J. C. Lancelot [a], C. Saturnino [a], H. El-Kashef [b], D. Perrine [a], C. Mahatsekake [a], H. Prunier [a] and M. Robba [a]

[a] Centre d'études et de Recherche sur le Médicament de Normandie, UFR des Sciences Pharmaceutiques, 1, rue Vaubénard, 14032 Caen, France

[b] Chemistry Department, Faculty of Science, Assiut University, 71516 Assiut, Egypt Received October 16, 1995

Several new β -lactams have been synthesized in good yields, via the cyclization of 3-chloro-N-arylpropionamides in a mixture of N,N-dimethylformamide and anhydrous sodium carbonate under a nitrogen atmosphere.

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The synthesis of β -lactams is accessible by several methods under anhydrous conditions [1]. One of these methods [2] involves the reaction between β -haloacyl chlorides and α -amino acid derivatives in a mixture of benzene and 40% sodium hydroxide solution in the presence of a phase transfer catalyst. Yamazaki [3] has reported another method which includes the cyclization of N-alkyl- β -halocarboxamides [4] using potassium hydroxide as a phase transfer.

In the present paper, we report the preliminary results of a facile synthesis of new β-lactams by cyclization of N-substituted-3-chloropropionamides without the use of any phase transfer catalyst. Thus when the methyl 3-aminothiophene-2-carboxylate derivatives 1a-f [5] were allowed to interact with pivaloyl chloride and an equivalent amount of pyridine at reflux in dioxane, the corresponding chloroamides 2a-f were obtained in 60 to 70% yield. Upon heating at 160° in DMF in the presence of sodium carbonate these latter compounds, 2a-f, were subjected to a dehydrochlorination reaction with concomitant cyclization where the lactams 3a-f resulted in 70 to 90% yield. The acids 4a-f could be obtained by alkaline hydrolysis of the ester function of the corresponding lactams 3a-f. In an attempt to obtain the amide derivative 5a, the ester 3f was heated in neat pyrrolidine under reflux. The spectral and elemental analysis of the product proved that the ester function is intact and that the halogen atom is absent. The product is analyzed for the pyrrolidinyl derivative 5.

On the other hand, amines 6a-b were reacted with 3,3'-dichloropivaloyl chloride under the same reaction conditions as those of 2a-f to give the dichloropropionamide derivatives 7a-b. Cyclization of these amides gave the corresponding chloromethyl β -lactam derivatives 8a-b. The labile chlorine atom of the latter derivatives was substituted by the 4-benzylpiperazino group to give compounds 9a-b.

The antibacterial screening of these prepared β -lactams revealed that they are active against several stains of

Gram positive bacteria. However, the detailed study, along with the synthesis of other derivatives with the object to improve their antibacterial activity will be the subject of a future publication.

Scheme 1

Scheme 2

R-NH₂

$$C_{3}H_{5}N$$

CH₃

CH₂

CH₂-Cl

CH₂-Cl

CH₂-Cl

CH₂-Cl

Ta-7b

S-CO₂CH₃

Ch

Na₂CO₃

DMF

Na₂CO₃

DMF

R-N

CH₂

S-CO₂CH₃

Pa R=

CH

S-CO₂CH₃

OCH₃

1) Benzylpiperidine

R-N

CH

CH₂-Cl

R-N

R-N

R-N

CH

S-CO₂CH

Sa

Sa-8b

EXPERIMENTAL

Melting points were determined on Köfler type WME apparatus and are uncorrected. Their ir spectra were recorded on Philips PU spectrometer. The nmr spectra were recorded on a varian EM 390 spectrometer at 90 MHz in hexadeuteriodimethylsulfoxide with tetramethylsilane as an internal reference, chemical shifts are expressed as δ (ppm) relative to TMS. The 3-chloropivaloyl chloride and 3,3'-dichloropivaloyl chloride started from the commercially Aldrich limited.

Methyl 3-(3-Chloro-2,2-dimethylpropionylamino)-4-(4-fluorophenyl)thiophene-2-carboxylate (2a).

General Procedure.

A solution of 10 g (0.0398 mole) of methyl 3-amino-4-(4-fluorophenyl)thiophene-2-carboxylate (1a) and 6.17 g (0.0398 mole) of 3-chloropivaloyl chloride in 100 ml of dioxane was refluxed with 3.14 g (0.0398 mole) of pyridine under a nitrogen atmosphere for 1 hour. The solvent was evaporated *in vacuo* and the residue dissolved in water and extracted with ether. The solvent was removed to leave a solid 11 g (75%), mp 110° (ether); ir (potassium bromide): 3270 (NH), 1690 (CO); ¹H-nmr (DMSO-d₆): 10.20 (s, 1H, NH), 8.10 (s, 1H, H5), 7.63 (d, 2H, ArH), 7.10 (d, 2H, ArH), 3.85 (s, 3H, COOCH₃), 3.70 (s, 2H, CH₂), 1.30 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₇H₁₇FClNO₃S: C, 55.20; H, 4.63; N, 3.78; Cl, 9.58. Found: C, 55.30; H, 4.70; N, 3.82, Cl, 9.69.

Methyl 3-(3-Chloro-2,2-dimethylpropionylamino)-4-(4-chlorophenyl)thiophene-2-carboxylate (2b).

This compound was obtained by the procedure described for compound 2a as colorless crystals (79%), mp 81° (ether); ir (potassium bromide): 3320 (NH), 1700 (CO); ¹H-nmr (DMSOd₆): 9.34 (s, 1H, NH), 7.97 (s, 1H, H5), 7.44 (m, 4H, ArH), 3.80 (s, 3H, COOCH₃), 3.69 (s, 2H, CH₂), 1.24 (s, 6H, CH₃).

Anal. Caled. for C₁₇H₁₇C₁₂NO₃S: C, 52.85; H, 4.43; N, 3.62; Cl, 18.35. Found: C, 52.90; H, 4.50; N, 3.76; Cl, 18.42.

Methyl 3-(3-Chloro-2,2-dimethylpropionylamino)-4-(4-anisyl)thiophene-2-carboxylate (2c).

This compound was obtained by the procedure described for compound **2a** as colorless crystals (76%), mp 98° (ether); ir (potassium bromide): 3280 (NH) 1700 (CO); ¹H-nmr (DMSOd₆): 9.27 (s, ¹H, NH), 7.85 (s, 1H, H5), 7.39 (d, 2H, ArH), 6.94 (d, 2H, ArH), 3.78 (s, 6H, OCH₃, COOCH₃), 3.70 (s, 2H, CH₂), 1.25 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₈H₂₀ClNO₄S: C, 56.61; H, 5.27; N, 3.66; Cl, 9.28. Found: C, 56.90; H, 5.30; N, 3.76; Cl, 9.32.

Methyl 3-(3-Chloro-2,2-dimethylpropionylamino)-4(2-thienyl)-thiophene-2-carboxylate (2d).

This compound was obtained by the procedure described for compound 2a as colorless crystals (82%), mp l02° (ether); ir (potassium bromide): 3260 (NH), 1700 (CO); 1 H-nmr (DMSO- 4 d₆): 9.36 (s, 1H, NH), 8.00 (s, 1H, H5), 7.56 (dd, 1H, H5'), 7.33 (dd, 1H, H3'), 7.06 (dd, 1H, H4), 3.83 (s, 3H, COOCH₃), 3.70 (s, 2H, CH₂), 1.29 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₅H₁₆ClNO₃S₂: C, 50.33; H, 4.50; N, 3.91; Cl, 9.90. Found: C, 50.38; H, 4.55; N, 4.00; Cl, 10.00.

Methyl 3-(3-Chloro-2,2-dimethylpropionylamino)-5-(4-chloro-phenyl)thiophene-2-carboxylate (2e).

This compound was obtained by the procedure described for compound **2a** as colorless crystals (60%), mp 137° (acetonitrile); ir (potassium bromide): 3280 (NH), 1700 (CO); ¹H-nmr (DMSO-d₆): 9.60 (s, 1H, NH), 8.12 (s, 1H, H4), 7.40 (m, 4H, ArH), 3.80 (s, 3H, COOCH₃), 3.70 (s, 2H, CH₂), 1.30 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₇H₁₇Cl₂NO₃S: C, 52.85; H, 4.43; N, 3.62; Cl, 18.35. Found: C, 53.00; H, 4.40; N, 3.70; Cl, 18.42.

Methyl 3-(3-Chloro-2,2-dimethylpropionylamino)-5-(4-fluorophenyl)thiophene-2-carboxylate (2f).

This compound was obtained by the procedure described for compound **2a** as colorless crystals (64%), mp 157° (acetonitrile); ir (potassium bromide): 3270 (NH), 1700 (CO); ¹H-nmr (DMSO-d₆): 10.33 (s, 1H, NH), 8.16 (s, 1H, H4), 7.63 (d, 2H, ArH), 7.16 (d, 2H, ArH), 3.83 (s, 3H, COOCH₃), 3.73 (s, 2H, CH₂), 1.36 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₇H₁₇FClNO₃S: C, 55.20; H, 4.63; N, 3.78; Cl, 9.58. Found: C, 55.34; H, 4.65; N, 3.86; Cl, 9.72.

N-Benzhydryl-2,2-dichloromethylpropionylamine (7a).

This compound was obtained by the procedure described for compound **2a** as colorless crystals (70%), mp 176° (acetonitrile); ir (potassium bromide): 3310 (NH), 1640 (CO); ¹H-nmr (DMSO-d₆): 8.60 (d, 1H, NH), 7.13 (m, 10H, ArH), 6.10 (d, 1H, CH), 3.83 (d, 4H, (CH₂)₂), 1.26 (s, 3H, CH₃).

Anal. Calcd. for C₁₈H₁₉Cl₂NO: C, 64.29; H, 5.69; N, 4.16; Cl, 21.08. Found: C, 64.31; H, 5.62; N, 4.21; Cl, 21.15.

Methyl (2,2-Dichloromethylpropionylamino)-4-(4-anisyl)thio-phene-2-carboxylate (7b).

This compound was obtained by the procedure described for compound (2a) as colorless crystals (65%), mp 158° (acetonitrile); ir (potassium bromide): 3320 (NH), 1650 (CO); ¹H-nmr (DMSO-d₆): 9.20 (s, 1H, NH), 7.80 (s, 1H, H5), 7.40 (d, 2H, ArH), 6.80 (d, 2H, ArH), 3.80 (s, 6H, OCH₃, COOCH₃), 3.76 (d, 4H, (CH₂)₂), 1.20 (s, 3H, CH₃).

Anal. Calcd. for C₁₈H₁₉C₁₂NO₄S: C, 51.92; H, 4.59; N, 3.36; Cl, 17.03. Found: C, 52.00; H, 4.65; N, 3.40; Cl, 17.23.

N-[2-Methoxycarbonyl-4-(4-fluorophenyl)thien-3-yl]-3,3-dimethylazetidin-2-one (3a).

General Procedure.

To a solution of 4 g (0.0108 mole) of methyl 3-(3-chloro-2,2-dimethylpropionylamino)-4-(fluorophenyl)thiophene-2-carboxylate (2a) in 40 ml of dry *N*,*N*-dimethylformamide and 1.14 g (0.0108 mole) of sodium carbonate was heated at 160° with stirring under nitrogen for 1 hour. The solution was poured into ice/water (150 ml) and extracted with ethylacetate 150 ml. The dry residue was washed twice by ether-hexane, to give 3a as a white solid, 2.90 g (80%), mp 84°; ir (potassium bromide): 1740, 1700 (CO); ¹H-nmr (DMSO-d₆): 7.90 (s, 1H, H5), 7.30 (m, 4H, ArH), 3.80 (s, 3H, COOCH₃), 3.30 (s, 2H, CH₂), 1.23 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₇H₁₆FNO₃S: C, 61.24; H, 4.83; N, 4.20; S, 9.61. Found: C, 61.36; H, 4.90; N, 4.28; S, 9.72.

N-[2-Methoxycarbonyl-4-(4-chlorophenyl)thien-3-yl]-3,3-dimethylazetidin-2-one (3b).

This compound was obtained by the procedure described for compound **3a** as colorless crystals (78%), mp 70° (ether-hexane); ir (potassium bromide): 1750, 1680 (CO); ¹H-nmr (DMSO-d₆): 7.96 (s, 1H, H5), 7.40 (q, 4H, ArH), 3.80 (s, 3H, COOCH₃), 3.10 (s, 2H, CH₂), 1.26 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₇H₁₆CNO₃S: C, 58.36; H, 4.61; N, 4.00; S, 9.16. Found: C, 58.45; H, 4.65; N, 4.10; S, 9.24.

N-[2-Methoxycarbonyl-4-(4-anisyl)thien-3-yl]-3,3-dimethylazetidin-2-one (3c).

This compound was obtained by the procedure described for compound 3a as colorless crystals (81%), mp 90° (ethanol); ir (potassium bromide): 1780, 1720 (CO); ¹H-nmr (DMSO-d₆): 7.80 (s, 1H, H5), 7.23 (d, 2H, ArH), 6.90 (d, 2H, ArH) 3.73 (s, 6H, OCH₃, COOCH₃), 3.23 (s, 2H, CH₂), 1.23 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₈H₁₉NO₄S: C, 62.58; H, 5.54; N, 4.05; S, 9.28. Found: C, 62.70; H, 5.60; N, 4.10; S, 9.31.

3-Chloromethyl-3-methyl-1-(benzhydryl)azetidin-2-one (8a).

This compound was obtained by the procedure described for compound 3a as colorless crystals (92%), mp 122° (ether); ir (potassium bromide): 1750 (CO); ¹H-nmr (DMSO-d₆): 7.20 (m, 10H, ArH), 5.95 (s, 1H, CH), 3.73 (s, 2H, CH₂), 3.21, 2.90 (qq, 2H, CH₂-Cl), 1.25 (s, 3H, CH₃).

Anal. Calcd. for C₁₈H₁₈ClNO: C, 72.11; H, 6.05; N, 4.67. Found: C, 72.30; H, 6.10; N, 4.72.

N-[2-Methoxycarbonyl-4-(4-anisyl)thien-3-yl]-3-chloromethyl-3-methylazetidin-2-one (8b).

This compound was obtained by the procedure described for compound 3a as colorless crystals (79%), mp 110° (ether); ir (potassium bromide): 1740, 1680 (CO); ¹H-nmr (DMSO-d₆):

7.92 (s, 1H, H5), 7.50 (m, 4H, ArH), 3.80 (s, 6H, OCH₃, COOCH₃), 3.30 (s, 2H, CH₂), 3.20, 2.95 (qq, 2H, CH₂-Cl), 1.26 (s, 3H, CH₃).

Anal. Calcd. for C₁₈H₁₈ClNO₄S: C, 56.91; H, 4.77; N, 3.68; S, 8.44. Found: C, 57.00; H, 4.62; N, 3.72; S, 8.57.

N-[2-Methoxycarbonyl-4-(2-thienyl)thien-3-yl]-3,3-dimethylazetidin-2-one (**3d**).

This compound was obtained by the procedure described for compound 3a as colorless crystals (69%), mp 136° (acetonitrile); ir (potassium bromide): 1745, 1710 (CO); ¹H-nmr (DMSO-d₆): 8.10 (s, 1H, H5), 7.56 (q, 1H, H5'), 7.30 (q, 1H, H3'), 7.00 (q, 1H, H4'), 3.80 (s, 3H, COOCH₃), 3.43 (s, 2H, CH₂), 1.40 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₅H₁₅NO₃S₂: C, 56.05; H, 4.70; N, 4.35; S, 19.95. Found: C, 56.15; H, 4.76; N, 4.42; S, 19.82.

N-[2-Methoxycarbonyl-5-(4-chlorophenyl)thien-3-yl]-3,3-dimethylazetidin-2-one (3e).

This compound was obtained by the procedure described for compound 3a as colorless crystals (73%), mp 123° (acetonitrile); ir (potassium bromide): 1750, 1720 (CO); ¹H-nmr (DMSO-d₆): 7.90 (s, 1H, H4), 7.60 (d, 2H, ArH), 7.40 (d, 2H, ArH), 3.80 (s, 3H, COOCH₃), 3.30 (s, 2H, CH₂), 1.33 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₇H₁₆ClNO₃S: C, 58.36; H, 4.61; N, 4.00; S, 9.16. Found: C, 58.42; H, 4.70; N, 4.25; S, 9.22.

N-[2-Methoxycarbonyl-5-(4-fluorophenyl)thien-3-yl]-3,3-dimethylazetidin-2-one (3f).

This compound was obtained by the procedure described for compound 3a as colorless crystals (78%), mp 102° (ether); ir (potassium bromide): 1760, 1700 (CO); ¹H-nmr (DMSO-d₆): 7.90 (s, 1H, H4), 7.66 (m, 2H, ArH), 7.23 (m, 2H, ArH), 3.90 (s, 3H, COOCH₃), 3.76 (s, 2H, CH₂), 1.36 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₇H₁₆FNO₃S: C, 61.24; H, 4.83; N, 4.20; S, 9.61. Found: C, 61.36; H, 4.84; N, 4.32; S, 9.76.

N-[2-Carboxy-4-(4-fluorophenyl)thien-3-yl]-3,3-dimethylazetidin-2-one (4a).

General Procedure.

A mixture of 3.5 g (0.0104 mole) of N-[2-Methoxycarbonyl-4-(4-fluorophenyl)thien-3-yl]-3,3-dimethylazetidin-2-one (3a) and 4N sodium hydroxide (100 ml) were refluxed for 2 hours. The solution was cooled to 5°, neutralized with concentrated hydrochloric acid and acidified with acetic acid. The precipitate thus obtained was filtered, washed with water, dried and recrystallized from acetonitrile yield 2.90 g (87%), mp 210°; ir (potassium bromide): 3430, 2820, 2580 (COOH), 1700 (CO); ¹H-nmr (DMSO-d₆): 12.83 (s, 1H, OH), 7.83 (s, 1H, H5), 7.30 (m, 4H, ArH), 3.30 (s, 2H, CH₂), 1.20 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₆H₁₄FNO₃S: C, 60.17; H, 4.41; N, 4.38; S, 10.04. Found: C, 60.27; H, 4.46; N, 4.42; S, 10.20.

N-[2-Carboxy-4-(4-chlorophenyl)thien-3-yl]-3,3-dimethylaze-tidin-2-one (4b).

This compound was obtained by the procedure described for compound **4a** as colorless crystals (79%), mp 200° (acetonitrile); ir (potassium bromide): 3300, 2500, 2400 (COOH), 1730, 1690 (CO); ¹H-nmr (DMSO-d₆): 11.86 (s, 1H, NH), 7.86 (s, 1H, H5), 7.40 (q, 4H, ArH), 3.33 (s, 2H, CH₂), 1.23 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₆H₁₄ClNO₃S: C, 57.22; H, 4.20; N, 4.17; S, 9.54. Found: C, 57.34; H, 4.24; N, 4.22; S, 9.58.

N-[2-Carboxy-4-(4-anisyl)thien-3-yl]-3,3-dimethylazetidin-2-one (4c).

This compound was obtained by the procedure described for compound 4a as colorless crystals (81%), mp 120° (ether); ir (potassium bromide): 3300, 2600, 2500 (COOH), 1700 (CO); ¹H-nmr (DMSO-d₆): 13.66 (s, 1H, NH), 7.83 (s, 1H, H5), 7.33 (d, 2H, ArH), 6.96 (d, 2H, ArH), 3.83 (s, 3H, OCH₃), 3.30 (s, 2H, CH₂), 1.30 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₇H₁₇NO₄S: C, 61.61; H, 5.17; N, 4.22; S, 9.67. Found: C, 61.80; H, 5.21; N, 4.36; S, 9.72.

N-[2-Carboxy-4-(2-thienyl)thien-3-yl]-3,3-dimethylazetidin-2-one (4d).

This compound was obtained by the procedure described for compound 4a as colorless crystals (86%), mp 134° (ethanol); ir (potassium bromide): 3340, 2600, 2500 (COOH), 1700 (CO); $^1\text{H-nmr}$ (DMSO-d₆): 12.50 (s, 1H, OH), 7.80 (s, 1H, H5), 7.56 (q, 1H, H5'), 7.24 (m, 2H, H3', H4'), 3.35 (s, 2H, CH₂), 1.25 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₁₄H₁₃NO₃S₂: C, 54.70; H, 4.26; N, 4.55; S, 20.86. Found: C, 54.84; H, 4.28; N, 4.61; S, 20.92.

N-[2-Carboxy-5-(4-chlorophenyl)thien-3-yl]-3,3-dimethylaze-tidin-2-one (4e).

This compound was obtained by the procedure described for compound 4a as colorless crystals (81%), mp 149° (acetonitrile); ir (potassium bromide): 3300, 2600, 2500 (COOH), 1690 (CO); ¹H-nmr (DMSO-d₆): 7.36 (q, 4H, ArH), 6.93 (s, 1H, H4), 5.83 (s, 1H, OH), 3.00 (s, 2H, CH₂), 1.13 (s, 6H, (CH₂)).

Anal. Calcd. for C₁₆H₁₄ClNO₃S: C, 57.22; H, 4.20; N, 4.17; S, 9.54. Found: C, 57.31; H, 4.18; N, 4.26; S, 9.61.

N-[2-Carboxy-5-(4-fluorophenyl)thien-3-yl]-3,3-dimethylazetidin-2-one (4f).

This compound was obtained by the procedure described for compound 4a as colorless crystals (79%), mp 110° (ether); ir (potassium bromide): 3320, 2600, 2500 (COOH), 1700 (CO); ¹H-nmr (DMSO-d₆): 12.06 (s, 1H, OH), 7.63, 7.20 (m, 4H, ArH), 7.03 (s, 1H, H4), 3.36 (s, 2H, CH₂), 1.06 (s, 6H, (CH₃)₂).

Anal. Caled. for C₁₆H₁₄FNO₃S: C, 60.17; H, 4.41; N, 4.38; S, 10.04. Found: C, 60.24; H, 4.46; N, 4.50; S, 10.24.

N-[2-Carboxy-5-(4-pyrrolidinophenyl)thien-3-yl]-3,3-dimethylazetidin-2-one (5).

A stirred solution of **3f**, 2.5 g (0.0074 mole) in pyrrolidine (30 ml) was refluxed for 6 hours. The mixture was stirred at room temperature for 2 hours. The precipitate product was filtered and recrystallized from acetonitrile to give **5**, yield 2.4 g, 84%, mp 190°; ir (potassium bromide): 1750, 1700 (CO); ¹H-nmr (DMSO-d₆): 7.66 (s, 1H, H4), 7.36, (d, 2H, ArH), 6.43 (d, 2H, ArH), 3.80 (s, 3H, CH₃), 3.63 (s, 2H, CH₂), 3.16, 1.90 (m, 8H, pyrrolidine), 1.26 (s, 6H, (CH₃)₂).

Anal. Calcd. for C₂₁H₂₄N₂O₃S: C, 65.59; H, 6.29; N, 7.28; S, 8.33. Found: C, 65.70; H, 6.31; N, 7.40; S, 8.50.

3-Methyl-2-(4-benzyl-1-methylpiperazinyl)-*N*-(benzhydryl)azetidin-2-one Dihydrochloride (**9a**).

General Procedure.

To a solution of 5 g (0.0167) of 3-chloromethyl-3-methyl-1-(benzhydryl)azetidin-2-one (8a) in 35 ml of dry N,N-dimethyl-formamide was added 1.77 g (0.0167 mole) of sodium carbonate and 2.93 g (0.0167 mole) of benzylpiperazine. The mixture was stirred at 160° for 1 hour. The solution was poured into ice/water (150 ml) and extracted with ethyl acetate (150 ml). The extract was dried (sodium sulfate), the solvent was removed under reduced pressure. The oil, 5.25 g (0.0119 mole, 72%), was dissolved in 2-propanol (30 ml) and (5 ml) hydrochloric acid and was converted to the dihydrochloride salt 9a as a white solid, 4.20 g, 69%, mp 165° (acetonitrile); ir (potassium bromide): 3400, 2600, 2500 (NH+), 1730 (CO); ¹H-nmr (DMSO-d₆): 7.50, 7.20 (m, 15H, ArH), 5.88. (s, 1H, CH), 3.96 (s, 2H, NH+, deuterium oxide exchangeable), 4.28, 3.40, 3.26 (m, 14H, (CH₂)₇), 1.33 (s, 3H, CH₃).

Anal. Calcd. for $C_{29}H_{35}Cl_2N_3O$: C, 67.95; H, 6.88; Cl, 13.83. Found: C, 68.10; H, 6.92; Cl, 14.05.

N-(4-Anisyl-2-methoxycarbonylthien-3-yl)-3-methyl-3-(4-benzylpiperazinomethyl)azetidin-2-one Dihydrochloride (9b).

This compound was prepared as described for 9a (35%), mp 188° (acetonitrile); ir (potassium bromide): 3320, 2600, 2500 (NH+), 1720 (CO); ¹H-nmr (DMSO-d₆): 7.98 (s, 1H, H5), 7.50, 7.42 (m, 9H, ArH), 4.82 (s, 2H, NH+, deuterium oxide exchangeable), 3.80 (s, 6H, OCH₃, COOCH₃), 4.30, 3.47, 3.20 (m, 14H, (CH₂)₇), 1.30 (s, 3H, CH₃).

Anal. Calcd. for C₂₉H₃₅Cl₂N₃O₄S: C, 58.77; H, 5.95; N, 7.09; S, 5.41. Found: C, 58.92; H, 5.99; N, 7.16; S, 5.59.

REFERENCES AND NOTES

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