

1,3-Dipolar cycloaddition reactions of Munchnone and Sydnone derivatives obtained from 4,5,6,7-tetrahydrothieno(3,2-c)pyridine-4 and -6 carboxylic acids.

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Abstract - The 1,3-dipolar cycloaddition of dimethyl acetylenedicarboxylate with mesoionic munchnones and sydnones derived from 4,5,6,7-tetrahydrothieno(3,2-c)pyridine-4 and -6 carboxylic acids afforded respectively new ring-fused pyrroles and pyrazoles.

The conversion of secondary amino acids into pyrroles via intermediate mesoionic 1,3-oxazolium-5-olates (munchnones)¹ has been utilized in converting the "cyclic" amino acids, tetrahydro- β -carboline-1 and -3 carboxylic acids² and tetrahydroisoquinoline-1³ and -3⁴ carboxylic acids into novel ring-fused pyrroles. These reactions involved a 1,3-dipolar cycloaddition of the munchnone, behaving like a cyclic azomethine ylide⁵, to the corresponding acetylenic or olefinic dipolarophile followed by CO₂ evolution, and aromatization or tautomerization.

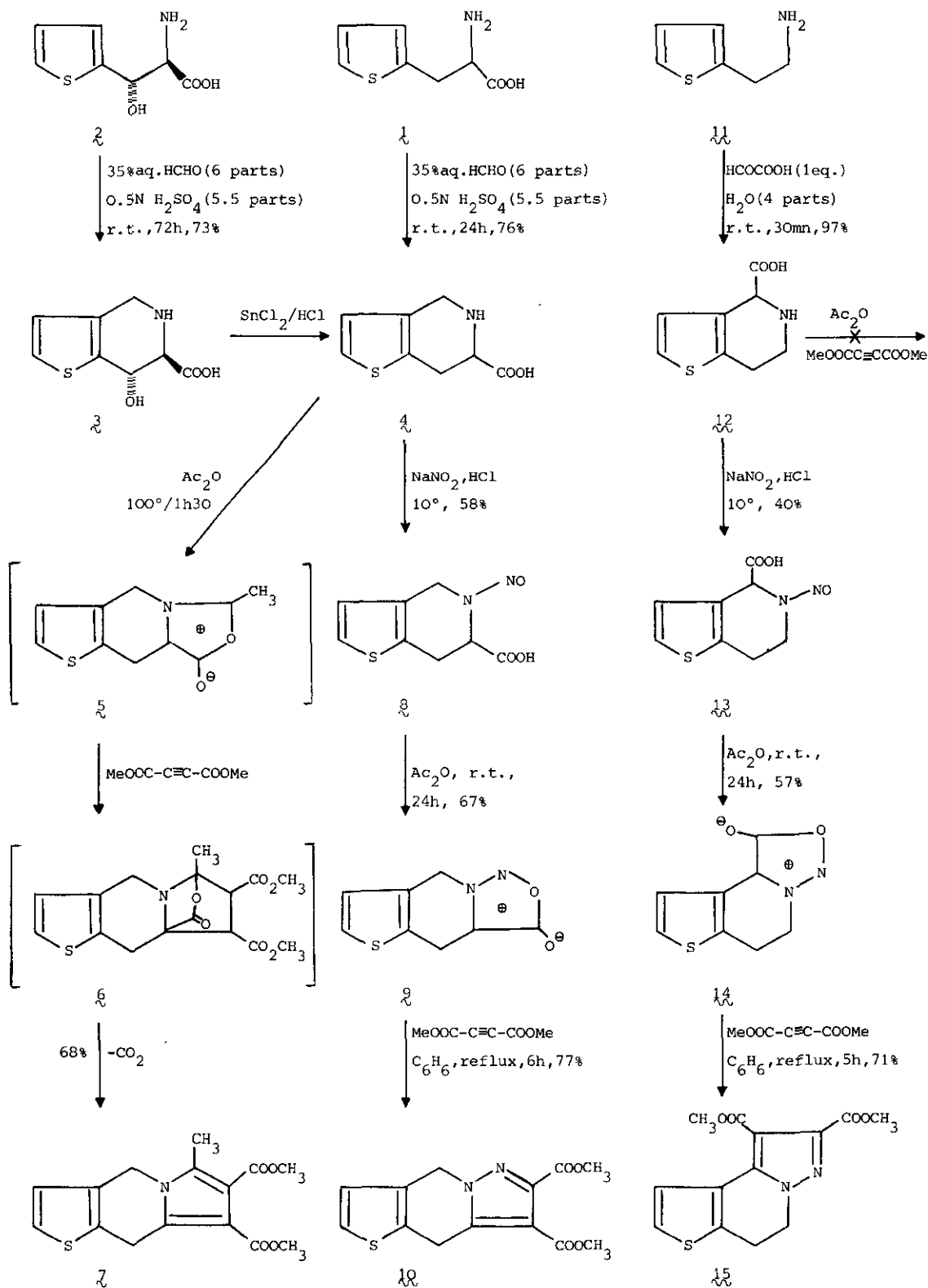
The present paper deals with the application of the above reaction on two other types of cyclic amino acid ring systems, namely 4,5,6,7-tetrahydrothieno(3,2-c)pyridine-4 and -6 carboxylic acids. Moreover it will describe the synthesis of fused-pyrazoles by a similar reaction with the corresponding 1,2,3-oxadiazolium-5 olates (sydnones)².

The amino-acid **4** was prepared⁶ by Pictet-Spengler cyclisation with formaldehyde of $(\pm)$ - β -(2-thienyl) alanine **1** or by hydrogenolysis of compound **3**⁶ with stannous chloride-hydrochloric acid in acetic acid.

The amino acid **12** (F > 260°) was easily obtained by condensation of 2-(2-thienyl)ethyl amine with glyoxylic acid, in water, at room temperature. The conversion of **4** into the 5,9-dihydro-thieno(3,2-f)indolizine **7**, involved treatment with dimethyl acetylenedicarboxylate in acetic anhydride. No attempt was made to isolate the highly reactive intermediate munchnone **5** and rearrangement of the presumed adduct **6** could be followed by CO₂ evolution. But all attempts to convert **12** in the same way were unsuccessful.

The N-nitroso- α -amino-acid **8** (F = 155° (H₂O-EtOH)) was cyclodehydrated using acetic anhydride and the resulting sydnone **9** (F = 182° (EtOH)) underwent a 1,3-dipolar cycloaddition with dimethyl acetylenedicarboxylate in refluxing benzene to give the fused-pyrazole **10** (F = 143° (iPrOH)). Similarly, the crude N-nitroso-derivative **13** (F_{dec} = 145-150°) was transformed into **15** (F = 80° (iPrOH-iPr₂O)) via the sydnone **14** (F = 165° (iPrOH)).

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N°	IR ν (cm ⁻¹)	¹ H. N.M.R. δ (ppm) , J (Hz)
7 λ	ν_{CO} :1725,1700	(CDCl ₃) : 2,35 (s,3H) ; 3,75 (s,3H) ; 3,77 (s,3H) ; 4,18 (t,2H,J=3) ; 4,78 (t,2H,J=3) ; 6,78 , 7,18 (2d,2H,J=5,5)
8 λ	ν_{CO} :1710	(DMSO d ₆) : 4,27 , 5,17 (2d,2H) ; 6,07 (q,1H) ; 6,88 , 7,37 (2d,2H,J=5,5)
9 λ	ν_{CO} :1730	(DMSO d ₆) : 3,87 (t,2H,J=4) ; 5,50 (t,2H,J=4) ; 6,95 , 7,48 (2d,2H,J=5,5)
10 λ	ν_{CO} :1745,1702	(CDCl ₃) : 3,84 (s,3H) ; 3,88 (s,3H) ; 4,30 (t,2H,J=4,0) ; 5,23 (t,2H,J=4) ; 6,83 , 7,25 (2d,2H,J=5,5)
12 λ	ν_{COO^-} :1555,1625	(CF ₃ COOH) : 3,25 (s ^{bc} ,2H) ; 3,85 (s ^{bc} ,2H) ; 5,50 (s ^{bc} ,1H) ; 7,15 , 7,33 (2d,2H,J=5,5)
13 λ	ν_{CO} :1730	(DMSO d ₆) : 4,21 (m,1H) ; 4,93 (m,1H) ; 5,82 (s,1H) ; 6,98 , 7,30 (2d,2H,J=5,5)
14 λ	ν_{CO} :1740,1755	(DMSO d ₆) : 3,37 (t,2H,J=7,5) ; 4,67 (t,2H,J=7,5) ; 7,12 , 7,43 (2d,2H,J=5,5)
15 λ	ν_{CO} :1705	(CDCl ₃) : 3,28 (t,2H,J=7,5) ; 3,92 (s,3H) ; 3,97 (s,3H) ; 4,45 (t,2H,J=7,5) ; 7,25 , 7,73 (2d,2H,J=5,5)

s^{bc} : broadened singlet

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