Novel Cyclization and Rearrangement to 1,4-Dihydropyridazino[4,5-*c*]pyridazinones

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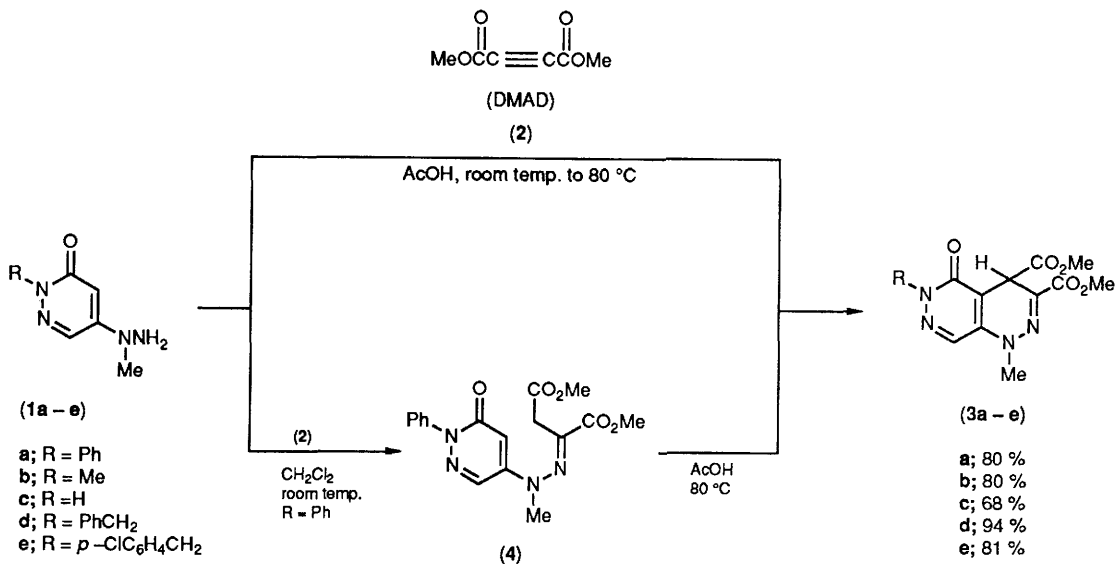
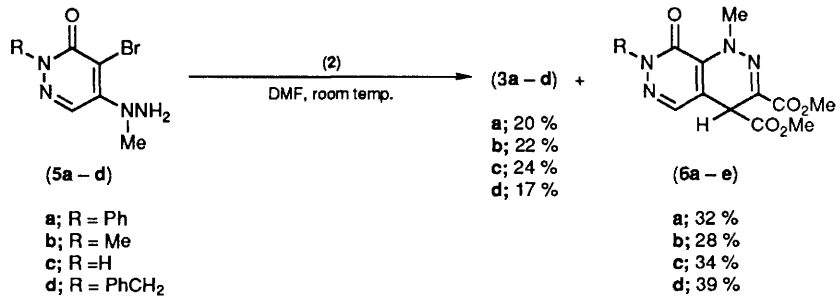
1,4-Dihydropyridazino[4,5-*c*]pyridazinones were prepared by a novel one-pot cyclization and dehydrogenation from hydrazinopyridazinones and dimethyl acetylenedicarboxylate.

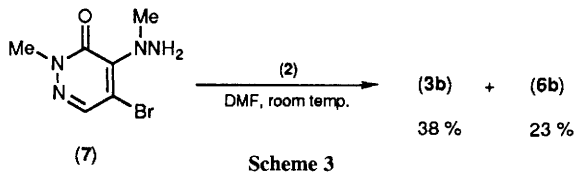
Fused pyridazinones have attracted attention because of their potential biological and pharmacological activities.[1] In order to study the synthesis of fused heterocyclic ring systems containing the pyridazinone moiety, we investigated the condensations of the hydrazinopyridazin-3-ones (**1**) and the bromo compounds (**5**) and (**7**),[2] whose structures include the synthetically interesting enehydrazine moiety, with dimethyl acetylenedicarboxylate (DMAD, **2**), in an attempt to obtain 1,4-dihydropyridazino[4,5-*c*]pyridazine-4,5-diones. Unexpectedly the reaction of (**1**) with (**2**) gave 1,4-dihydropyrid-



Scheme 1. (**3a**), m.p. 189—190; (**3b**), 147; (**3c**), 218—220; (**3d**), 97—98; (**3e**), 162—163 °C.



Scheme 2



Scheme 3

azino[4,5-*c*]pyridazin-5(6*H*)-ones (**3**), which were formed by cyclization and dehydrogenation between the enehydrazine moiety and the carbon–carbon triple bond of DMAD (**2**). To our knowledge, there have been few reports of the preparation of 1,4-dihydropyridazinopyridazines, with the exception of ring transformation by hydrazinolysis of 4-acyl-3*H*-imidazo[1,5-*b*]pyridazine-5,7(6*H*)-diones.[3] In the reactions of (**5**) and (**7**) with DMAD (2), an entirely unexpected rearrangement occurred together with the formation of the expected products.

Treatment of (**1**) with DMAD (**2**) in AcOH at room temperature—80 °C gave (**3**) in good yields by the initial Michael addition of the hydrazino group of (**1**) to a triply bonded carbon atom of (**2**) followed by cyclization with dehydrogenation (Scheme 1). In order to elucidate the reaction pathway, compound (**1a**) was allowed to react with DMAD (**2**) under milder conditions in CH_2Cl_2 at room temperature, and the intermediate Michael adduct (**4**) was successfully isolated. Heating of the intermediate (**4**) at 80 °C in AcOH afforded (**3a**) as expected. Such a dehydrogenative cyclization of enehydrazines[4] with DMAD to give 1,4-dihydropyridazines has not been reported so far.

When 4-bromo-5-hydrazinopyridazin-3-ones (**5**) were treated with DMAD (**2**) in dimethylformamide (DMF) at room temperature, compounds (**3**) and the regioisomers (**6**) were produced in 17—20 and 28—39% yields, respectively (Scheme 2). The structure of compounds (**6**) was established on the basis of analytical data together with IR, ^{13}C NMR, ^{1}H NOE difference, and mass spectral data. Compound (**7**), a regioisomer of (**5b**), also afforded (**3b**) and (**6b**) on reaction with DMAD (**2**) under the same conditions in 38 and 23% yields, respectively (Scheme 3).

This is the first example of this route to fused 1,4-dihydropyridazines using DMAD by direct cyclization with

dehydrogenation, and applications to the preparation of other fused heterocycles are being investigated.

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