AN APPROACH TOWARDS FUSED THIENO[3,2-*b*]PYRIDINES

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Abstract - A series of fused thieno[3,2-*b*]pyridines was prepared *via* the condensation of substituted 2-acetyl-3-aminothiophenes and acid anhydrides. In addition, selected examples of these compounds were prepared *via* an intramolecular Wittig reaction.

INTRODUCTION

Thieno[3,2-*b*]pyridine and its derivatives represent an important class of heterocyclic compounds. Their isosterism with the 4-quinolone ring system and the known antibacterial activity of some of them such as nalidixic acid,[1] enoxacin and cinoxacin,[2] resulted in developing a variety of methods for their syntheses.[3-7] The parent ring system has mainly been prepared *via* three routes using 3-substituted pyridine, 2-substituted thiophene or 3-substituted thiophene[3] and more recently 2,3- disubstituted thiophene.[4,5] Different derivatives have been prepared and tested for antibacterial activities[2] and as NADH models.[6,7] In the present work we describe an approach for the synthesis of fused thieno[3,2-*b*]pyridines in one step from 2-acetyl-3-aminothiophene, as well as the use of an intramolecular Wittig reaction in another approach for their syntheses.

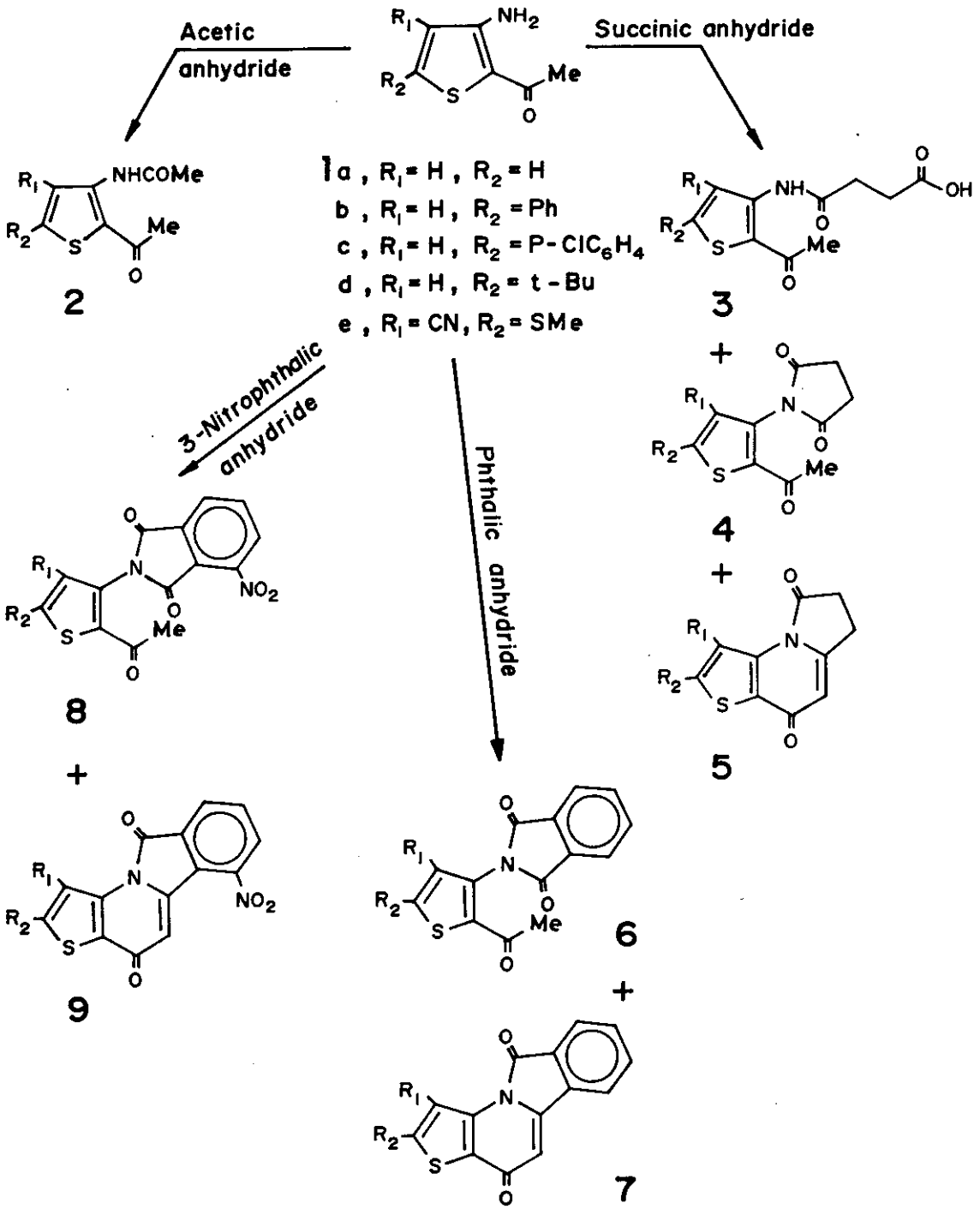
RESULTS AND DISCUSSION

In the first part of this paper, the cyclization of 2-acetyl-3-aminothiophenes with acid anhydrides is investigated. The substituted thiophenes (**1a-e**) were treated with acetic, succinic, phthalic and 3-nitrophthalic anhydrides

under basic conditions and the products of these reactions were identified (Scheme 1).

It was found that the type of product obtained in each case (whether an acid, amide, imide, or a thieno[3,2-*b*]-pyridine derivative) was dependent mainly on type of acid anhydride and to some extent on reaction conditions Acetic anhydride, when condensed with compounds **(1a-e)** under acetic acid or triethylamine conditions, gave the amides **(2a-d)**. None of the thieno[3,2-*b*]pyridines were obtained. The exception in this case was compound **(1e)** which did not react at all with acetic anhydride or in this sense with other acid anhydrides. Succinic anhydride, on the other hand, gave three types of products **(3, 4,** and **5)** depending on reaction conditions. When the reaction was conducted in solution (xylene, Et_3N), the succinamates **(3a-d)** were obtained as sole products. These compounds show absorbances for three carbonyl groups at δ 169 for the amide, δ 173-177 for the acid and at δ 192 for the ketone in their ^{13}C nmr spectra. Products of types **(4)** and **(5)** were obtained when the reaction was conducted without solvent. Compound **(4a)** was obtained as major product when compound **(1a)** and succinic anhydride were heated at 180 °C without solvent. Compound **(5)** was found in minor quantities in this case (another method for the preparation of this compound is discussed later in the text). The type of product obtained when compounds **(1a-d)** were condensed with phthalic anhydride was dependent to some extent on the type of substituents on the thiophene derivatives **(1a-d)** and as mentioned above, on reaction conditions. Compound **(1a)** gave compound **(6a)** as major product under both conditions used (1 ml, 7.17 mmol, of Et_3N, 125 °C and 3 ml, 21.52 ml of Et_3N, 140 °C), while compound **(7a)** was obtained in minor quantities under the latter conditions. Compound **(1b)** in contrast gave both compounds **(6b)** and **(7b)** depending on reaction conditions. The latter compound is obtained as major product when stronger basic condition and higher temperature were used, while the former is obtained using milder condition. These compounds were easily separated from each other under both conditions by fractional recrystallization (see Experimental). The major product crystallized first while the other one was obtained from the filterate. Similarly compounds **(6c)** and **(7c)** were obtained from compound **(1c)** except that the former was always the major product. Compound **(1d)** on the other hand gave only compound **(6d)** and none of compound **(7d)**. A major difference between compounds of types **6** and **7** in their nmr spectra was the disappearance of the absorbance of the methyl group of compound **(6)** and the appearance of a new one in the spectrum of compound **(7)** for C (10). This latter position appeared

Scheme 1


Acetic anhydride
Succinic anhydride
3-Nitrophthalic anhydride
Phthalic anhydride
1a , R1 = H , R2 = H
b , R1 = H , R2 = Ph
c , R1 = H , R2 = P-ClC6H4
d , R1 = H , R2 = t-Bu
e , R1 = CN, R2 = SMe
2
3
4
5
6
7
8
9

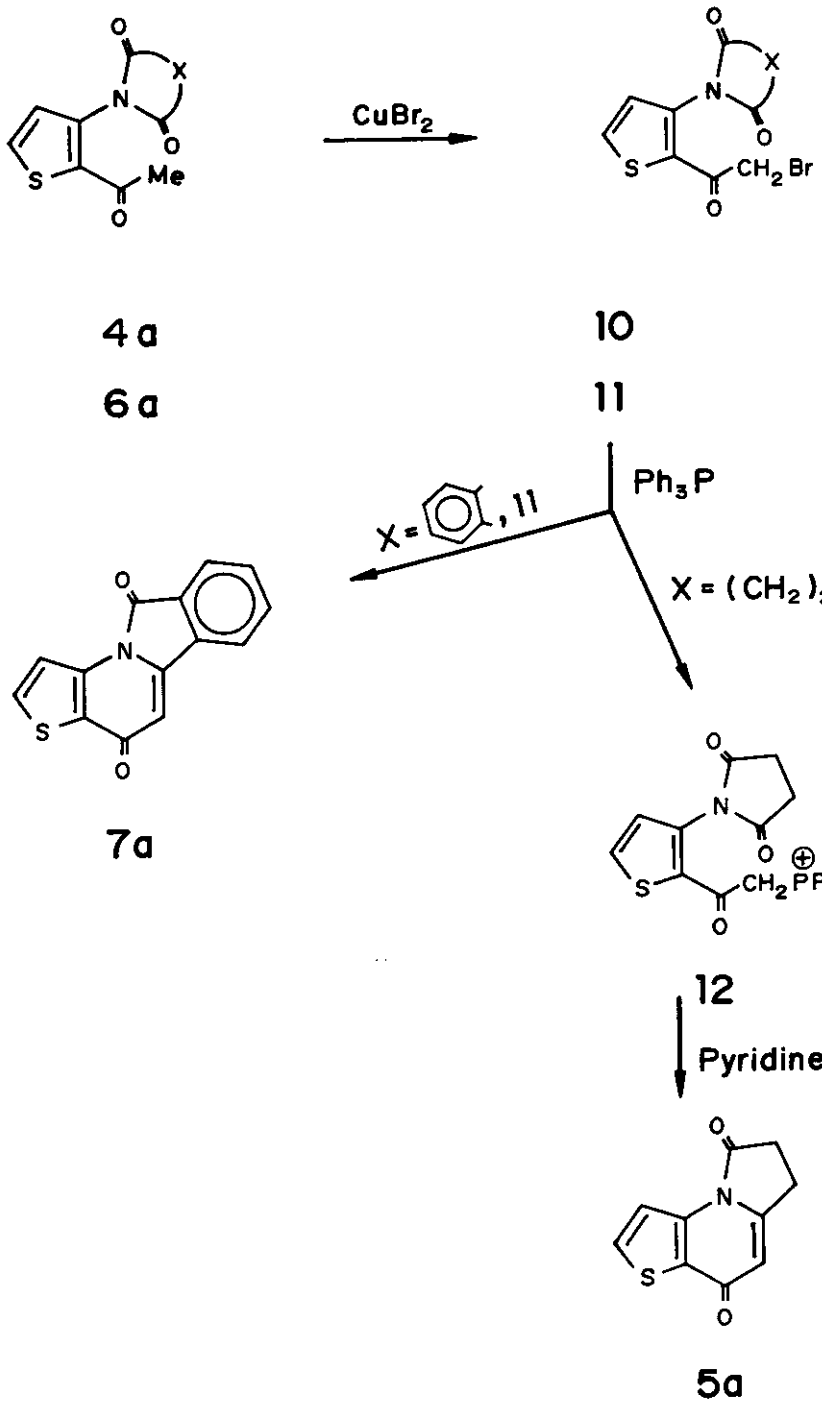
in the ^{1}H nmr spectrum at about δ 6.7-6.8 and in the ^{13}C nmr spectrum at about δ 107 which is in close agreement with previous studies on related compounds.[2]

Although the heterocyclic system thieno[3,2-*b*]pyridine and many of its fused derivatives are well known, to the best of our knowledge the heterocyclic system thieno[2,3:5,6]pyrido[2,1-*a*]isoindole has never been reported.

Finally when 3-nitrophthalic anhydride reacted with compounds **(1a-d)** products of types **(8)** and **(9)** were obtained with different ratios in each case. Compound **(1a)** gave a mixture of compounds **(8a)** and **(9a)** with the latter as major product while compounds **(1b)** and **(1c)** gave only the fused derivatives **(9b)** and **(9c)** respectively. In contrast, compound **(1d)** did not give any of the fused derivative **(9d)**, instead only **8d** was produced. It is probably worth mentioning here that although the reaction with 3-nitrophthalic anhydride could produce two isomers of the fused derivatives **(9a-c)** (the one shown in Scheme 1 and the other with the nitro group at 6-position), only one isomer was isolated under our conditions (see Experimental). The choosing of which isomer is produced was based upon a noticeable down field shift in the ^{1}H nmr absorption of the 10-position of these compounds when compared with their unsubstituted analogs **(7a-c)**. In the isomer shown in Scheme 1 the nitro group is in a place where a resonance is possible with position (10) which could explain the big down field shift. This shift is big enough not to be attributed only to the presence of the nitro group in these compounds. The isomer with the nitro group at the 6-position will not have this kind of resonance. This latter isomer was probably not produced because of the presence of some sort of steric interaction between the nitro group and the lactam carbonyl group.

In the second part of this paper we have used another approach for the synthesis of these fused thieno[3,2-*b*]pyridine derivatives. An intramolecular Wittig reaction was utilized for the conversion of the *N*-substituted imides to our target compounds. The imides **(4a)** and **(6a)** were chosen as examples in this case (Scheme 2). The bromination of compounds **(4a)** and **(6a)** with copper bromide afforded their bromo derivatives **(10)** and **(11)**, respectively. These latter compounds reacted with triphenylphosphine differently. Compound **(10)** when treated with triphenylphosphine gave the phosphonium salt **(12)**. The ^{1}H nmr spectrum of this compound showed a distinct doublet at δ 6.34 (J=14.6 Hz) for the CH_2 group. The treatment of compound **(12)** with pyridine and triethylamine afforded the cyclic compound **(5a)**. The carbonyl groups of this compound absorb in the ^{13}C nmr

Scheme 2



spectrum at δ 169.32 (lactam) and δ 172.21 (ketone) while the C(8) absorbs at δ 109.14. This latter position absorbs in the ^{1}H nmr spectrum as singlet at δ 6.29 while C-2 and C-3 protons appeared as two doublets (J=5.39 Hz) at δ 8.20 and δ 7.75, respectively. Compound **(11)** on the other hand did not give the expected phosphonium salt when reacted with triphenylphosphine. Instead, compound **(7a)** was obtained directly. The carbonyl groups of this compound appeared in the ^{13}C nmr spectrum at δ 160.32 (lactam) and δ 176.52 (ketone) while C(10) absorbed at δ 107.24.

EXPERIMENTAL

All melting points are uncorrected. Ir spectra were recorded on a Perkin-Elmer 883 spectrophotometer as KBr pellets. Nmr spectra were recorded on a Jeol FX-100 (100 MHz) using TMS as an internal standard in the indicated solvents and reported in δ (ppm) values. Microanalysis was performed at KACST research laboratories.

***N*-[(2-Acetyl-3-thienyl)]acetamide (2a)**

To a solution of 2-acetyl-3-aminothiophene **(1a)** (1.00 g, 7.08 mmol) was added dropwise 2 ml (21.20 mmol) of acetic anhydride. The solution was heated at 90 °C for 3 h and then poured into iced water. The resulting solid was collected and recrystallized from water and ethanol. 84% yield (1.1 g), colorless solid, mp 104-105 °C. ^{1}H Nmr ($CDCl_3$): 2.23 (s, 3H), 2.50 (s, 3H), 7.45(d, J=5.1 Hz, 1H), 8.15 (d, J=5.1 Hz, 1H). ^{13}C Nmr: 24.6, 28.90, 122.90, 131.92, 135.50, 145.56, 168.33, 192.35. Anal. Calcd for $C_8H_9NO_2S$: C, 52.44; H, 4.95; N, 7.64. Found: C, 52.24; H, 4.83; N, 7.57.

***N*-[(2-Acetyl-5-phenyl-3-thienyl)]acetamide (2b)**

This compound was prepared analogously from 2-acetyl-3-amino-5-phenylthiophene **(1b)**. 85% yield, light yellow solid (water and ethanol), mp 108-110 °C. ^{1}H Nmr ($CDCl_3$): 2.24 (s, 3H), 2.50 (s, 3H), 7.44 (m, 3H), 7.65 (m, 2H), 8.40 (s, 1H). ^{13}C Nmr: 24.66, 28.89, 118.58, 126.27, 127.04, 129.10, 129.50, 132.85, 145.07, 50.36, 168.32, 192.76. Anal. Calcd for $C_{14}H_{13}NO_2S$: C, 64.84; H, 5.05; N, 5.40. Found: C, 64.95; H, 4.92; N, 5.58.

***N*-(2-Acetyl-5-(4-chlorophenyl)-3-thienyl))acetamide (2c)**

This compound was prepared analogously from 2-acetyl-3-amino-5-(4-chlorophenyl)thiophene **(1c)**. 88% yield, colorless solid (water and ethanol), mp 165-166 °C. ^{1}H Nmr ($CDCl_3$): 2.24 (s, 3H), 2.50 (s, 3H), 7.40 (d, J= 8.8

Hz, 2H), 7.60 (d, J=8.8 Hz, 2H), 8.40 (s, 1H). ^{13}C Nmr: 24.72, 28.95, 118.93, 127.5, 129.38, 131.44, 135.67, 145.13, 168.45, 192.82. Anal. Calcd for $C_{14}H_{12}NO_2ClS$: C, 57.24; H, 4.12; N, 4.77. Found: C, 57.06; H, 4.03; N, 4.62.

***N*-[(2-Acetyl-5-t-butyl-3-thienyl)]acetamide (2d)**

This compound was prepared analogously from 2-acetyl-3-amino-5-*tert*-butylthiophene **(1d)**. 79% yield, colorless solid (water and ethanol), mp 71-73 °C. ^{1}H Nmr ($CDCl_3$): 1.40 (s, 9H), 2.20 (s, 3H), 2.44 (s, 3H), 7.98 (s, 1H). ^{13}C Nmr: 24.66, 28.73, 31.83, 35.47, 117.29, 118.18, 144.60, 165.34, 168.33, 192.88. Anal. Calcd for $C_{12}H_{17}NO_2S$: C, 60.22; H, 7.16; N, 5.85. Found: C, 60.07; H, 7.04; N, 5.66.

***N*-[(2-Acetyl-3-thienyl)]succinamate (3a)**

A solution of compound **(1a)** (1.00 g, 7.08 mmol), succinic anhydride (0.85 g, 8.50 mmol) and 1 ml (7.17 m mol) of Et_3N in xylene (200 ml) was refluxed for 5 h. The solvent was evaporated and the product was precipitated by the addition of ether (50 ml). 52% yield (0.88 g), yellow solid (ethanol), mp 120-121 °C. ^{1}H Nmr (DMSO-d_6): 2.47 (s, 3H), 2.57 (br s, 4H), 7.94 (s, 2H), 10.84 (br s, 1H). ^{13}C Nmr: 28.89, 31.42, 119.87, 122.22, 133.56, 143.31, 169.91, 173.55, 192.64. Ir (ν, cm^{-1}): 3350 - 2500, 1714, 1695, 1605, 1563, 1415. Anal. Calcd for $C_{10}H_{11}NO_4S$: C, 49.78; H, 4.60; N, 5.81. Found: C, 49.92; H, 4.48; N, 5.67.

***N*-[(2-Acetyl-5-phenyl-3-thienyl)]succinamate (3b)**

This compound was obtained analogously from compound **(1b)**. 78% yield, yellow solid (ethanol), mp 174-176 °C. ^{1}H Nmr ($CDCl_3$): 2.50 (s, 3H), 2.75 (s, 4H), 7.43 (m, 3H), 7.69 (m, 2H), 8.44 (s, 1H), 11.16 (br s, 1H). ^{13}C Nmr: 28.8, 32.01, 118.64, 126.21, 129.01, 129.50, 132.85, 144.89, 169.97, 174.43, 192.85. Ir (ν, cm^{-1}): 3800-2600, 1712, 1690, 1610, 1557, 1420. Anal. Calcd for $C_{16}H_{15}NO_4S$: C, 60.55; H, 4.76; N, 4.41. Found: C, 60.31; H, 4.84; N, 4.57.

***N*-[(2-Acetyl-5-(4′-chlorophenyl)-3-thienyl)]succinamate (3c)**

This compound was obtained analogously from compound **(1c)**. 68% yield, yellow solid (ethanol), mp 223-224 °C. ^{1}H Nmr ($CDCl_3$ - DMSO-d_6): 2.50 (s, 3H), 2.75 (s, 4H), 7.35 (m, 2H), 7.55 (m, 2H), 8.42 (s, 1H), 11.13 (br s, 1H). ^{13}C Nmr: 28.70, 31.63, 118.73, 126.83, 129.58, 132.65, 135.61, 144.93, 169.89, 175.32, 192.76. Ir (ν, cm^{-1}): 3300-2550, 1717, 1691, 1621, 1560, 1430. Anal. Calcd for $C_{16}H_{14}NO_4ClS$: C, 54.62; H, 4.01; N. 3.98. Found: C. 54.45; H. 4.13; N. 3.78.

***N*-[(2-Acetyl-5-t-butyl-3-thienyl)]succinamate (3d)**

This compound was obtained analogously from compound **(1d)**. 72% yield, colorless solid (ethanol), mp 160-162 °C. ^{1}H Nmr ($CDCl_3$): 1.39 (s, 9H), 2.44 (s, 3H), 2.76 (s, 4H), 7.96 (s, 1H), 11.19 (br s, 1H). ^{13}C Nmr: 28.78, 31.60, 31.83, 35.47, 117.35, 118.34, 144.25, 165.87, 169.62, 177.19, 192.99. Ir (ν, cm^{-1}): 3300- 2600, 1717, 1691, 1620, 1566, 1438. Anal. Calcd for $C_{14}H_{19}NO_4S$: C, 56.55; H, 6.44; N, 4.71. Found: C, 56.73; H, 6.25; N, 4.85.

***N*-[(2-Acetyl-3-thienyl)]-2,5-pyrrolidinedione (4a)**

A mixture of compound **(1a)** (1.00 g, 7.08 mmol) and succinic anhydride (0.85 g, 8.50 mmol) was heated at 185 °C for 6 h. The resulting solid was purified over silica gel *tlc* plates using $CHCl_3$ as solvent. 46% yield (0.72 g), colorless solid, mp 66-68 °C. ^{1}H Nmr ($CDCl_3$): 2.50 (s, 3H), 2.91 (s, 4H), 7.05 (d, J=5.13 Hz, 1H), 7.60 (d, J= 5.13 Hz, 1H). ^{13}C Nmr: 28.83, 29.30, 118.22, 128.39, 129.68, 132.44, 135.65, 175.55, 188.71. Anal. Calcd for $C_{10}H_9NO_3S$: C, 53.80; H, 4.06; N, 6.27. Found: C, 53.52; H, 4.16; N, 6.10.

***N*-[(2-Acetyl-3-thienyl)]phthalimide (6a)**

A mixture of compound **(1a)** (1.00 g, 7.08 mmol) and phthalic anhydride (1.15 g, 7.79 mmol) was refluxed for 6 h in xylene (200 ml) in the presence of 3 ml (21.52 mmol) of triethylamine. After evaporation of the solvent, ethanol was added and the resulting solid was collected and recrystallized from ethanol/ chloroform. 63% yield (1.20 g), light yellow solid, mp 132-133 °C. ^{1}H Nmr ($CDCl_3$): 2.48 (s, 3H), 7.15 (d, J=5.10 Hz, 1H), 7.60 (d, J=5.10 Hz, 1H), 7.75 (m, 2H), 7.90 (m, 2H). ^{13}C Nmr: 29.07, 123.98, 128.86, 129.57, 132.15, 134.44, 158.23, 170.11, 192.15. Anal. Calcd for $C_{14}H_9NO_3S$: C, 61.98; H, 3.34; N, 5.16. Found: C, 61.81; H, 3.45; N, 5.28.

***N*-[(2-Acetyl-5-phenyl-3-thienyl)]phthalimide (6b)**

A solution of compound **(1b)** (1.00 g, 4.60 mmol), phthalic anhydride (0.75 g, 5.06 mmol) and 1 ml (7.17 mmol) of triethylamine in xylene (200 ml) was heated at 125 °C for 8 h. After evaporation of the solvent, the resulting solid was recrystallized from ethanol. 45% yield (0.72 g), light yellow solid, mp 158-159 °C. ^{1}H Nmr ($CDCl_3$): 2.49 (s, 3H), 7.45 (m, 4H), 7.80 (m, 6H). Anal. Calcd for $C_{20}H_{13}NO_3S$: C, 69.15; H, 3.77; N, 4.03. Found: C, 69.27; H, 3.62; N, 3.91. Light yellow crystals precipitated from the filterate after two days which turned out to be compound **(7b)** (0.23 g, 15% yield).

2-Phenylthieno[2',3':5,6]pyrido[2,1-*a*]isoindole-5,11-dione (7b)

This compound was prepared using the procedure described above except that 3 ml of triethylamine were used and the temperature was 140 °C. Evaporation of the solvent and recrystallization of the resulting solid from chloroform afforded light yellow crystals **(7b)** (0.60 g, 40%), mp 199-200 °C. ^{1}H Nmr ($CDCl_3$-DMSO-d_6): 6.78 (s, 1H), 7.40 (m, 4H), 7.60 (m, 5H), 8.59 (s, 1H). Anal. Calcd for $C_{20}H_{11}NO_2S$: C, 72.93; H, 3.36; N, 4.25. Found: C, 72.51; H, 3.12; N, 4.45. From the filterate compound **(6b)** was obtained (0.35 g, 22% yield).

***N*-[(2-Acetyl-5-(4'-chlorophenyl)-3-thienyl)]phthalimide (6c)**

This compound was obtained from compound **(1c)** using the procedure described for compound **(6b)**. 43% yield, light yellow solid (ethanol and chloroform), mp 167-168 °C. ^{1}H Nmr ($CDCl_3$): 2.49 (s, 3H), 7.32 (s, 1H), 7.40 (d, J=9.04 Hz, 2H), 7.60 (d, J=9.04 Hz, 2H), 7.80 (m, 2H), 7.90 (m, 2H). Anal. Calcd for $C_{20}H_{12}NO_3ClS$: C, 62.91; H, 3.17; N, 3.67. Found: C, 63.05; H, 3.25; N, 3.49.

2-(4'-Chlorophenyl)thieno[2',3':5,6]pyrido[2,1-*a*]isoindole-5,11-dione (7c)

The filterate of the above experiment contained two compounds on *tlc*. The one with the lower R_f value was isolated over *tlc* silica gel plates with chloroform and identified as compound **(7c)** (the other one was compound **(6c)**; 18% yield, yellow solid (ethanol and chloroform), mp 182-183 °C. ^{1}H Nmr ($CDCl_3$): 6.75 (s, 1H), 7.40 (m, 4H), 7.65 (m, 4H), 8.52 (s, 1H). Anal. Calcd for $C_{20}H_{10}NO_2SCl$: C, 66.02; H, 2.77; N, 3.87. Found: C, 66.25; H, 2.63; N, 3.64.

***N*-[(2-Acetyl-5-t-butyl-3-thienyl)]phthalimide (6d)**

This compound was obtained from compound **(1d)** using the procedure described for compound **(6b)**. 38% yield, yellow solid (ethanol and chloroform), mp 139-142 °C. ^{1}H Nmr ($CDCl_3$): 1.44 (s, 9H), 2.43 (s, 3H), 6.91 (s, 1H), 7.81 (m, 2H), 7.90 (m, 2H). Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.04; H, 5.23; N, 4.28. Found: C, 66.28; H, 5.09; N, 4.11.

***N*-[(2-Acetyl-3-thienyl]-3-nitrophthalimide, (8a) and 9-nitrothieno[2',3':5,6]pyrido[2,1-*a*]isoindole-5,11-dione (9a)**

Compound **(1a)** (1.00 g, 7.09 mmol), 3-nitrophthalic anhydride (1.51 g, 7.81 mmol), and 3 ml (21.52 mmol) of triethylamine were refluxed in xylene (200 ml) for 6 h. The resulting solid was collected and recrystallized from

ethanol and chloroform to give compound **(9a)**. 63% yield (1.33 g), light yellow solid, mp 295-297 °C. ^{1}H Nmr (DMSO-d_6), 6.91 (s, 1H), 7.95(m, 2H), 8.16 (d, J=5.15 Hz, 1H), 8.30 (m, 2H). ^{13}C Nmr: 112.41, 118.41, 126.23, 129.80, 130.51, 133.33, 136.32, 149.17, 164.32, 173.53. Ir (ν, cm^{-1}): 3104, 1756, 1622, 1520, 1360. Anal. Calcd for $C_{14}H_6N_2O_4S$: C, 56.37; H, 2.03; N, 9.39. Found: C, 56.13; H, 1.85; N, 9.14. The recrystallization filterate contained two compounds, the one with the higher R_f value was purified over *tlc* silica gel plates with chloroform and identified as compound **(8a)**. 15% yield (0.34 g), yellow solid, mp 152-153 °C. ^{1}H Nmr ($CDCl_3$): 2.58 (s, 3H), 7.51 (d, J=5.10 Hz, 1H), 7.63 (d, J=5.10 Hz, 1H), 8.32 (m, 2H), 8.91 (m, 1H). ^{13}C Nmr: 28.89, 122.82, 123.06, 126.04, 130.04, 132.39, 132.69, 135.35, 148.27, 162.21, 193.80. Anal. Calcd for $C_{14}H_8N_2O_5S$: C, 53.16; H, 2.55; N, 8.86. Found: C,53.36; H, 2.44; N, 8.98.

9-Nitro-2-phenylthieno[2',3':5,6]pyrido[2,1-*a*]isoindole-5,11dione (9b)

This compound was prepared from compound **(1b)** using the procedure described for compound **(9a)**. 58% yield, yellow solid (ethanol and chloroform), mp 312-314 °C. ^{1}H Nmr (DMSO-d_6): 6.98 (s, 1H), 7.50 (m, 2H), 7.80 (m, 3H), 8.23 (s, 1H), 8.40 (m, 2H), 8.47 (m, 1H). Anal. Calcd for $C_{20}H_{10}N_2O_4S$: C, 64.16; H 2.69; N, 7.48. Found: C, 64.05; H, 2.59; N, 7.11.

2-(4'-Chlorophenyl)-9-nitrothieno[2',3':5,6]pyrido[2,1-*a*]isoindole- 5,11-dione (9c)

This compound was prepared analogously from compound **(1c)**. 55% yield, light yellow solid (ethanol and chloroform), mp 320-322 °C. ^{1}H Nmr (DMSO-d_6): 6.88 (s, 1H), 7.45 (s, 2H), 7.67 (m, 2H), 7.82 (m, 1H), 8.30 (m, 2H), 8.45 (s, 1H). ^{13}C Nmr: 109.12, 118.36, 127.32, 128.75, 137.11, 149.53, 150.61, 172.47, 183.18. Anal. Calcd for $C_{20}H_9N_2O_4SCl$: C, 58.76; H, 2.21; N, 6.85. Found: C, 58.53; H, 2.08; N, 6.61.

***N*-[(2-Acetyl-5-t-butyl-3-thienyl]-3-nitrophthalimide (8d)**

This compound was obtained from compound **(1d)** using the procedure described for compound **(6d)**. 32% yield (0.6 g), yellow solid (ethanol), mp 93-95 °C. ^{1}H Nmr ($CDCl_3$): 1.45 (s, 9H), 2.48 (s, 3H), 7.27 (s, 1H), 7.55 (m, 1H), 8.05 (m, 1H), 8.31 (m, 1H). ^{13}C Nmr: 28.71, 31.88, 35.58, 118.18, 126.75, 130.51, 131.98, 135.85, 143.96, 162.51, 165.85, 193.28. Anal. Clacd for $C_{18}H_{16}N_2O_5S$: C, 58.05; H, 4.33; N, 7.52. Found: C, 57.85; H, 4.23; N, 7.37.

***N*-[(2-Bromoacetyl)-3-thienyl]-2,5-pyrrolidinedione (10)**

To a refluxing suspension of $CuBr_2$ (2.20 g, 9.8 mmol) in ethyl acetate (80 ml) was added dropwise a solution of compound **(4a)** (1.00 g, 4.47 mmol) in chloroform (80 ml). The mixture was refluxed for 3 h or until a white precipitate was formed. The solid precipitates were filtered off and the filterate was washed with water and dried over magnesium sulfate. The solvent was evaporated and the resulting solid was recrystallized from ethanol. 64% yield (0.86 g), colorless solid, mp 151-152 °C. ^{1}H Nmr ($CDCl_3$): 2.93 (s, 4H), 4.31 (s, 2H), 7.12 (d, J=5.20 Hz, 1H), 7.67 (d, J=5.20 Hz, 1H). Anal. Calcd for $C_{10}H_8NO_3BrS$: C, 39.75; H, 2.67; N, 4.64. Found: C, 39.52; H, 2.54; N, 4.79.

(3-Succinimido-2-thienoyl)methyl triphenylphosphonium bromide (12)

A solution of compound **(10)** (0.50 g, 1.65 mmol) and triphenylphosphine (0.52 g, 1.98 mmol) in THF (150 ml) was refluxed for 5 h. The resulting solid was filtered and washed with THF. 68% yield (0.63 g), colorless solid, mp 217-219 °C. ^{1}H Nmr ($CDCl_3$): 2.92 (s, 4H), 6.34 (d, J=14.6 Hz, 2H), 7.07 (d, J=5.10 Hz, 1H), 7.70 (m, 16H). Anal. Calcd for $C_{28}H_{23}NO_3BrPS$: C, 59.58; H, 4.10; N, 2.48. Found: C, 59.23; H, 4.21; N, 2.29.

Pyrrolo[1,2-*a*]thieno[2,3-*e*]pyridine-5,9-dione (5a)

A solution of compound **(12)** (0.50 g, 0.885 mmol) in pyridine (50 ml) was refluxed in the presence of 1 ml (7.17 mmol) of triethylamine for 4 h. After evaporation of the solvent, water was added and the mixture was extracted with chloroform (100 ml x 3). The organic layer was dried over magnesium sulfate and then evaporated to dryness. The resulting solid was recrystallized from ethanol to give 0.092 g (51% yield) of light yellow crystals, mp 212-213 °C. ^{1}H Nmr ($CDCl_3$): 2.90 (m, 2H), 3.20 (m, 2H), 6.29 (s, 1H), 7.75 (d, J=5.39 Hz, 1H), 8.20 (d, J=5.39 Hz, 1H). ^{13}C Nmr: 23.1, 28.76, 109.14, 118.53, 132.86, 136.23, 154.56, 169.32, 172.21. Anal. Calcd for $C_{10}H_7NO_2S$: C, 58.52; H, 3.43; N, 6.82. Found: C, 58.61; H, 3.25; N, 6.51.

***N*-[(2-(Bromoacetyl)-3-thienyl]phthalimide (11)**

This compound was prepared from compound **(6a)** using the procedure described for compound **(10)**. 76% yield (0.98 g), colorless solid (ethanol), mp 192-193 °C. ^{1}H Nmr ($CDCl_3$): 4.30 (s, 2H), 7.21(d, J=5.15 Hz, 1H), 7.70 (d, J=5.15 Hz, 1H), 7.85 (m, 4H). ^{13}C Nmr: 32.90, 124.10, 128.98, 130.68, 131.57, 134.56, 135.87, 146.31, 171.32, 195.27. Anal. Calcd for $C_{14}H_8NO_3BrS$: C, 48.02; H, 2.30; N, 4.00. Found: C, 47.83; H, 2.41; N, 4.12.

Thieno[2',3':5,6]pyrido[2,1-*a*]isoindole-5,11-dione (7a)

A solution of compound **(11)** (0.50 g, 1.42 mmol) and triphenylphosphine (0.45 g, 1.72 mmol) in THF (200 ml) was refluxed for 7 h. The solvent was evaporated and the resulting solid was recrystallized from ethanol and chloroform. 56% yield (0.20 g), light greenish solid, mp 280-282 °C. ^{1}H Nmr ($CDCl_3$): 6.68 (s, 1H), 7.75 (s, 4H), 7.90 (d, J= 5.56 Hz, 1H), 8.16 (d, J=5.56 Hz, 1H). ^{13}C Nmr: 107.24, 118.46, 121.87, 125.74, 131.97, 134.38, 134.91, 141.74, 149.15, 160.32, 176.52. Anal. Calcd for $C_{14}H_7NO_2S$: C, 66.39; H, 2.78; N, 5.53. Found: C, 66.25; H, 2.54; N, 5.61.

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