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CATIONIC HETEROCYCLIZATION

ONE STEP SYNTHESIS OF CONDENSED HETEROCYCLICS

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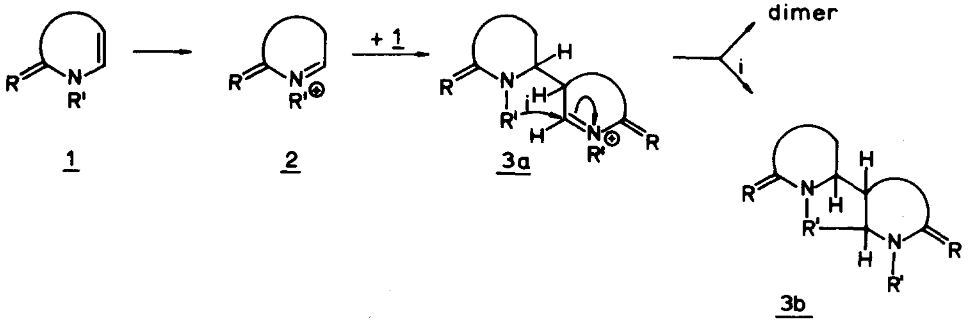
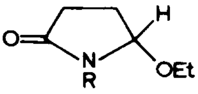
Dimerizations of cyclic enamines 1 ($R=H_2$) occurring via iminium intermediates 2 ($R=H_2$) are well-known[1] and have been applied recently in alkaloid synthesis[2]. Schematically the overall process can be represented as follows:



In general the H$^{\oplus}$elimination in 3a will be fast and leads to dimeric products. If, however R^1 possesses sufficient nucleophilic character a further cyclization might become favoured (route i) which will lead to condensed heterocyclics 3b in a single step. The recent report by Swan and Wilcock[3] on a closely related subject prompts us to disclose our results and this letter reports an example of this novel type of ring closure as applied to certain lactam derivatives structurally related to 1 ($R=O$). O-Ethyl-α-carbinollactams[4] 4 or alternatively pyrrolin-2-ones 5[4] which are easily prepared from 4 dimerize under influence of acid in different ways.

Treatment of 4a (4, R=Me) or either 5a (5, R=Me) with pTsOH in refluxing benzene afforded exclusively 6a[5] (6, R=Me) mp 81-92°C (dec), PMR, δ(CDCl$_3$), 6,80S (H$_4$)[6] in 79% yield. On the contrary, reflux of 4a in benzene solution containing a silica-alumina catalyst[7] provided dimer 7a (7 R=CH$_3$), m.p. 95° (dec) PMR, δ(CDCl$_3$). 6.00S (H$_3$)[6], none of 6a being detected (TLC). It thus appears possible to control the selectivity of the dimerization process by the appropriate choice of the acid catalyst.



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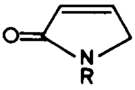

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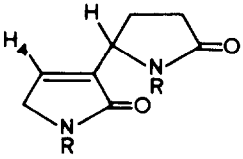

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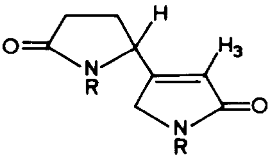

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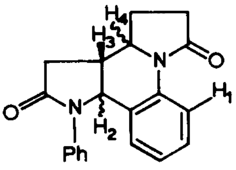
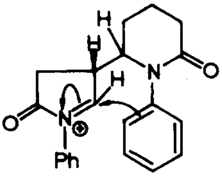
Similarly, p-TsOH treatment of 4b (4 R=Ph) afforded mainly 6b (6 R=Ph) m.p. 156-158° PMR δ(CDCl$_3$) 6.69 (H$_4$), although TLC analysis revealed the presence of a small amount of an unknown compound X. Reaction of 4b or 5b (5 R=Ph) in presence of the silica-alumina catalyst gave a 1:1 mixture of X and a second isomer Y in essentially quantitative yield, which was separated via fractional crystallization. TLC-monitoring of the reaction showed the presence of a transient intermediate, presumably 7b (7, R=Ph) PMR δ(CDCl$_3$) 6,08 (H$_3$)ppm. On the basis of PMR and mass spectral analysis structures 8 and 9 were assigned X and Y respectively.



8 α-H$_2$, β-H$_4$

9 β-H$_2$, ξ-H$_4$



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8: m.p. 241°C (dec), PMR $\delta(CDCl_3)$ 8.51 d J=9.5 Hz (H_1); 5.51 d $J_{2,3}$=8.0 Hz (H_2); 4.21 m $J_{3,4}$=3.0 Hz (H_4) and 3.29 m $J_{2,3}$=8.0 Hz, $J_{3,4}$=3.0 Hz (H_3); MS m/e 318 ($M^{\oplus}$) 65%; 184 $(M-134)^{\oplus}$ 100%. For 9 the following data are found: m.p. 250°C (dec) PMR $\delta(CDCl_3)$ 8.68 d J=9.5 Hz (H_1); 5.02 d $J_{2,3}$=5.0 Hz (H_2); 3.95 m (H_4) and 2.95 m (H_3); MS m/e 318 ($M^{\oplus}$) 35%, 184 $(M-134)^{\oplus}$ 100%. The stereochemical assignments have been based upon a consideration of all possible isomers and are tentative. Furthermore it should be emphasized that only initial C-4 attack can lead to the cyclized product via the intermediate 10 and therefore reaction conditions favouring C-4 attack are a prerequisite. In addition the yield in this novel reaction compares most favourable with those found in a related process3).

This double cationic cyclization mimics in a way the presently well-established olefinic cyclization8) and can be applied to a variety of N-aryl succinimides. Synthetic and mechanistic implications9) as well as further examples of mixed condensations and introduction of nitrogen substituents of different electronic character will be discussed in our full paper.

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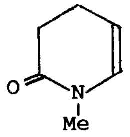
9. Reaction of *i* under both conditions affords exclusively one dimer. The present results may be accounted for by assuming the intermediacy of the elusive 2-OH-pyrrole[10] under strongly acidic conditions.



i

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