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Reaction of α-Lactams with Alkynyl-lithium Reagents: a Novel Synthesis of Pyrrolinones

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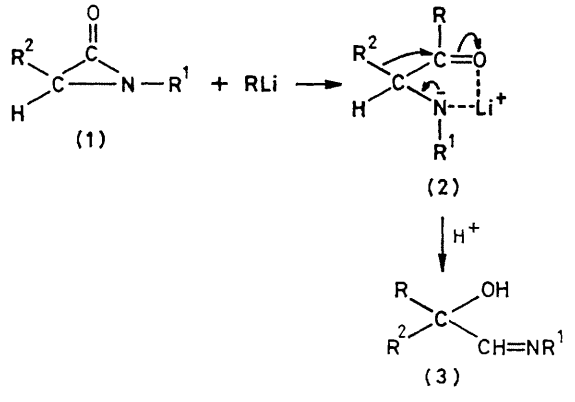
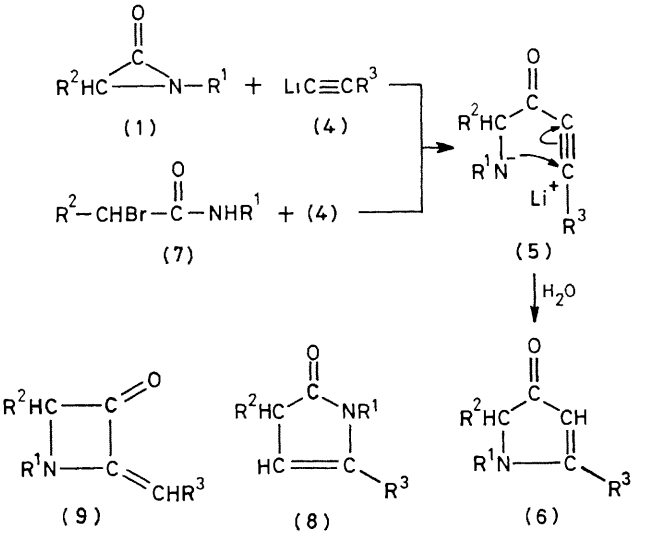
Summary The reaction of α-lactams with alkynyl-lithium reagents affords 2-pyrrolin-4-ones and constitutes a useful synthesis of this class of heterocycles bearing bulky aliphatic substituents.

α-Lactams (**1**) undergo reaction with alkyl-lithium compounds to produce α-hydroxy-imines (**3**).[1] Although other pathways are not ruled out, initial cleavage of the acyl–nitrogen bond, followed by rearrangement of the resulting anion (**2**), accounts for the observed products. In fact, under very carefully controlled conditions that prevent the rearrangement of (**2**), α-amino-ketones, derived from (**2**) by protonation, could be isolated.[2] We now describe a reaction of α-lactams with alkynyl-lithium reagents that gives an entirely different product.

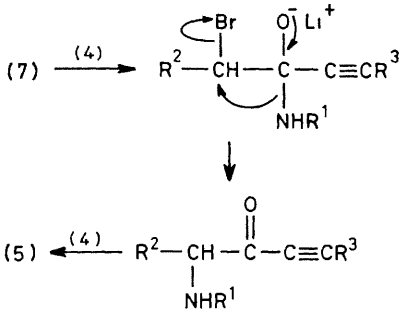


Treatment of (**1a**) in tetrahydrofuran with propynyl-lithium (**4a**) in an atomsphere of nitrogen at 25—30 °C yielded a solid (54%), which, after crystallization from pentane, afforded white crystals, m.p. 91·2—92·0 °C, to which we assign the structure (**6a**) on the basis of the following spectral data: ν_{max} (CCl_4) 1680 vs cm^{-1}; ^1H n.m.r. ($CDCl_3$) δ 1.00 (s, 9H), 1·33 (s, 9H), 2·25 (s, 3H),



a; $R^1 = R^2 = Bu^t$, $R^3 = Me$
b; $R^1 = R^2 = 1$-adamantyl, $R^3 = Me$
c; $R^1 = Bu^t$, $R^2 = 1$-adamantyl, $R^3 = Me$
d; $R^1 = 1$-adamantyl, $R^2 = Bu^t$, $R^3 = Me$

3·25 (s, 1H), and 5·22 (s, 1H), u v [(95% EtOH) λ_{max} 288 (ϵ 5200) and 344 (ϵ 5320), (2,2,4-trimethylpentane) λ_{max} 288 (ϵ 6875) and 350 (ϵ 1965) nm], M^+ 209 Thus, selective cleavage of the acyl–nitrogen bond of the lactam ring to give (**5**) and subsequent regiospecific ring-closure constitutes a novel synthesis of 2-pyrrolin-4-ones (**6**), devoid of complications caused by the rearrangement of (**2**) to (**3**) Alternative products derived from other possible modes of cleavage followed by cyclization, such as (**8a**) and (**9a**), are clearly ruled out by the spectral data cited Compound (**6a**) was also obtained by treatment of the α-bromo-amide (**7a**) with an excess of (**4a**), presumably by cyclization to (**1a**) and subsequent reaction of (**1a**), although a direct conversion of (**7**) into (**5**) can also be envisaged This observation enhances the utility of the present synthesis of (**6**) by obviating the necessity of isolating α-lactams, however, thermal decomposition of especially unstable α-lactams may make this impossible Other 2-pyrrolin-4-ones (**6b**—**d**) were similarly synthesized



Attempted ring expansions of α-lactams with diazomethane and dimethylsulphoxonium methylide by other workers were unsuccessful [3] Only three successful ring expansions of α-lactams have been reported one leading to a derivative of azetidin-2-one,[4a] another leading to a mixture of imidazolidine-2,4-diones,[4b] and the third yielding a succinimide [4c] Thus, the production of 2-pyrrolin-4-ones described herein represents only the fourth successful ring expansion of the aziridinone ring Although other syntheses of 2-pyrrolin-4-ones have been reported,[5] only one of them[5f] provides examples where all substituents are aliphatic, and, in this particular method (photo-oxygenation), the starting material is a pyrrole Since (**6**) does not tautomerize to a pyrrole, obviously steric factors militate against the preparation of (**6**) from the corresponding pyrrole by photo-oxygenation Thus, the preparation of 2-pyrrolin-4-ones from α-lactams or their precursors constitutes a useful alternative for the synthesis of at least some members of this class of heterocyclic compounds

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