Tetrahedron Letters,Vol.24,No.13,pp 1407-1410,1983 0040-4039/83/131407-04$03.00/0
Printed in Great Britain

COMPLETELY REGIOSELECTIVE α-ACYLIMINIUM ION CYCLIZATIONS WITH ALLYL AND PROPARGYL SILANES

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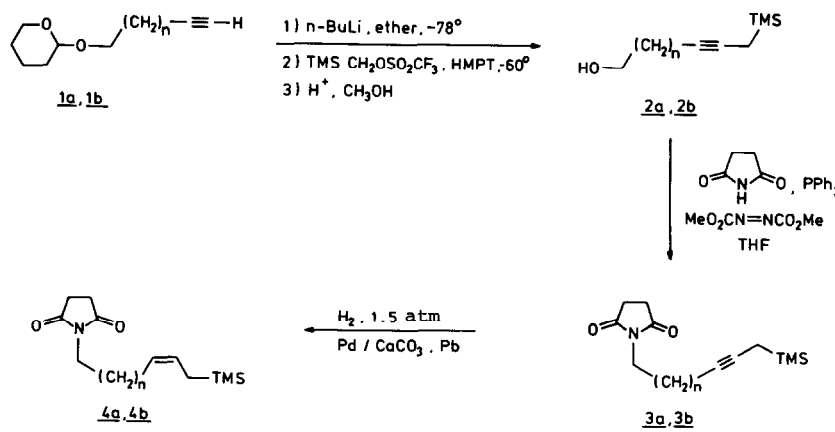
Abstract: Intramolecular reactions of α-acyliminium ions with allyl and propargyl silanes occur under the influence of trifluoroacetic acid, to afford in high yield and with complete regioselectivity bridgehead nitrogen bicyclic compounds 5 - 8.

The use of silicon as an auxiliary element in organic synthesis continues to receive wide-spread attention since the late sixties[1]. Allyl and propargyl silanes are among the most rewarding silicon containing functionalities due to their high reactivity and marked regio- and stereo-control in reactions with electrophiles[2,3]. We now wish to report that use of these unsaturated silanes gives excellent results also in cyclization reactions of the very electrophilic α-acyliminium ions[4,5].

Since α-acyliminium ions derived from succinimide have proved to be excellent cyclization substrates[4], we chose to synthesize the imides 3a, 3b, 4a and 4b (Scheme I).



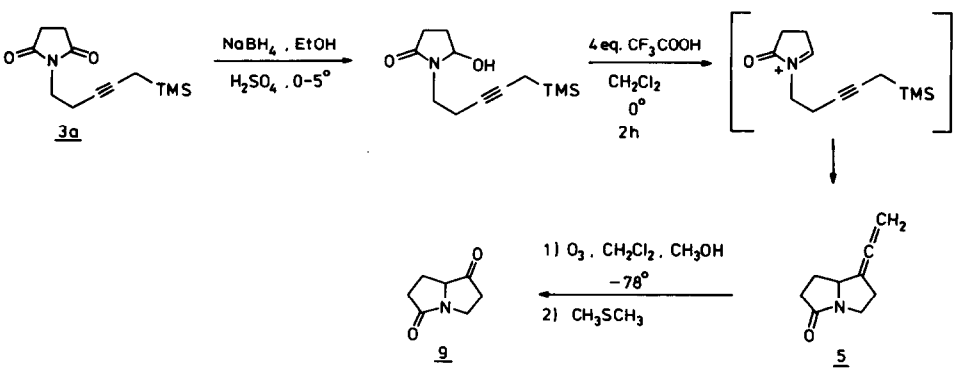
1a, 1b — 2a, 2b — 3a, 3b — 4a, 4b

Scheme I (n = 1 : 1a–4a ; n = 3 : 1b–4b)

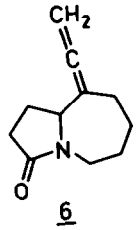
Propargyl silanes 2a (45%) and 2b (59%) were prepared from the THP-ethers of 3-butyn-1-ol (1a)[6] and 5-hexyn-1-ol (1b)[7], respectively, by using the procedure of Peterson et al[8]. Imides 3a (74%)[9] and 3b (89%)[10] were obtained from 2a and 2b through reaction with succinimide in the presence of triphenylphosphine and dimethyl azodicarboxylate (Mitsunobu reaction)[11]. Catalytic hydrogenation of the propargyl silanes 3a and 3b afforded the Z-allyl silanes 4a[12] and 4b[13] in nearly quantitative yields. It is noteworthy, that synthesis of allyl silanes from propargyl silanes offers the opportunity to obtain them in isomerically pure state, whereas many other synthetic procedures yield allyl silanes as Z,E-mixtures[1a].

Reduction of the imides 3a, 3b, 4a and 4b to the corresponding hydroxylactams (Scheme II) occurred in high yield by using excess sodium borohydride in ethanol at 0-5°C and slow addition of a 4% solution of sulfuric acid in ethanol until TLC indicated complete conversion[10]. The hydroxylactams could be purified by using flash chromatography, but were usually pure enough for the ring closure reaction. Upon addition of a CH_2Cl_2 solution of hydroxylactam to a CH_2Cl_2 solution of 4 eq of trifluoroacetic acid at 0°C[15], complete cyclization took place in all four cases within two hours. The reactions were clean and the products (5-8) were obtained in overall yields (from the imides) of 70-90%. These results show that formation of the α-acyliminium ion is a much more facile process than (undesired) protodesilylation. Furthermore, complete regioselectivity was observed, as from 3a and 4a only pyrrolizidones 5 and 7 were obtained and from 3b and 4b only the seven-membered ring compounds 6 and 8.

The structures of the cyclization products 5-8 (all colorless oils) were proved by spectroscopic means and exact mass determination. Allene 5 showed



Scheme II



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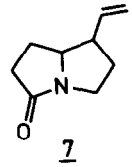

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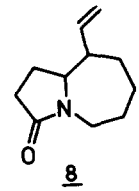

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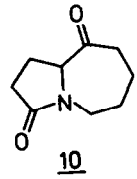

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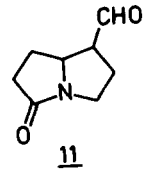

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characteristic IR absorptions ($CHCl_3$) at 1970 and 1680 cm^{-1} and ^1H NMR ($CDCl_3$): δ 4.92 (m, 2H), 4.48 (m, 1H), 3.93 (dt, J=11.0, 5.5 Hz, 1H), 1.7-3.1 (m, 7H). It was rather unstable and therefore was treated with ozone (CH_2Cl_2/CH_3OH 1:1, -78°C; then CH_3SCH_3) to yield ketone 9 (IR($CHCl_3$): 1760 and 1690 cm^{-1}). From 3b was obtained allene 6 (IR($CHCl_3$): 1960 and 1675 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.82 (m, 2H), 4.31 (m, 1H), 4.05 (m, 1H), 2.71 (m, 1H), 1.2-2.5 (m, 10H); ^{13}C NMR ($CDCl_3$): δ 206.8, 174.7, 104.6, 75.8, 62.0, 42.0, 30.7, 29.7, 28.6, 28.2 and 25.7 ppm), which was more stable than 5, and could also be easily ozonolyzed to give ketone 10 (IR($CHCl_3$): 1710 and 1685 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.34 (m, 1H), 4.07 (m, 1H), 1.4-2.9 (m, 11H)).

Imide 4b gave after reduction and ring closure 8 as a 2:1 mixture of two isomers (IR($CHCl_3$): 1665 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.50-5.75 (m, 1H), 4.95-5.10 (m, 2H), 3.82 (ddd, $^2/_3$ H, 3.55-3.75 (m, 1H), 3.38 (ddd, $^1/_3$ H), 3.00-3.20 (m, 1H), 1.3-2.5 (m, 11H)). Cyclization of the hydroxylactam from 4a yielded 7 as a single isomer (IR($CHCl_3$): 1675, 995 and 925 cm^{-1} and ^1H NMR ($CDCl_3$): δ 5.43-5.78 (m, 1H), 5.00-5.22 (m, 2H), 4.03 (ddd, J=6,6,6 Hz, 1H), 3.61 (ddd, J=11,7,7 Hz, 1H), 3.07 (m, 1H), 1.4-2.9 (m, 7H)). Ozonolysis of this product (O_3, CH_3OH, CH_2Cl_2, -78°C; then CH_3SCH_3) afforded in 90% yield a single isomer of aldehyde 11 (IR($CHCl_3$): 1725 and 1680 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.84 (d, J=3 Hz, 1H), 3.27 (ddd, J=6.5, 6.5, 6.5 Hz, 1H), 2.78 (ddd, J=11, 6.5, 6.5 Hz, 1H), 2.9-3.3 (m, 2H), 1.7-2.8 (m, 6H)).

These results indicate that the cyclization reaction of α-acyliminium ions

with allyl and propargyl silanes constitutes a useful method for the preparation of various bridgehead nitrogen bicyclic systems. In future papers we will report on the stereochemistry of the process as well as on its application to the synthesis of natural products, especially pyrrolizidine alkaloids[16].

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9. Imide 3a: solid, mp 48-51°C; IR($CHCl_3$): 2225, 1780, 1710, 1165, 850 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.64 (t, J=7 Hz, 2H), 2.71 (s, 4H), 2.47 (tt, J=7, 2.5 Hz, 2H), 1.40 (t, J=2.5 Hz, 2H), 0.08 (s, 9H).
10. Imide 3b: oil; IR($CHCl_3$): 2220, 1780, 1705, 1155, 850 cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.55 (t, J=7 Hz, 2H), 2.72 (s, 4H), 2.20 (m, 2H), 1.3-1.9 (m, 4H), 1.42 (t, J=2.5 Hz, 2H), 0.09 (s, 9H).
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13. Imide 4b: oil, IR($CHCl_3$): 1775, 1700, 1140, 850 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.1-5.6 (m, 2H), 3.52 (t, J=6.5 Hz, 2H), 2.72 (s, 4H), 2.04 (dt, 2H); 1.2-1.9 (m, 4H), 1.48 (d, J=7 Hz, 2H), 0.0 (s, 9H).
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(Received in UK 24 January 1983)