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Intramolecular Amidoalkylation Cyclizations in Synthesis of Novel Pyrrolo(or Isoindolo)thieno[2]benzazepines

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Thieno[2]benzazepines annulated to pyrrole 8a,b or isoindole 8c have been synthesized utilizing the acid-catalyzed cyclization of hydroxylactams 7a-c as key step.

As a part of our program aimed at the synthesis of products which have most potent CNS activity, we have previously reported some thieno[2]azepinones annulated to isoindole [1] or pyrrolidine [2] rings. These compounds are structurally related to some natural isoindolo(or pyrrolo)benzazepine alkaloids: and derivatives [3] isolated from Chilean Berberidaceae, Berberis darwinii Hook and Taxus baccata [4]. On the other hand, it was found that prominent examples of structures which bear a benzazepine moiety such as pyridobenzazepinone [5], hexahydrodibenz[o,c]pyrazino[1,2-d]azepine [6] and trans-2,3,5,6,11,11a-hexahydro-6-phenyl-1H-pyrrolo[2,1-b][3]benzazepine [7], exhibit more significant clinical antidepressant effects. Furthermore, any number derivatives of dibenzo[c,e; b,e; b,f]azepines are known and display hypolipidermic activity [8], CNS activity [9], and antiarrhythmic activity [10], respectively. In view of our interest in the synthesis of diversely substituted polycyclic systems, we wish to report herein an interesting approach to thieno[2]benzazepines annulated to a pyrrolidinone moiety as 8a,b or annulated to an isoindole moiety as 8c.

We recently developed a method for the preparation of indolizidines annulated to both thiophene and benzene rings. The Heck reaction of aryl radical cyclization of suitable enamides was the key step [11]. From this result and in a similar manner we thought to arrive to the thieno[2]benzazepines 8a-c. Unfortunately, whereas the addition of a Grignard reagent (phenylmagnesium bromide) to the imide function of the reported phthalimide derivative 3c [1] gave the expected alcohol 4c (65%) (Scheme 1), no reaction was observed with the imides 3a,b. The resulting hydroxylactam 4c was reduced using triethylsilane in trifluoroacetic acid to afford lactam 5c in a good yield of 91% (Scheme 1).

As shown in Scheme 1, the lactam 5c was subjected to the usual radical cyclization conditions (2,2'-azobisisobutyronitrile, tributyltin hydride, toluene) without success. Likewise, an intramolecular Heck reaction did not give the expected
isoindolothieno[2]benzazepine 8c. These failures were similar to those reported in the literature for related compounds [12,13,14]. Nevertheless a partial success had been observed for cyclization, under the action of tri-\(n\)-butyltin hydride, of a non-conjugate enamide to a 7-membered ring [15].

![Scheme 1](image)

From these results we were then led to examine another approach using \(N\)-acyliminium-aromatic cyclization. Actually, heterocyclization involving \(N\)-acyliminium ions (intramolecular \(\alpha\)-amidoalkylation reaction) has been widely studied [16]. In this field, we recently presented our preliminary studies concerning the synthesis of dibenzo[c,e]azepines [17]. Our results were in accordance with the Baldwin's rules [18]. Since a 7-endo-trigonal ring forming process is favored rather than a 5-endo-trigonal one, the hydroxylactams 7a-c (Scheme 2) should lead to the thienobenzazepines 8a-c. \(N\)-acyliminium ion precursors 7a-c were obtained from phthalimide derivative 3c or succinimide derivatives 3a,b. The latter compounds were prepared by alkylation of the commercially available succinimide (2a) and tetramethylsuccinimide (2b) [19] with 2-bromo-3-bromomethylthiophene (1) [20] under
solid-liquid phase transfer catalysis using anhydrous potassium carbonate as base and a mixture of potassium iodide and 18-crown-6 as the catalysts [21].

A palladium(0) catalyzed cross-coupling of bromo derivatives 3a-c with phenylboronic acid provided the diaryl compounds 6a-c in high yields (95 to 98%). Reduction of imides 6a-c by sodium borohydride in anhydrous methanol and in the presence of acid, to avoid the formation of the opened amide-alcohol [2,22], afforded the hydroxylactams 7a-c (85 to 96%). Speckamp reported [22,23] that with succinimides bearing two relatively large substituents at a single carbon atom, the reduction did not need addition of acid. Likewise in the case of
tetramethylsuccinimide derivative 6b, in the absence of hydrochloric acid we have never observed the ring opened amide-alcohol.

Hydroxylactams 7a-c were then subjected to trifluoroacetic acid in dry dichloromethane at room temperature [11], and led exclusively to the thienobenzazepines 8a-c. This reaction provides a new example of N-acyliminium cyclization resulting in a nitrogen containing 7-membered ring. The structures of 8a-c were assigned on the basis of their mass, ir, and nmr (1H and 13C) spectra as well as by their microanalyses. Thus, the two protons of the thiophene ring appear as doublets (AB system) with a coupling constant of 5 Hz characteristic of α,β-substituted thiophene. Furthermore in the 1H nmr spectra of 8a-c the methylene protons (CH2-N) appear as an AB system due to the diastereotopic effect with a coupling constant of about 15 Hz characteristic of gem protons. Likewise, the key feature in the 13C nmr spectra of 8a-c was the appearance of ten signals for 8a and 8b and sixteen signals for 8c in the aromatic region. Moreover, one of these resonances disappears in the corresponding DEPT program spectra, as a consequence of the intramolecular amidoalkylation cyclization.

The present work shows a general methodology for the synthesis of biaryl(c,e)azepines annulated to an isoindole or pyrrolidinone moiety starting from hydroxylactams and according to the Baldwin's rules the cyclization process gives a 7-membered ring rather than a 5-membered ring.

EXPERIMENTAL

All melting points were determined using a Leitz heat plate apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer FT-IR paragon 1000 spectrometer. The nuclear magnetic resonance spectra (1H and 13C) were taken on a Bruker AC-200 (200 MHz) instrument in the solvent indicated. Chemical shifts values are reported in ppm from TMS as an internal reference and are given in δ units and the following abbreviations are used: s for singlet, d for doublet, dd for doublet of doublet, br for broad and finally m for multiplet. Elemental analyses were obtained in the microanalysis laboratory of the I.N.S.A at Rouen, F 76130 Mt-St-Aignan. Mass spectral measurements were recorded on an AEI MS 902 S Spectrometer. Thin layer chromatography was performed on precoated plates of silica gel 60F 254 (Merck) and the spots visualized using an ultraviolet lamp or iodine vapor. E. Merck silica gel
60F (70-300 mesh) was used for column chromatography. The starting materials 1, 2b and 3c were prepared according to known procedures [1,19,20].

General Procedure for \(N\)-alkylation of Halides 2a,b.

To a mixture of succinimide (2a) or tetramethylsuccinimide (2b) (10 mmoles) and 18-crown-6 (1% w/w) in dry toluene (15 ml) was added solid potassium carbonate (1.34 g, 11 mmoles) and 0.1 equivalent per mmole of potassium iodide. After stirring for 10 minutes, 2-bromo-3-bromomethylthiophene (1) (3.07 g, 12 mmoles) in dry toluene (10 ml) was added slowly dropwise over a period of 15 minutes. The mixture was then refluxed for 24 hours under nitrogen atmosphere and cooled. The heterogeneous solution was filtered over a short column of Celite which was washed with toluene (3 x 10 ml). The organic phase was evaporated in vacuo and the resulting crude solid was recrystallized from anhydrous ethanol.

1-(2'-Bromothien-3'-ylmethyl)succinimide (3a).

This product was isolated as colorless needles in 92% yield, mp 110°; \(R_f\) 0.87 (dichloromethane/acetone, 9:1); ir: \(\nu\) 2896 (CH), 1653 (C=O) \(\text{cm}^{-1}\); \(^1\)H nmr (deuteriochloroform): \(\delta\) 2.70 (s, 4H, 4H-succinimide), 4.62 (s, 2H, CH\(_2\)-N), 6.90 (d, 1H, \(J = 5.6\) Hz, \(H_4\)-thiophene), 7.16 (d, 1H, \(J = 5.6\) Hz, \(H_5\)-thiophene); \(^{13}\)C nmr (deuteriochloroform): \(\delta\) 28.0 (2CH\(_2\)), 36.4 (CH\(_2\)), 111.7 (C), 125.9 (CH), 128.3 (CH), 134.9 (C), 176.3 (2CO); ms: (EI) \(m/z\) 274 (M\(^+\)).


3,3,4,4-Tetramethyl-l-(2'-bromothien-3'-ylmethyl)succinimide (3b).

This product was obtained similarly from 1 and 2b in a yield of 85%, mp 66°; \(R_f\) 0.45 (chloroform/acetone, 9:1); ir: \(\nu\) 2942 (CH), 1677 (C=O) \(\text{cm}^{-1}\); \(^1\)H nmr (deuteriochloroform): \(\delta\) 1.10 (s, 12H, 4CH\(_3\)), 4.60 (s, 2H, CH\(_2\)-N), 7.64 (d, 1H, \(J = 5.6\) Hz, \(H_4\)-thiophene), 7.29 (d, 1H, \(J = 5.6\) Hz, \(H_5\)-thiophene); \(^{13}\)C nmr (deuteriochloroform): \(\delta\) 21.2 (4CH\(_3\)), 36.3 (CH\(_2\)), 46.8 (2C), 116.6 (C), 126.1 (CH), 127.6 (CH), 135.2 (C), 181.1 (2CO); ms: (EI) \(m/z\) 330 (M\(^+\)).

Anal. Calcd. for C\(_{13}\)H\(_{10}\)BrNO\(_2\)S (330.24): C, 47.28; H, 4.88; N, 4.24. Found: C, 47.12; H, 4.69; N, 4.15.

2,3-Dihydro-3-hydroxy-3-phenyl-2-(2'-bromothien-3'-ylmethyl)-lH-isouindol-1-one (4c).

To a stirred solution of (2'-bromothien-3'-ylmethyl)-1-phthalamide (3c) (3.23 g, 10 mmoles) in 100 ml of dry dichloromethane was added dropwise over a period of 10 minutes 3.63 g (20
mmoles) of phenylmagnesium bromide (prepared by classical procedure from magnesium (0.535 g, 22 g-atoms) and phenyl bromide (3.14 g, 20 mmoles) in dry tetrahydrofuran). After 3 hours of reaction at room temperature, the reaction mixture was poured into a solution of 20% ammonium chloride (100 ml) and decanted. The organic phase was washed with water, brine, dried over magnesium sulfate and concentrated in vacuo. The resulting solid was purified by chromatography on silica gel column eluting with dichloromethane/hexane (9:1) ($R_f$ 0.78) to isolate ω-carbinol lactam 4c as white crystals in a yield of 65%, mp 182°; ir: ν 3270 (br, O-H), 1667 (C=O) cm$^{-1}$; $^1$H nmr (deuteriochloroform): δ 3.30 (s, 1H, O-H), 4.16 (d, 1H, J = 15.3 Hz, CH$_2$-N), 4.57 (d, 1H, J = 15.3 Hz, CH$_2$-N), 6.88 (d, 1H, J = 5.6 Hz, H$_4$-thiophene), 7.03 (d, 1H, J = 5.6 Hz, H$_5$-thiophene), 7.17-7.32 (m, 6H, 6H-benzene), 7.41-7.49 (m, 2H, 2H-benzene), 7.74-7.82 (m, 1H, 1H-benzene); $^{13}$C nmr (deuteriochloroform): δ 36.9 (CH$_2$), 90.5 (C), 109.1 (C), 122.7 (CH), 122.9 (CH), 125.9 (2CH), 126.1 (CH), 127.9 (CH), 128.1 (2CH), 128.6 (CH), 129.2 (CH), 130.2 (C), 132.7 (CH), 137.9 (C), 139.4 (C), 149.7 (C), 166.9 (CO); ms: (EI) m/z 400 (M$^+$).

Anal. Calcd. for C$_{19}$H$_{14}$BrN$_2$O$_2$S (400.29): C, 57.01; H, 3.53; N, 3.50. Found: C, 56.97; H, 3.40; N, 3.39.

2,3-Dihydro-3-phenyl-2-(2′-bromothien-3′-ylmethyl)-1H-isooindol-1-one (5c).

A solution of 4c (4.1 g, 10.24 mmoles) in a mixture of 10 ml of trifluoroacetic acid and 20 ml of dry dichloromethane was stirred under an atmosphere of nitrogen and cooled in an ice bath. The solution was treated with 1.2 g (10.3 mmoles) of triethylsilane, added over a period of 5 minutes. After removal of this ice bath, the stirring was continued for 1 hour. The mixture was then poured into ice-water, made alkaline by the addition of ammonia and extracted with dichloromethane. The extracts were combined, dried and evaporated in vacuo. The oily residue was purified by flash chromatography on silica gel column eluting with dichloromethane/ligroin (9:1) ($R_f$ 0.82) to isolate ω-carbinol lactam 5c as orange crystals in a yield of 94%, ir (neat): ν 3070 and 2958 (CH), 1697 (C=O) cm$^{-1}$; $^1$H nmr (deuteriochloroform): δ 3.97 (d, 1H, J = 15.1 Hz, CH$_2$-N), 5.07 (d, 1H, J = 15.1 Hz, CH$_2$-N), 5.25 (s, 1H, CH), 6.87 (d, 1H, J = 5.6 Hz, H$_4$-thiophene), 7.03-7.17 (m, 6H, 1H$_3$-thiophene and 5H-benzene), 7.27-7.33 (m, 2H, 2H-benzene), 7.8-7.9 (m, 2H, 2H-benzene); $^{13}$C nmr (deuteriochloroform): δ 33.2 (CH$_2$), 64.1 (CH), 111.2 (C), 123.1 (CH), 123.6 (CH), 126.2 (CH), 127.6 (2CH), 128.2 (CH), 128.6 (2CH), 128.9 (2CH), 130.9 (C), 131.9 (CH), 136.5 (C), 136.7 (C), 146.4 (C), 168.6 (CO); ms: (EI) m/z 384 (M$^+$).
General Procedure for Synthesis of Diarylimides 6a,b,c.

To a stirred solution of N-alkylated imide 3a, 3b or 3c (20.6 mmoles) in dimethyl ether (40 ml) under dry nitrogen was added slowly by portions tetrakis(triphenylphosphine)palladium (0.72 g, 0.6 mmole). After 30 minutes of reaction a solution of anhydrous potassium carbonate (2.85 g, 20.6 mmoles) in water (20 ml) and phenyl boronic acid (3.02 g, 24.8 mmoles) were added to the mixture which was then boiled under reflux. After 24 hours of reaction, the solvent was evaporated in vacuo and the aqueous solution was extracted with dichloromethane. Drying and evaporation of the extract gave a brown solid which was purified by flash chromatography on silica gel column (ethyl acetate/hexane).

1-(2'-Phenylthien-3'-ylmethyl)succinimide (6a).

This compound was isolated as a white solid by crystallization from diethyl ether in 98% yield, mp 98°; Rf 0.55 (ethyl acetate/diethyl ether, 3:1); ir: υ 2899 (CH), 1592 (C=O) cm\(^{-1}\); \(^1\)H nmr (deuteriochloroform): δ 2.60 (s, 4H, 4H-succinimide), 4.70 (s, 2H, CH\(_2\)-N), 6.95 (d, 1H, J = 5.4 Hz, H\(_4\)-thiophene), 7.22 (d, 1H, J = 5.4 Hz, H\(_5\)-thiophene), 7.35-7.45 (m, 3H, 3H-benzene), 7.61-7.72 (m, 2H, 2H-benzene); \(^13\)C nmr (deuteriochloroform): δ 28.1 (2CH\(_2\)), 36.5 (CH\(_2\)), 124.6 (CH), 127.9 (CH), 128.3 (CH), 128.4 (CH), 128.7 (CH), 129.2 (CH), 129.7 (CH), 131.2 (C), 133.4 (C), 140.9 (C), 176.3 (2CO); ms: (EI) m/z 271 (M\(^+\)).


3,3,4,4-Tetramethyl-1-(2'-phenylthien-3'-ylmethyl)succinimide (6b).

This product was obtained in the same manner from 3b in 96% yield, mp 92° (ethanol/diethyl ether); Rf 0.82 (ethyl acetate/diethyl ether, 4:1); ir: υ 2909 (CH), 1683 (C=O) cm\(^{-1}\); \(^1\)H nmr (deuteriochloroform): δ 2.67 (s, 12H, 4CH\(_3\)), 4.60 (s, 2H, CH\(_2\)-N), 6.87 (d, 1H, J = 5.4 Hz, H\(_4\)-thiophene), 7.18 (d, 1H, J = 5.4 Hz, H\(_5\)-thiophene), 7.22-7.37 (m, 3H, 3H-benzene), 7.39-7.71 (m, 2H, 2H-benzene); \(^13\)C nmr (deuteriochloroform): δ 21.2 (4CH\(_3\)), 36.2 (CH\(_2\)), 46.7 (2C), 124.6 (CH), 127.7 (CH), 127.8 (CH), 128.5 (CH), 129.6 (CH), 131.6 (C), 131.9 (CH), 132.1 (CH), 133.4 (C), 140.9 (C), 182.5 (2CO); ms: (EI) m/z 327 (M\(^+\)).

Anal. Calcd. for C\(_{19}\)H\(_{21}\)NO\(_2\)S (327.44): C, 69.69; H, 6.46; N, 4.28. Found: C, 69.51; H, 6.30; N, 4.11.

2-(2'-Phenylthien-3'-ylmethyl)phthalimide (6c).
This product was obtained in the same manner from 3c in a yield of 95%, mp 157°; Rf 0.70 (dichloromethane/diethyl ether, 4:1); ir: v 3085 and 2909 (CH), 1703 (C=O) cm$^{-1}$; $^1$H nmr (deuteriochloroform): $\delta$ 4.85 (s, 2H, CH$_2$-N), 7.00 (d, 1H, J = 5.4 Hz, H$_4$-thiophene), 7.16 (d, 1H, J = 5.4 Hz, H$_5$-thiophene), 7.25-7.50 (m, 3H, 3H-benzene), 7.52-7.61 (m, 2H, 2H-benzene), 7.63-7.70 (m, 2H, 2H-phthalimide), 7.71-7.80 (m, 2H, 2H-phthalimide); ms: (EI) m/z 319 (M$^+$).

Anal. Calcd. for C$_{19}$H$_{13}$N$_2$O$_2$S (319.37): C, 71.45; H, 4.10; N, 4.39. Found: C, 71.31; H, 4.00; N, 4.22.

General Procedure for Reduction of Imides 6a,b,c.

To a stirred solution of N-alkylated imide 6a, 6b or 6c (12.6 mmoles) in dry methanol (15 ml) was added slowly in portions sodium borohydride (2.83 g, 75 mmoles) at -5-0° over a period of 10 minutes. While the temperature was kept at -5-0°, 2N hydrochloric acid solution in dry ethanol (3 drops) was added to the reaction mixture at regular intervals of 10 minutes during 3 hours. The excess of sodium borohydride was destroyed by adding cold water (10 ml) then a solution of 10% hydrochloric acid in dry ethanol at 0-5° to pH 3. After removal of the solvent, the residue was diluted with water (45 ml) and extracted with dichloromethane. The organic layers were washed with saturated brine, dried over sodium sulfate and evaporated in vacuo. The oily residue after trituration with diethyl ether was recrystallized from ethanol to give o-carbinol lactams 7a, 7b or 7c.

1-(2'-Phenylthien-3'-ylmethyl)succinamidal (7a).

This product was obtained as yellow crystals in 85% yield, mp 148°; Rf 0.75 (dichloromethane/acetone, 9:1); ir: v 3345 (br, O-H), 1662 (C=O) cm$^{-1}$; $^1$H nmr (deuteriochloroform): $\delta$ 0.75-0.95 (m, 1H, 1H-pyrrolidinone), 1.13-2.22 (m, 1H, 1H-pyrrolidinone), 1.62-1.93 (m, 1H, 1H-pyrrolidinone), 1.97-2.21 (m, 1H, 1H-pyrrolidinone), 3.78 (d, 1H, J = 15 Hz, CH-N), 3.76-3.81 (m, 1H, 1H-pyrrolidinone), 4.91 (d, 1H, J = 15 Hz, CH$_2$-N), 6.82 (d, 1H, J = 5.4 Hz, H$_4$-thiophene), 7.07 (d, 1H, J = 5.4 Hz, H$_5$-thiophene), 7.09 (d, 1H, J = 7.8 Hz, 1H-benzene), 7.30-7.35 (m, 4H, 4H-benzene); $^{13}$C nmr (deuteriochloroform): $\delta$ 25.5 (CH$_2$), 28.4 (CH$_2$), 36.3 (CH$_2$), 88.4 (CH), 125.3 (CH), 128.1 (CH), 128.4 (CH), 128.8 (2CH), 129.6 (2CH), 132.1 (C), 133.1 (C), 140.9 (C), 174.2 (CO); ms: (EI) m/z 273 (M$^+$).


3,3,4,4-Tetramethyl-1-(2'-phenylthien-3'-ylmethyl)succinamidal (7b).
This compound was isolated after 24 hours of reaction at room temperature from 6b as colorless solid in 96% yield, mp 154°C; Rₚ 0.66 (dichloromethane/hexane, 9:1); IR: ν 3224 (br, OH), 1651 (C=O) cm⁻¹; ¹H NMR (deuteriochloroform): δ 0.77 (s, 3H, CH₃), 0.87 (s, 3H, CH₃), 0.92 (s, 3H, CH₃), 1.11 (s, 3H, CH₃), 4.31 (d, 1H, J = 15 Hz, CH₂-N), 4.33–4.36 (m, 1H, 1H-pyrrolidinone), 4.82 (d, 1H, J = 15 Hz, CH₂-N), 6.96 (d, 1H, J = 5.2 Hz, H₄-thiophene), 7.21 (d, 1H, J = 5.2 Hz, H₅-thiophene), 7.35–7.42 (m, 4H, 4H-benzene), 7.56–7.62 (m, 1H, 1H-benzene); ¹³C NMR (deuteriochloroform): δ 17.2 (CH₃), 19.3 (CH₃), 23.2 (CH₃), 23.6 (CH₃), 37.3 (CH₂), 42.3 (C), 45.8 (C), 88.2 (CH), 124.7 (CH), 128.0 (CH), 128.8 (2CH), 129.1 (CH), 129.4 (2CH), 132.7 (C), 133.5 (C), 140.8 (C), 178.5 (CO); MS: (EI) m/z 329 (M⁺).


2,3-Dihydro-3-hydroxy-2-(2'-phenylthien-3'-ylmethyl)-1H-isindol-1-one (7c).

This compound was isolated as a white solid in 96% yield, mp 155°C; Rₚ 0.66 (dichloromethane/hexane, 9:1); IR: ν 3313 (br, OH), 1658 (C=O) cm⁻¹; ¹H NMR (deuteriochloroform): δ 2.73 (d, 1H, J = 10.8 Hz, OH), 4.42 (d, 1H, J = 15.1 Hz, CH₂-N), 4.88 (d, 1H, J = 15.1 Hz, CH₂-N), 5.55 (d, 1H, J = 10.8 Hz, 1H-isooindole), 6.95 (d, 1H, J = 5.1 Hz, H₄-thiophene), 7.19 (d, 1H, J = 5.1 Hz, H₅-thiophene), 7.30–7.55 (m, 8H, 8H-benzene), 7.56 (d, 1H, J = 7 Hz, 1H-benzene); MS: (EI) m/z 321 (M⁺).

Anal. Calcd. for C₁₉H₁₅N₂O₂S (321.39): C, 71.01; H, 4.70; N, 4.36. Found: C, 70.92; H, 4.55; N, 4.29.

General Procedure for the Synthesis of Pyrrolo(or isoindolo)thienobenzazepines 8a, 8b and 8c.

To a stirred solution of hydroxylactam 7a, 7b or 7c (2 mmoles) in dichloromethane (50 ml) was added trifluoroacetic acid (6 ml). After 24 hours of reaction at room temperature, the reaction mixture was diluted with water (50 ml) and neutralized with an aqueous 10% sodium hydroxide solution. The organic layer was separated, washed with water (50 ml), dried over magnesium sulfate and concentrated in vacuo to give after flash chromatography (silica gel; dichloromethane/hexane, 9:1) and recrystallization from suitable solvent the expected tetracyclic products 8a-c.


This product was obtained as a white solid in 80% yield, mp 128°C (ethanol); Rₚ 0.74 (chloroform/ligroin, 8:2); IR: ν 2894 (CH), 1673 (C=O) cm⁻¹; ¹H NMR (deuteriochloroform): δ
2.24-2.59 (m, 4H, 4H-pyrrolidinone), 3.74 (d, 1H, J = 14.5 Hz, CH₂-N), 4.51 (dd, 1H, J = 8 Hz and J = 13.6 Hz, 1H-pyrrolidinone), 4.55 (d, 1H, J = 14.5 Hz, CH₂-N), 7.03 (d, 1H, J = 5.2 Hz, H₄'-thiophene), 7.21-7.23 (m, 1H, 1H-benzene), 7.28 (d, 1H, J = 5.2 Hz, H₅'-thiophene), 7.35-7.49 (m, 3H, 3H-benzene); ¹³C nmr (deuteriochloroform): δ 22.6 (CH₂), 31.5 (CH₂), 39.7 (CH₂), 58.5 (CH), 125.3 (CH), 125.6 (CH), 128.1 (CH), 128.5 (CH), 128.9 (CH), 129.1 (CH), 133.9 (C), 134.7 (C), 135.1 (C), 139.8 (C), 173.1 (CO); ms: (EI) m/z 255 (M⁺).

Anal. Calcd. for C₁₅H₁₃NOS (255.33): C, 70.59; H, 5.13; N, 5.49. Found: C, 70.34; H, 5.05; N, 5.29.

2,3,3a,11-Tetrahydro-2,2,3,3-tetramethylpyrrolo[2,1-a]thieno[3,2-d][2]benzazepin-1-one (8b).

This product was obtained similarly from 7b in a yield of 85%, mp 130° (ethanol); R₇ 0.85 (ethyl acetate/hexane, 9:1); ir: ν 2978 (CH), 1680 (C=O) cm⁻¹; ¹H nmr (deuteriochloroform): δ 0.19 (s, 3H, CH₃), 0.88 (s, 3H, CH₃), 0.91 (s, 3H, CH₃), 1.10 (s, 3H, CH₃), 3.73 (d, 1H, J = 14.2 Hz, CH₂-N), 4.96 (s, 1H, 1H-pyrrolidinone), 3.73 (d, 1H, J = 14.2 Hz, CH₂-N), 7.03 (d, 1H, J = 5.2 Hz, H₄'-thiophene), 7.13 (d, 1H, J = 5.2 Hz, H₅'-thiophene), 7.28-7.33 (m, 2H, 2H-benzene), 7.50-7.55 (m, 2H, 2H-benzene); ¹³C nmr (deuteriochloroform): δ 18.1 (CH₃), 18.8 (CH₃), 18.9 (CH₃), 20.6 (CH₃), 38.5 (CH₂), 47.1 (C), 47.4 (C), 72.4 (CH), 123.9 (CH), 126.6 (CH), 128.2 (CH), 128.5 (CH), 130.4 (CH), 130.8 (CH), 133.9 (C), 134.2 (C), 138.2 (C), 139.7 (C), 177.9 (CO); ms: (EI) m/z 311 (M⁺).

Anal. Calcd. for C₁₉H₂₁NOS (311.44): C, 73.27; H, 6.80; N, 4.50. Found: C, 73.18; H, 6.59; N, 4.22.

4,10b-Dihydroisoindolo[1,2-a]thieno[3,2-d][2]benzazepin-6-one (8c).

This product was obtained similarly from 7c in a yield of 88%, mp 241° (ethanol); R₇ 0.76 (dichloromethane/hexane, 9:1); ir: ν 2985 (CH), 1684 (C=O) cm⁻¹; ¹H nmr (deuteriochloroform): δ 4.07 (d, 1H, J = 15 Hz, CH₂-N), 5.20 (d, 1H, J = 15 Hz, CH₂-N), 5.60 (s, 1H, CH), 6.99-7.77 (m, 7H, 7H-benzene), 7.13 (d, 1H, J = 5 Hz, H₄'-thiophene), 7.38 (d, 1H, J = 5 Hz, H₅'-thiophene), 7.95 (d, 1H, J = 6 Hz, 1H-benzene); ¹³C nmr (deuteriochloroform): δ 40.4 (CH₂), 61.4 (CH), 123.9 (CH), 124.5 (CH), 125.6 (CH), 126.7 (CH), 128.2 (CH), 128.6 (CH), 128.9 (C), 129 (CH), 129.3 (CH), 131 (CH), 134 (C), 134.2 (C), 134.5 (C), 135 (C), 139.7 (C), 141.9 (CH), 166.4 (CO); ms: (EI) m/z 303 (M⁺).

REFERENCES AND NOTES


