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UNPRECEDENTED REARRANGEMENTS VIA ALLENES AS π-PARTICIPANTS IN α-ACYLIMINIUM ION CYCLISATIONS[1]

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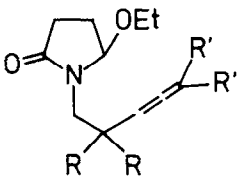
Abstract: Upon HCOOH reaction of ethoxylactams 1a-1d the terminally unsubstituted allenes 1a and 1d underwent a [3,3] sigmatropic rearrangement. The dimethyl allenes 1b and 1c afforded only products from an α-acyliminium ion cyclisation.

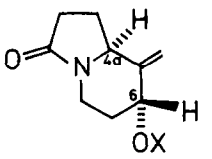
Cationic π-cyclisation of α-acyliminium ions has been applied in the synthesis of various heterocyclic systems[2]. Generally the formation of sixmembered rings is favored although minor variations in the electronic bias of the π-moiety severely influence the mode of ring closure[3]. Aiming at the development of novel methods for selective formation of heterocyclic rings of different sizes the allenic bond has been investigated in its behaviour towards α-acyliminium ions. Terminal allenes have been shown to possess sufficient reactivity as π-nucleophiles in cationic cyclisation reactions[4]. HCOOH treatment (18 hr, r.t.) of ethoxylactam 1a[5], obtained in the usual manner by $NaBH_4/H^+$ reduction and acid work-up (HCl-EtOH)[6] of the corresponding imide, yielded a mixture of 4 formates 2a-5a in an estimated ratio of 2:1:1:2 (^{1}H-NMR), which after hydrolysis (K_2CO_3, MeOH, H_2O) easily could be separated by column chromatography (combined yield 96%). The expected C_6 epimeric alcohols 2b and 3b (Scheme I) were isolated as a non-separable crystalline fraction (47%) in which the epimer ratio mounted to 7:2. In addition alcohol 4b was obtained as a minor product (15%), m.p. 102.5-106.0°C (EtOAc - hexane).

Quite unexpectedly the other major isomer proved to be the ringopened product 5b possessing an unusual diene structure. Yield: 34%, m.p. 5b: 66.5-68.0°C (dipe). (250 MHz) ^{1}H-NMR δ($CDCl_3$): 6.34 (d of d, J = 11.9 and 17.9 Hz, 1H, C<u>H</u> =

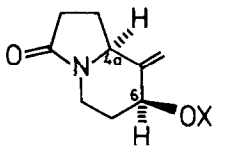
CH_2); 5.29 (d, J_{trans} = 17.9 Hz, 1H, CH=C$\underline{H}_2$); 5.17 (d, J_{cis} = 11.9 Hz, 1H, CH=C$\underline{H}$)$_2$; 5.20 and 4.94 (2 broad s, 2H, C=C$\underline{H}_2$); 5.04 and 4.21 (2 x d, J = 10.4 Hz, 2H, sec-NC$\underline{H}$); 4.57 (d of d, J = 3.7 and 8.2 Hz, 1H, tert-NC$\underline{H}$); 2.60-1.70 (m, 4H). UV(EtOH): λ_{max} = 204 nm (ε = 11.600); λ_{max} = 216 nm (ε = 11.000) and λ_{max} = 222 nm (ε = 10.900). Its structure was also verified chemically upon prolonged reaction with K_2CO_3aq of 5b, which produced amide 5c with loss of formaldehyde; m.p. 52.5-56.0°C (dipe).



1a R=R'=H
1b R=R'=Me
1c R=H, R'=Me
1d R=Me, R'=H

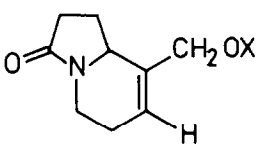


2a X=OCH
2b X=H

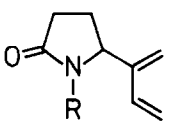


3a X=OCH
3b X=H

SCHEME I

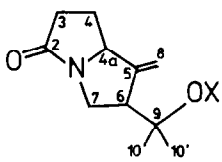


4a X=OCH
4b X=H



5a R=CH_2OOCH
5b R=CH_2OH
5c R=H

6a R=H
6b R=Me



7a X=OCH
7b X=H

The formation of 5a can be rationalized by either assuming an anchimeric assistance of the amide nitrogen in the fragmentation of A[8] (Scheme II) or via a direct [3.3] sigmatropic rearrangement of the α-acyliminium ion B. Eventually the process depicted in B could be followed by a ring closure via the alternate primary acyliminium ion C, which formally opens a second cyclisation pathway (Scheme II). Until recently examples of the 2-aza-Cope rearrangement B were unknown[9].

By carrying out the cyclisation in different solvent combinations the ratio of (5/2 + 3 + 4) could be influenced to a considerable extent (Table). However, we were not able to promote exclusive formation of 5a. Also the submission of either 2, 3, 4 or 5 (a and b) to the conditions of its formation did not indicate a possible conversion of cyclic compounds into acyclic dienes and

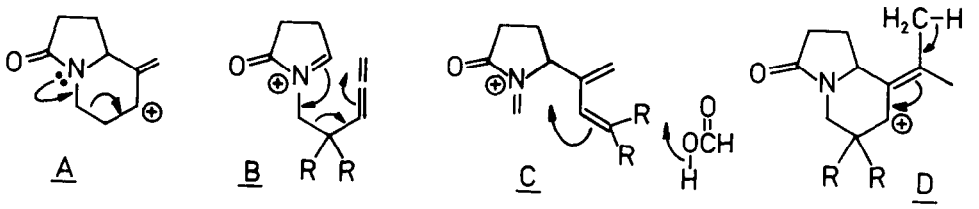
TABLE: Cyclisation of Ethoxylactam 1a

Acid	temp.(°C)	time (hr)	product ratio[a]
HCOOH	r.t.	18	35/65
HCOOH/3 eq NaOOCH	r.t.	18	27/73
HCOOH	76	5	0/100
$CHCl_2COOH$	r.t.	18	50/50
CF_3COOH/CH_2Cl_2 1:7 (by vol)	0-5	0.5	45/55
C_6H_6/1.5 eq pTsA	80	5	45/55
$HCOOH/CH_2Cl_2$ 1:1 (by vol)	r.t.	18	47/53

a) estimated ratio ringopened/ringclosed (5/2 + 3 + 4) as determined by ^{1}H-NMR. Accuracy ca 5%.

vice versa. Therefore it seems likely that both types of compounds are formed irreversibly via separate pathways. To investigate this phenomenon a number of structurally related allenes were selected. While HCOOH-cyclisation (18 hr, r.t.) of 1b[5] and 1c[5] proceeded quantitatively the products formed possessed the cyclic diene structures 6a and 6b. Thus instead of the fragmentation route to the acyclic diene an alternative pathway is followed which is depicted in D (Scheme II). Loss of a proton from the gem-dimethyl group supposedly is of lower energy in both the cyclisation and fragmentation routes. Therefore the latter process could only be expected in case the terminal carbon atom of the allene function is not possessing β-hydrogens. The obvious target compound 1d[5] upon HCOOH-treatment at r.t. (18 hr) afforded a 4 : 1 mixture of the pyrrolizidines 7a and 7b in 94% yield.

The characterisation of 7a rests upon the following ^{1}H- and ^{13}C-NMR data: 7a oil: (100 MHz) ^{1}H-NMR δ($CDCl_3$): 7.98 (s, 1H, OCH); 5.28 and 5.19 (2 x t, J = 2 Hz, 2H, C = CH_2); 4.52 (t, J = 7 Hz, 1H, H_{4a}); 3.99 (m, 1H, deshielded H_7); 3.38 (d of d, J = 8.5 and 1.5 Hz, 1H, H_6); 3.13 (d of d, J = 12 and 8.5 Hz, 1H, H_7); 1.55 and 1.48 (2 x s, 6H, CH_3); 2.90 - 0.85 (m, 4H). (250 MHz) ^{13}C-NMR δ($CDCl_3$): 175.04 (C_2); 159.83 (OCH); 149.63 (C_5); 111.10 (C_8); 84.57 (C_9); 64.13 (C_{4a}); 53.25 (C_7); 43.46 and 33.65 (C_3 and C_6); 27.06 (C_4); 23.86 and 23.78 (C_{10} and $C_{10'}$). The relative stereochemistry at C_{4a} and C_6 could not be established. The formation of 7a and 7b can be rationalized on the basis of a process in which fragmentation and ring closure are successive steps (B → C, Scheme II).



SCHEME II

Apparently the fragmentation is the preferred route because in the final cyclisation a relatively stable tertiary $C^{\oplus}$-ion can be formed. Further investigation on this novel aspect of allene chemistry is in progress.

REFERENCES AND NOTES.

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5. The starting imides are readily prepared via the oxidation-reduction coupling technique[7] of succinimide with the appropriate alcohols. 1,2-Pentadien-5-ol is synthesized as described by P. Crabbé, H. Fillion, D. André and J.-L. Luche, J.Chem.Soc.Chem.Comm., 859 (1979); 2-methyl-2,3-hexadien-6-ol by L.-I. Olsson, A. Claesson and C. Bogentoft, Acta Chem. Scand., B 28, 765 (1974); 2,2,5-trimethyl-3,4-hexadien-1-ol and 2,2-dimethyl 3,4-pentadien-1-ol by R.S. Bly and S.U. Koock, J.Am.Chem.Soc., 91, 3292 (1969). Ethoxylactams were isolated after column chromatography as homogeneous samples in almost quantitative yields prior to cyclisation. All new compounds gave correct analytical data.
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