A convenient synthesis of Carbocyclic fused Thieno [2,3-b] Pyridines and Carbocyclic fused 1H-Pyrazolo [3,4-b] Pyridines

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ABSTRACT

A synthesis of carbocyclic fused thieno [2,3-b] pyridines and carbocyclic fused 1H- pyrazolo [3,4-b] pyridines utilizing carbocyclic fused 2(1h)-pyridinethiones as starting components is described. The structures of the products were assigned and confirmed on the basis of their elemental analysis and spectral data.
We have described several novel syntheses of 2 (1H)-pyridinethiones. These compounds are considered important intermediates for the synthesis of the biologically active deazafloric acid and deazaaminopterine ring systems. One of these papers has described the novel reaction of cyanothioacetamid 1 with sodium salts of 2-(hydroxymethylene)-1-cycloalkanones 2 producing the carbocyclic fused 2(1H)-pyridinethiones. In conjunction with this work we report in this paper a novel synthesis of fused 1H-pyrazolo [3,4-b] pyridines and fused thieno [2,3-b] pyridines. The structure of compounds 5 was established and confirmed on the basis of elemental analysis and spectral data (IR, MS, 1H NMR). The IR spectra of compound 5 showed absence of a CN band, the mass spectrum was compatible with the molecular formula C17H14N2SO, and 1H NMR contained a broad band at δ 7.20 ppm assignable to an amino function. A 2-chloro derivative 6 corresponding to the cycloalkane ring fused 3-cyano 2-(ethylthio)pyridines. The structure of compounds 7 was established on the basis of elemental analysis and spectral data (IR, MS, 1H NMR). The IR spectra of compound 7 showed absence of a NH band.

Experimental

All melting points are uncorrected. IR spectra were obtained (KBr disc) on a Pye Unicam Spectra-1000 or on a Shimadzu IR 200 instrument. The mass spectra were recorded on a Varian MAT 112 spectrometer. Analytical data were obtained from the Microanalytical Data Centre at Cairo University.

Cycloalkane ring fused 3-cyano 2-(ethylthio) pyridines (4a-d):

A mixture of 3 (0.01 mol), NaOH (0.02 mol), and Etl (0.015 mol) in dry dichloromethane (50 ml) was stirred at room temperature for 24 h and then diuted with cold water (100 ml). The dichloromethane layer was washed several times with water, dried and then evaporated. The resulting solid product was collected by filtration and crystallized from the appropriate solvent.

4a: Yield (55%); m.p. 113°C; IR (KBr) ν 2220 (CN); 1H NMR (DMSO) δ 1.10 (t, 3H CHJ), 1.92 (m, 2H, CH2), 2.55-2.90 (m, 4H, 2CH2); 4.10 (q, 2H, CH2), 7.56 (s, H, pyridine H); (Calcd for C13H19N2S; C, 67.0; H, 7.3; N, 12.0). Found: C, 66.9; H, 7.5; N, 12.0%.

4b: Yield (40%); m.p. 89°C; IR (KBr) ν 2222 (CN); 1H NMR (DMSO) δ 1.02 (t, 3H CHJ), 1.52 - 1.75 (m, 6H, 3CH2), 2.50-2.77 (m, 2H, 2CH2); 400 (q, 2H, CH2), 7.58 (s, 1H, pyridine H-4); MS, m/e 218; (Calcd for C13H17N2S; C, 65.7; H, 6.8; N, 13.7. Found: C, 66.0; H, 6.5; N, 13.3%)

4c: Yield (33%); m.p. 92°C; IR (KBr) ν 2218 (CN); 1H NMR (DMSO) δ 1.11 (t, 3H CHJ), 1.38 - 1.77 (m, 6H, 3CH2), 2.40-2.75 (m, 2H, 2CH2); 2.80 - 2.95 (q, 2H, CH2), 3.99 (q, 2H, CH2), 7.88 (s, 1H, pyridine H-4); (Calcd for C13H19N2S; C, 67.0; H, 7.3; N, 12.0. Found: C, 67.0; H, 7.0; N, 12.0%).

4d: Yield (30%); m.p. 105°C; IR (KBr) ν 2228 (CN); 1H NMR (DMSO) δ 1.08 (t, 3H CHJ), 1.28 (m, 4H, 2CH2), 1.51 (s, 2H, 2CH2); 2.85 (m, 2H, CH2), 3.95 (q, 2H, CH2), 7.85 (s, 1H, pyridine H-4); (Calcd for C13H19N2S; C, 68.0; H, 7.7; N, 11.5. Found: C, 68.0; H, 7.5; N, 11.4%)

Cycloalkane ring-fused 3-amino-2-benzoylthiieno (2,3-b)-pyridines (5a-d):

A mixture of 3 (0.01 mol), C2H5ONa (0.02 mol), and phenacyl bromide (0.01 mol) in EtOH (50 ml) was...
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\begin{align*}
\text{1} & \quad \text{2} \\
\text{3} & \quad \text{4} \\
\text{5} & \quad \text{6} \\
\text{7} & \quad \text{d} \\
\end{align*}
\]

\[
\begin{array}{cccccccc}
4 & n & R & 5 & n & R & 3,6,7 & n \\
a & 3 & \text{CH}_3 & a & 3 & \text{COPh} & a & 3 \\
b & 4 & \text{CH}_3 & b & 4 & \text{COPh} & b & 4 \\
c & 5 & \text{CH}_3 & c & 5 & \text{COPh} & c & 5 \\
d & 6 & \text{CH}_3 & d & 6 & \text{COPh} & d & 6 \\
\end{array}
\]
stirred at 50-60°C for 3h and then diluted with cold water (50ml). The resulting solid product was collected by filtration and crystallized from the appropriate solvent.

5a: Yield (70%); m.p. 214-216°C; IR (KBr) v 3577, 3285 (NH); 'H NMR (DMSO) δ 1.90 (m, 2H CH2), 2.57-2.88 (m, 4H, 2CH2), 7.20 (s, 2H, NH); 7.32-7.82 (m, 5H, C6H5), 7.95 (s, H, pyridine H-4); MS, m/e 294; (Calcd for C12H10NS; C, 69.4; H, 4.8; N, 9.5. Found: C, 69.0; H, 5.1; N, 9.3%).

5b: Yield (80%); m.p. 202-03°C; IR (KBr) v 3520, 3440 (NH); 'H NMR (DMSO) δ 1.50-1.80 (m, 2H CH2), 2.00-2.77 (m, 2H, 2CH2), 7.21 (s, br, 2H, NH), 7.32-7.89 (s, 5H, C6H5), 7.8-8.4 (s, 1H, pyridine H-4); MS, m/e 308; (Calcd for C12H10NS; C, 69.4; H, 4.8; N, 9.5. Found: C, 70.0; H, 5.2; N, 8.8%).

5c: Yield (70%); m.p. 103-104°C; IR (KBr) v 3480, 3400 (NH); 'H NMR (DMSO) δ 1.40-1.78 (m, 6H 3CH3), 2.42-2.78 (m, 2H, 2CH2), 2.79-3.01 (m, 2H, CH3); 7.15 (s, br, 2H, NH), 7.28-7.68 (m, 5H, C6H5), 7.91 (s, 1H, pyridine H-4); Calcd for C12H10NSO: C, 70.8, H, 5.6, N, 8.7. F Found: C, 70.0; H, 5.2; N, 8.8%).

5cd: Yield (60%); m.p. 120-21°C; IR (KBr) v 3450, 3400 (NH); 'H NMR (DMSO) δ 1.30 (m, 4H 2CH2), 1.60 (s, 2H, CH2), 2.40 (m, 2H, CH3), 2.60 (s, 2H, CH2), 2.91 (m, 2H, CH2), 7.20 (s, br, 2H, NH), 7.28 - 7.80 (m, 5H, C6H5), 7.88 (s, 1H, pyridine H-4); Calcd for C12H10NSO: C, 71.4, H, 6.0; N, 8.3. Found: C, 71.0; H, 5.7; N, 8.0%).

Cycloalkane ring fused 2-chloro-3-cyanopyridines (6a-d):

A solution of 3 (0.01 mol) in chloroform (50ml) was stirred under a stream of dry chlorine gas for 2h, and then set aside overnight. The resultant precipitate was filtered off and crystallized from the appropriate solvent.

6a: Yield (55%); m.p. 167°C; IR (KBr) v 2220 (CN); 'H NMR (DMSO) δ 1.88 (m, 2H, CH2), 2.55-2.80 (m, 4H, 2CH2), 7.55 (s, 1H, pyridine H-4); MS m/e 178; (calcd for C10H9ClN; c, 60.5; H, 3.9, N, 15.7. Found: C, 60.1; H, 4.2; N, 15.5%).

6b: Yield (50%); m.p. 144°C; IR (KBr) v 2218 (CN); 'H NMR (DMSO) δ 1.65 (m, 2H, CH2), 1.80-1.89 (m, 4H, 2CH2), 2.55-2.70 (m, 2H, CH2), 7.8 (s, 1H, pyridine H-4); MS m/e 192; (calcd for C10H9ClN; c, 62.3; H, 4.7, N, 14.6. Found: C, 62.0; H, 5.0; N, 14.5%)

6c: Yield (60%); m.p. 112°C; IR (KBr) v 2230 (CN); 'H NMR (DMSO) δ 1.38-1.75 (m, 6H, 3CH3), 2.40-2.71 (m, 2H, CH2), 7.72-3.0 (m, 2H, CH2), 7.77 (s, 1H, pyridine H-4); (calcd for C12H12ClN; c, 63.9; H, 5.3, N, 13.6. Found: C, 64.0; H, 5.5; N, 13.5%).

6d: Yield (45%); m.p. 175°C; IR (KBr) v 2220 (CN); 'H NMR (DMSO) δ 1.28 (m, 4H, 2CH2), 1.62 (m, 2H, CH2), 238 (m, 2H, CH2), 2.58 (m, 2H, CH2), 7.80 (s, 1H, pyridine H-4); (calcd for C12H12ClN; c, 65.3; H, 5.9, N, 12.7. Found: C, 65.5; H, 5.6; N, 12.5%).

Cycloalkane ring fused 3-amino-1H-pyrazolo [3,4-b]pyridines (7a-d):

To a mixture of 4 or 6 (0.01 mol) and hydrazine hydrate (0.01 mol) in ethanol (50 ml), triethylamine (0.5 ml) was added. The mixture was heated under reflux for 3 h, and then allowed to stand overnight. The resultant precipitate was isolated by suction and crystallized from the appropriate solvent.

7a: Yield (40%); m.p. 250-252°C; IR (KBr) v 3570, 3380 (NH, NH); 'H NMR (DMSO) δ 1.85 (m, 2H, CH2), 2.50-2.82 (m, 4H, 2CH2), 5.28 (s, br, 2H, NH), 7.80 (s, 1H, pyridine H-4); 11.82 (s, br, 1H, NH); MS, m/e 174; (calcd for C13H11N5O: C, 62.1; H, 5.7, N, 32.2. Found: C, 62.0; H 5.5; N, 32.0%)

7b: Yield (56%), m.p. 201-203°C; IR (KBr) v 3435, 3279 (NH, NH); 'H NMR (DMSO) δ 1.43-1.80 (m, 6H, CH2), 2.50-2.72 (m, 2H, CH2), 5.21 (s, br, 2H, NH), 7.56 (s, 1H, pyridine H-4); 11.88 (s, br, 1H, NH); MS, m/e 188; (calcd for C13H11N5O: C, 63.8; H, 6.4, N, 29.8. Found: C, 63.6; H 6.1; N, 29.5%)

7c: Yield (60%), m.p. 156°C; IR (KBr) v 3480, 3450, 3300 (NH, NH); 'H NMR (DMSO) δ 1.48-1.73 (m, 6H, 3CH3), 2.45-2.70 (m, 2H, CH2), 2.70-2.92 (m, 2H, CH2), 5.13 (s, br, 2H, NH), 7.81 (s, 1H, pyridine H-4); 12.23 (s, br, 1H, NH); (calcd for C13H11N5O: C, 65.3; H, 6.9, N, 27.7. Found: C, 65.0; H 6.5; N, 27.5%)

7d: Yield (50%), m.p. 198-200°C; IR (KBr) v 3520, 3450, 3380 (NH, NH); 'H NMR (DMSO) δ 1.32 (m, 4H, 2CH2), 1.58 (m, 2H, CH2), 2.38 (m, 2H, CH2), 2.56 (m, 2H, CH2), 2.88 (m, 2H, CH2), 5.12 (s, br, 2H, NH); 7.80 (s, 1H, pyridine H-4); 11.98 (2, br, 1H, NH); (calcd for C13H11N5O: C, 66.7; H, 7.4, N, 25.9. Found: C, 66.6; H 7.1; N, 25.5%)
REFERENCES


