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A New Constructive Method for 1,4-Thiazepine Derivatives[1)]

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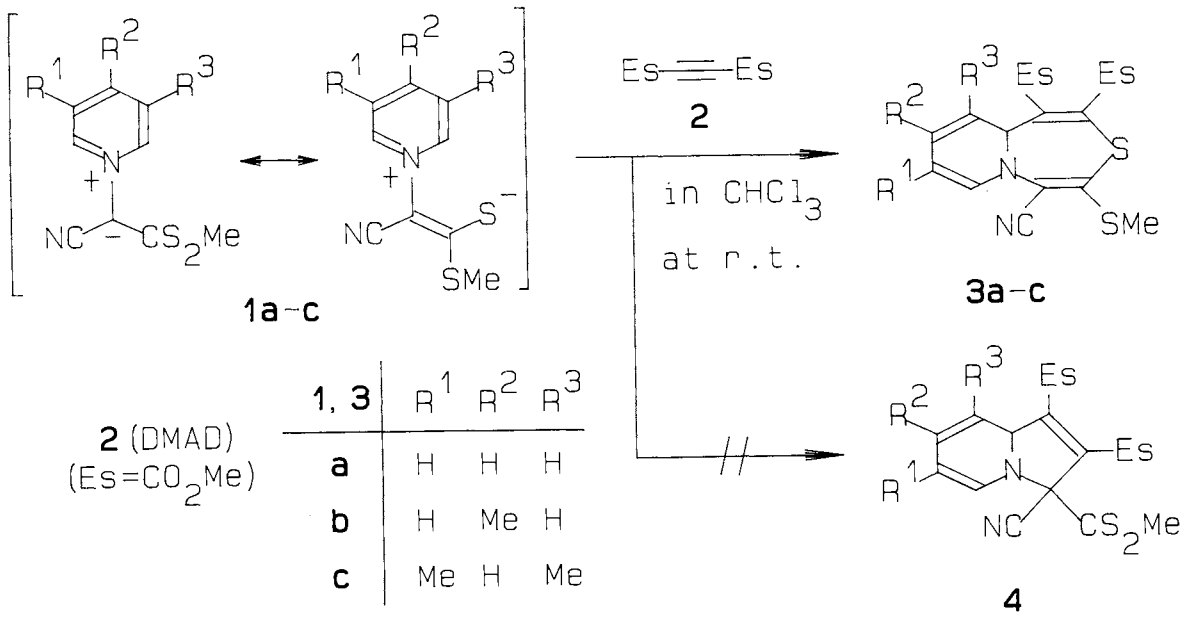
Some pyridinium 1-[(methylthio)thiocarbonyl]methylides reacted smoothly with dimethyl acetylenedicarboxylate in chloroform at room temperature to afford new heterocycles, 10a*H*-pyrido[1,2-*d*][1,4]thiazepine derivatives, in moderate yields.

Recently we have reported a simple and convenient preparative method for indolizines and pyrazolo[1,5-*a*]pyridines by way of the desulfurization or rearrangement of pyrido[2,1-*c*][1,4]thiazine and pyrido[1,2-*d*][1,3,4][1,4]thiazine intermediates.[2)] A characteristic feature in this method is the use of pyridinium salts which can be prepared from the regiospecific *S*-alkylations of the pyridinium *N*-methylides or *N*-aminides substituted by a thiocarbonyl group on the ylidic carbon atom. In continuation of this work, we are interested in the behavior of such pyridinium *N*-ylides toward electron-poor acetylenic compounds as dipolarophiles, since pyridinium *N*-ylides, in general, are better known as dipolar species rather than as nucleophiles. Their dipolar cycloadditions and cyclizations were well documented.[3)] In this paper we wish to report the reactions of some pyridinium 1-[(methylthio)thiocarbonyl]methylides with dimethyl acetylenedicarboxylate (DMAD) yielding new nitrogen-bridged heterocycles, dimethyl 2-methylthio-10a*H*-pyrido[1,2-*d*][1,4]thiazepine-1,2-dicarboxylates.

When an equimolar mixture of pyridinium 1-[cyano[(methylthio)-thiocarbonyl]]methylide (**1a**)[2b)] and DMAD (**2**) was allowed to react in

chloroform at room temperature for 12 h and then the reaction mixture was separated by column chromatography on silica gel using chloroform as an eluent, product **3a**, 34%, mp 127-128 °C, ν(KBr) 2218 (CN), and 1725 cm^{-1} (CO), δ ($CDCl_3$) 2,52 (3H, s, SMe), 3.71 and 3.78 (each 3H, s, COOMe) 5.1-5.7 (2H, m, 8-H and 10-H), 5.87 (br d, J=7.0 Hz, 10a-H), 6.20 (1H, m, 9-H), and 6.65 (1H, br d, J=8.0 Hz, 7-H), was obtained as red needles. Similar treatment of pyridinium N-ylides **1b,c** with the same reagent **2** gave the corresponding red adducts **3b,c** in 30 and 41% yields,[4] respectively.



1, 3	R^1	R^2	R^3
a	H	H	H
b	H	Me	H
c	Me	H	Me

The elemental analyses showed that these products were the 1 : 1 adducts between pyridinium N-ylides **1a-c** and DMAD (**2**),[5] and their ^1H NMR spectra exhibited clearly the presence of a nonaromatic 1,2-dihydropyridine moiety in these molecules because the chemical shifts of the skeletal protons (δ 5.10-5.65) and methyl protons (δ 1.71-1.88) were clearly different from those of aromatic indolizines. Of possible structures 1,3-dipolar cycloadduct, 3,8a-dihydroindolizine **4**, was excluded by the indication of an α,β-unsaturated cyano absorption bands (2209-2218 cm^{-1}) in the IR spectra. The 10a*H*-pyrido[1,2-*d*][1,4]thiazepine structure proposed for **3a-c** was finally confirmed by the single crystal

X-ray structural analysis of **3c**.[6]

Mechanistically, this reaction seems to proceed via the addition of DMAD (**2**) onto the anionic sulfur atom in ylide **1** followed by the 1,7-cyclization of the resulting zwitterionic species. The driving force of this reaction must be the soft-soft interaction[7] between the reactive centers of ylide **1** and DMAD (**2**). An alternative path, 1,5-dipolar cycloaddition of **1** with **2**, is less probable because such reaction is unprecedented and its reaction mode (π6a+π2s) has to involve a sterically and energetically unfavorable transition state.[8]

The scope and limitation of this reaction will be described in near future.

References

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4) **3b**, mp 128-129 °C, ν (KBr) 2214 (CN) and 1740 cm^{-1} (CO), δ ($CDCl_3$) 1.77 (3H, s, 9-Me), 2.49 (3H, s, SMe), 3.68 and 3.75 (each 3H, s, COOMe), 5.11 (1H, br d, J=7.0 Hz, 10-H), 5.11 (1H, br d, J=8.0 Hz, 8-H), 5.79 (1H, br d, J=7.0 Hz, 10a-H) and 6.54 (1H, d, J=8.0 Hz, 7-H). **3c**, mp 129-130 °C, ν (KBr) 2209 (CN), 1723 and 1738 cm^{-1} (CO), δ ($CDCl_3$) 1.77 and 1.88 (each 3H, s, 8-Me and 10-Me), 2.48 (3H, s, SMe),

3.69 and 3.77 (each 3H, s, COOMe), 5.75 (2H, br s, 10a-H and 9-H), and 6.23 (1H, br s, 9-H).

5) Satisfactory elemental analyses (within 0.3% for C.H.N) were obtained for all new compounds **3a-c**.

6) X-Ray crystallography was carried out on a RIGAKU AFC5S diffractometer. The diffraction data were collected with the use of MoKα radiation and 4477 independent reflections were used for solving the structure by the TEXSAN program (TEXSAN TEXRAY, Structure Analysis Package, Molecular Structure Corporation). Crystal data: $C_{17}H_{18}N_2O_4S_2$, FW = 378.46, monoclinic, space group $P2_1/n$, a = 7.542(2) Å, b = 12.142(2) Å, c = 20.442(2) Å, β = 95.99(2)°, V = 1861.8(5) Å^3, Z = 4, D_{calc} = 1.350 g/cm^3, R = 0.058, Rw =0.063.
Selected bond lengths (Å) and angles (°): C(1)-C(2) 1.333(7), C(1)-C(10a) 1.533(7), C(2)-S(3) 1.767 (6), S(3)-C(4) 1.765 (6), C(4)-C(5) 1.351 (7), C(5)-N(6) 1.406 (6), N(6)-C(7) 1.405(7), N(6)-C(10a) 1.473(7), C(7)-C(8) 1.327(8), C(8)-C(9) 1.434(8), C(9)-C(10) 1.332(8), C(10a)-C(1)-C(2) 120.3(5), C(1)-C(2)-S(3) 124.2(4), C(2)-S(3)-C(4) 109.1(3), S(3)-C(4)-C(5) 131.7(4), C(4)-C(5)-N(6) 127.3(5), C(5)-N(6)-C(7) 122.4(5), N(6)-C(7)-C(8) 120.1(5), N(6)-C(10a)-C(1) 112.0(4), N(6)-C(10a)-C(10) 109.2(4), C(5)-N(6)-C(10a) 117.6(4), C(7)-N(6)-C(10a) 119.2(4), C(7)-C(8)-C(9) 118.6(6), C(8)-C(9)-C(10) 122.5(6), C(9)-C(10)-C(10a) 118.9(5).

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