give the required product (3.48 g, 82%), mp 191-194°; nmr (deuteriochloroform/pyridine-*d*₃): 1.23 (q, 3H, J = 7 Hz), 2.8-3.13 (m, 2H), 3.33-3.66 (m, 2H), 3.91 (s, 3H), 4.16 (q, 2H, J = 7 Hz), 4.29 (s, 2H), 6.86 (d, 1H, J = 5 Hz), 7.43 (d, 1H, J = 5 Hz), 8.33 (broad s, 1H).

Anal. Calcd. for C₁₇H₁₇NO₅S: C, 58.78; H, 4.93; N, 4.03; S, 9.23. Found: C, 58.73; H, 4.85; N, 4.03; S, 9.16.

4,5,8,9-Tetrahydro-8-methyl-9-oxothieno[3',2':5,6]cyclohepta[1,2-*b*]pyrrole-7-acetic Acid, Ethyl Ester (**9d**).

The monoester **9c** (3.48 g, 10 mmoles) was heated under nitrogen at 210-220° in an oil bath for 1¾ hours. The mixture was cooled and dissolved in ethyl acetate. The organic layer was then washed with dilute sodium hydroxide, water, dried over anhydrous magnesium sulphate, filtered and the solvent removed *in vacuo* to give an oily solid (2.2 g). Purification by column chromatography using silica gel and elution with ether afforded the required product as a solid (1.8 g, 60%). Recrystallisation from pentane gave yellow crystals, mp 90-91°; nmr: 1.26 (q, 3H, J = 7 Hz), 2.92 (s, 4H), 3.62 (s, 2H), 3.88 (s, 3H), 4.15 (q, 2H, J = 7 Hz), 5.93 (s, 1H), 6.82 (d, 1H, J = 5 Hz), 7.35 (d, 1H, J = 5 Hz).

Anal. Calcd. for C₁₆H₁₇NO₅S: C, 63.34; H, 5.65; N, 4.62. Found: C, 63.29; H, 5.59; N, 4.61.

4,5,8,9-Tetrahydro-8-methyl-9-oxothieno[3',2':5,6]cyclohepta[1,2-*b*]pyrrole-7-acetic Acid (**1**).

The monoester **9c** (3.48 g, 10 mmoles) was heated under nitrogen at 210-220° in an oil bath for 3¾ hours. The mixture was cooled and dissolved in ethyl acetate. The organic layer was then washed with dilute sodium hydroxide, water, dried over anhydrous magnesium sulphate, filtered and the solvent removed *in vacuo* to give an oily solid (2.2 g). Purification by column chromatography using silica gel and elution with ether afforded the required product as a solid (1.8 g, 60%). Recrystallisation from pentane gave yellow crystals, mp 90-91°; nmr: 1.26 (q, 3H, J = 7 Hz), 2.92 (s, 4H), 3.62 (s, 2H), 3.88 (s, 3H), 4.15 (q, 2H, J = 6 Hz), 5.93 (s, 1H), 6.82 (d, 1H, J = 5 Hz), 7.35 (d, 1H, J = 5 Hz).

Anal. Calcd. for $C_{16}H_{17}NO_3S$: C, 63.34; H, 5.65; N, 4.62. Found: C, 63.29; H, 5.59; N, 4.61.

3,4,8,9-Tetrahydro-8-methyl-9-oxothieno[3',2':5,6]cyclohepta[1,2-*b*]pyrrole-7-acetic Acid (**1**).

The ester **9d** (9.2 g, 30.3 mmoles) was dissolved in ethanol (20 ml) and added to 5% sodium hydroxide solution (200 ml) and the mixture refluxed for 1 hour. The resulting solution was cooled, washed with ethyl acetate and acidified. The aqueous layer was extracted twice with chloroform and the combined organic layers washed with water, dried over anhydrous sodium sulphate, filtered and the solvent evaporated *in vacuo* to give a solid. Recrystallisation from chloroform/pentane afforded the required product (8.0 g, 97%), mp 157-158° (decarboxylation); nmr 2.93 (s, 4H), 3.7 (s, 2H), 3.9 (s, 3H), 6.0 (s, 1H), 6.9 (d, 1H, $J = 5$ Hz), 7.45 (d, 1H, $J = 5$ Hz), 10.13 (broad s, 1H).

Anal. Calcd. for $C_{14}H_{13}NO_3S$: C, 61.08; H, 4.76; N, 5.09; S, 11.64. Found: C, 60.93; H, 4.67; N, 5.08; S, 11.50.

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