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SIMULTANEOUS AND STEREOSPECIFIC FORMATION OF TWO C—C BONDS VIA α-ACYLIMMONIUM CYCLISATION

by

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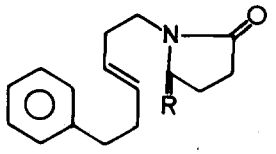
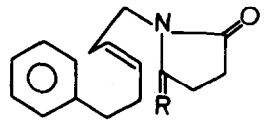
Single C—C bond formation through reaction of immonium type intermediates with monoolefins has been shown to function as an attractive route for the synthesis of heterocycles[1]. Yet in view of the numerous examples known to-day of the biomimetic carbocyclisations over more than one C=C bond[2], one might visualize useful applications for a heterocyclic alternative. In this communication we wish to describe the first successful heterocyclisations over two C=C bonds to form polyheterocyclics. The method employes the highly reactive α-acylimmonium ion[3] as a cationic initiating centre for arylolefin and diolefin cyclisations.

The E- and Z arylolefin imides 1 and 2, the acetylene analogue 3 and the E,E-diolefin 4, were selected as model substrates. The synthesis of imides 1-4 proceeded in satisfactory yields via oxidation-reduction coupling[4] of succinimide and the appropriate alcohols. The latter were synthesized by standard methods from 6-phenyl-3-hexenol-1 which in turn was prepared by the way of coupling of benzyl bromide and propargyl magnesium bromide and alkylation of the resulting adduct with ethyleneoxyde. 3,7-Octa-dienol-1 was obtained via a Julia-Johnson synthesis[5] of ethyl-3-cyclopropyl-2-oxopropionate and allyl bromide. $NaBH_4/H^{\oplus}$ reduction of imides 1-4, coupled with "acid work-up"[3], afforded the ethoxylactams 5-8 as homogeneous oils in quantitative yields. Prior to use the lactams were purified by chromatography.



1 R=O
5 R=H,OEt



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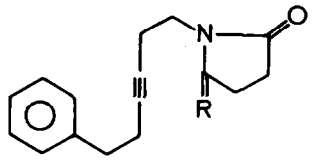
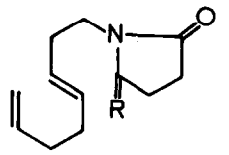
6 R=H,OEt



3 R=O
7 R=H,OEt



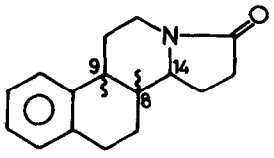
4 R=O
8 R=H,OEt

HCOOH-cyclisation of 5 (18 h/r.t.) gave a quantitative yield of cyclized material, which on the basis of previous results[6] and by ^{1}H-NMR analysis was shown to consist entirely out of the trans-anti isomer 9, m.p. 108-110°C, δ($CDCl_3$) 3·33 m (C_{14}-H); 4·31 m (C_{12}-H eq). Thus the cyclisation proceeded in a stereospecific manner in agreement with the results found earlier in the estrone series[7].

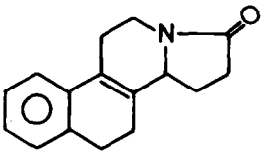
Interestingly, HCOOH-cyclisation of 6 (18 h/r.t.) resulted in quantitative formation of the cis-syn compound 10, m.p. 140-142°C, δ($CDCl_3$) 3·80 m (C_{14}-H); 4·15 m (C_{12}-H eq). Thus in spite of the "unnatural" Z geometry in 6 cyclisation occurs with complete retention of stereochemistry, which lend support to the idea of concerted formation of both C-C bonds in this type of substrate[8].

Contrary to earlier findings on the behaviour of acetylenic compounds in this type of cyclisation[9] the HCOOH-cyclisation of 7 proceeded relatively rapid (18 h/r.t.) to afford a quantitative yield of the slightly unstable 8,9-dehydroderivative 11, m.p. 117-119°C, δ($CDCl_3$) 4·29 m (C_{14}-H); 4·41 m (C_{12}-H eq). Apparently the built-in aromatic ring is a better nucleophilic capturing group for the intermediate vinylic cation as compared to the external solvent molecule[10].

From the aforementioned data it can be concluded that cationic heterocyclisations of arylolefinic ethoxylactams constitute a method of choice in the svnthesis



9 8,9-trans-8,14-anti
10 8,9-cis – 8,14 – syn.



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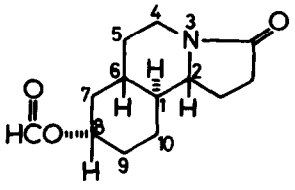

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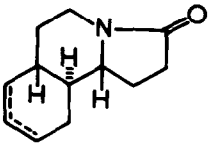

13

of this type of polyheterocyclics and obvious ramifications will be reported elsewhere. Within the latter context the diolefin 8 was considered as an interesting candidate since the incorporation of an unactivated 1,5-diene unit is anticipated to provide clear-cut information on the degree of reactivity of the cyclic α-acyl-immonium ion in olefin cyclisations. Furthermore the preparation of saturated bridgehead nitrogen tricyclics via the latter type of reaction offers interesting opportunities for future synthetic applications.

HCOOH treatment of 8 (18 h/r.t.) gave complete ringclosure to tricyclic nitrogen derivatives in which 12 was shown to be present (^{1}H-NMR) for about 60%. After chromatography and crystallisation a yield of 40% of 12 was obtained, m.p. 99-100°C; ^{1}H-NMR δ($CDCl_3$) (2·68 t, J=12·5 c/s, C_4-H_{ax}); 3·05 m, $J_{1,2}$=10 c/s; C_2-H_{ax}; 4·16 m, C_4-H_{eq}; 4·90 m, $J_{7,8} \approx J_{8,9}$=11 c/s and 5 c/s, C_8-H. On the basis of previous assignments coupled with the ^{1}H-NMR data the axial positions of H_2 and H_8 and the H_1-H_2 anti-relationship are immediately clear, while the trans H_1-H_6 relationship is indicated on the basis of mechanistic considerations[11].

In the remaining amount of crude cyclisation products the presence of 13 could be established.

The foregoing results obviously illustrate the possibility of simultaneous formation of two single C-C bonds in heterocyclisation. Furthermore, the unique properties of the cyclic α-acylimmonium ion as a highly reactive cationic centre for inducing olefin cyclisations are underlined.

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10) Additional data on the reactivity of acetylene derivatives in this type of heterocyclisation are given in the accompanying paper.

11) Details will be published in our full paper.

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