Tetrahedron Letters,Vol.26,No.1,pp 47 - 50,1985
Printed in Great Britain

0040-4039/85 $3.00 + .00

MECHANISTIC AND SYNTHETIC ASPECTS OF 2-AZA-1,3-DIENE PREPARATION THROUGH N-(1-TRIETHYLSILYLALLYL)IMINE PROTODESILYLATION

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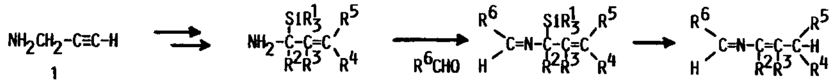
Summary. Features of a novel method for preparation of 2-aza-1,3-dienes involving CsF induced protodesilylation of N-(1-triethylsilylallyl)imines is described.

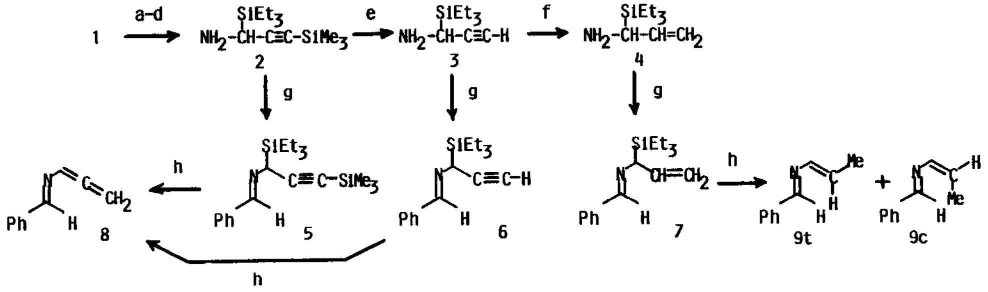
Substances containing the 2-aza-1,3-diene grouping represent a unique class of compounds as a result of their potentially interesting excited- and ground- state chemistry. Particularly significant is the Diels-Alder reactivity of these substances.[1] Several procedures with varying and often limited generality have been developed to prepare 2-aza-1,3-dienes.[2] In recent efforts designed to explore the chemistry of 2-aza-1,3-dienes,[1c] we have explored a potentially versatile method to prepare these substances (Scheme 1)involving N-(1-trialkylsilylallyl)-imine protodesilylation reactions.

Scheme 1.



In order to evaluate the feasibility of this route for azadiene synthesis, we have prepared the N-(1-triethylsilyl-allyl and -propargyl)imines 5 - 7 by condensation of the corresponding amines 2 - 4 with benzaldehyde (83-92%).[3] The requisite amines were prepared by use of the pathway (overall yield of 1 → 4 30 %) shown in Scheme 2.[4] This method for silylallyimine production should be sufficiently flexible to allow incorporation of complex substitution at the aldimine carbon and at the C=C positions.

Scheme 2.

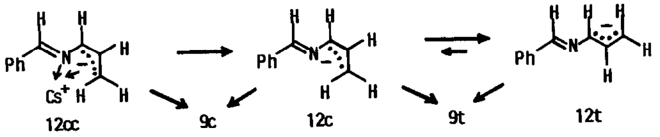


(a)$Me_2NCH(OMe)_2$; (b)n-BuLi, TMSCl; (c)nBuLi, TESCl; (d)N_2H_4; (e)LiOEt; (f)H_2,Pd/$CaCO_3$; (g)PhCHO, C_6H_6, ref; (h)CsF, H_2O

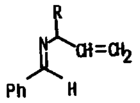
Cesium fluoride induced protodesilylation of the imines 5 - 7 is affected in either THF/H_2O/18-crown-6 or MeCN/H_2O (25°C, 1h) and leads to efficient (70-85%) formation of the 2-azatriene 8 and 2-azadienes 9 (Scheme 2). The presence of the allene grouping in 8 is readily established by ^{13}C-NMR (81.2/H_2C=,112.3/N-CH=,193.4/=C= ppm) and ^{1}H-NMR (5.34 dd, =CH_2; 6.89, t, NCH=) spectroscopic methods. Also, spectroscopic properties for the separable (glc) cis-trans isomeric azadienes 9 match those previously recorded.[2a]

The results from deuterium labeling studies and ^{1}H-NMR monitoring of these reactions provide mechanistic details about the protodesilylation processes. Firstly, desilylation of 7 (CsF/MeCN) conducted in the presence of D_2O leads to production of 9, mono-deuterated at the allylic methyl centers exclusively. This observation, coupled with the fact that N-allylbenzaldimine does not isomerize to 9 under the protodesilylation reaction conditions[5] suggests that formation of 9 involves kinetic γ-protonation of the intermediate iminoallylanion or its equivalent. Secondly, protodesilylation of 6 (CsF/d_8THF/18-crown-6) in the presence of D_2O provides the terminally mono-deutereated azatriene 8. ^{1}H-NMR monitoring of the reaction progress failed to reveal the presence of N-propargylbenzaldimine as an intermediate in this process. Finally, transformation of the bis-silylimine 5 to azatriene 8 (CsF/H_2O/d_8-THF/18-Crown-6) appears to involve sequential loss of the $SiEt_3$ (5 → 10) and $SiMe_3$ (10 → 11) groupings followed by isomerization of the propargylimine 11 to allenyl system 8. Accordingly, characteristic proton resonances associated with 10 and 11 rise and fall in a successive fashion when the conversion of 5 → 8 is monitored by ^{1}H-NMR spectroscopy. Independently prepared propargylimine 11 isomerized to 8 under reaction conditions[5] which mimic those present in the protodesilylation process.[6] These results demonstrate that a strong preference exists for γ-protonation of imino-allyl and -propargyl anions or their equivalents when sterically bulky (*e.g.*, $SiMe_3$) substituents are not present at this position.

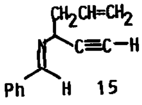
The synthetic significance of this method for 2-aza-1,3-diene preparation is heightened by observations which indicate the existence of a source of stereochemical control for protodesilylation of the silylallylimine 7. The azadiene 9t to 9c isomer ratio arising in reaction of 7 under the CsF/THF/18-crown-6 condition decreases dramatically when [H_2O] increases (*e.g.*, 9t:9c varies from 6 to 1 upon changing [H_2O] from 0.03 to 0.5M). An increase in [H_2O] has the opposite effect upon the 9t to 9c ratio for reactions in the CsF/MeCN system (*e.g.*, 9t:9c varies from 0.4 to 1 upon changing [H_2O] from 0.03 to 0.3M). This is a result of kinetic phenomena since 9t and 9c are configurationally stable under both reaction conditions. The comparative results hint at an unusual source of stereocontrol which perhaps is related to a kinetic preference for metal-chelated, cis-iminoallylanion 12cc formation,[7] and relative rates of geometric isomerization (12cc → 12c ⇆ 12t) versus protonation. In the THF/18-crown-6 system, isomerization to 12t should be rapid, owing to the external Cs^+ coordinating abilities of the solvent and macrocyclic ether, and competitive with γ-protonation at low [H_2O]. Conversion of 12cc should be slow in MeCN except at high [H_2O] where external complexation by H_2O is possible. In this case, the effect of [H_2O] on the 12cc protonation rate and the 12cc to 12c $\rightleftarrows$ 12t conversion could result in favored 9c formation at low [H_2O] and a 9t to 9c ratio which approaches 1.0 at high [H_2O]. The importance of metal ion complexation in controlling the azadiene isomer ratio gains support from the observation that addition of 18-crown-6 to reaction mixtures containing 7 under the CsF/MeCN/0.06M H_2O conditions causes a change in the 9t to 9c ratio from 0.5 to 0.9.



A final aspect of these studies concerns alkylative desilylation of the silicon substituted imines 6 and 7. Reaction of 7 (CsF, MeCN, 25°C, 16h) in the presence of either benzyl or allyl-bromide leads to formation of the products of α-alkylation 13 and 14 (70-74%). Similarly, the allylpropargylimine 15 is produced (73%) by desilylation of 6 in the presence of allybromide. In each case, products of α-alkylation were not detectable. The contrastingly different regiochemical selectivities displayed for protonation and alkylation of the iminoallyl anion intermediates derived from imines 6 and 7 are not simply rationalized.[8] However, this variability resembles that reported for alkylation and acylation of other heteroatom substituted allylanions.[9]



13 (R=Allyl)
14 (R=Benzyl)



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The results summarized above suggest that fluoride ion induced, protodesilylation of N-(1-trialkylsilylallyl)imines can serve as a useful method for 2-aza-1,3-diene synthesis. The versatility of this process in terms of its application to the synthesis of complex systems is under current scrutiny.

Acknowledgment. Support for this research from the Petroleum Research Fund administered by the American Chemical Society (1532-AC1) and from the National Institutes of Health (Gm-29016) is gratefully acknowledged.

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(1) (a) For a recent review of 2-azadiene Diels Alder chemistry, see Bolger, D., Tetrahedron, 1983, 39, 2869; (b) for early studies of electron rich 2-azadiene cycloadditions with electron

poor olefins see Sainte, F.; Serckx-Poncin, b.; Hesbain-Frisque, A.M.; Ghosez, L., J. Am. Chem. Soc., 1982, 104, 1428; Demoulin, A.; Gorissen, H.; Hesbain-Frisque, A.M.; Ghosez, L., J. Am. Chem Soc., 1975, 97, 4409; Gompper, R; Heinemann, U., Angew. Chem. Int. Ed., 1980, 19, 217; 1981, 20, 296; (c) more recently (Cheng, Y.S.; Mariano, P.S.; unpublished results) electronically neutral 2-azadienes have been shown to undergo Lewis-acid catalyzed Diels-Alder cycloadditions with electron rich olefins.

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(3) All new compounds reported in this communication have spectroscopic data in complete accord with the assigned structures.

(4) Chen, S.F.; Ullrich, J.W.; Mariano, P.S.; J. Am. Chem. Soc., 1983, 105. 6160.

(5) Conditions for the attempted isomerizations include Me_3SCl and $HClO_4$ since in the presence of H_2O, Me_3SiF is formed in the protodesilylation reactions.

(6) (a) Why N-propargylbenzaldimine rearranges to the azatriene 8 while N-allylbenzaldimine fails to rearrange to azadiene 9 under the reaction conditions[5] appears to be due to the added driving force in the former case resulting from the normal tendency of 3-alkyl substituted-1-alkynes to tautomerize to their allene counterparts. For example, the conversion of 1-butyne to 1,2-butadiene is exothermic by ca. 1 kcal/mol [6b] (b) Srinivasan, R., J. Am. Chem. Soc., 1960, 82, 5663; Haller, I; Srinivasan, R., J. Am. Chem. Soc., 1966, 88, 3694; Kebarle, P., J. Chem. Phys., 1963, 39, 2218.

(7) (a) Rationalizations for preferred formation of cis-enamines by protonation or alkylation of 1-aminoallyl anions also involve internal metal chelation;[7b] (b) Sauer, J.; Prahl, H., Tetrahedron Lett., 1966, 2863; Chem. Ber. 1969, 102, 1917; Riviere, M.; Lattes, A.; LeTran, M.; Ava, D., Bull. Soc. Chim. Fr., 1972, 730; Ahlbrecht, H., Chimia, 1977, 31, 391.

(8) Note that isomerization of the propargyl to the allenyl system does not occur in this case since a proton source is missing under these conditions.

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(Received in USA 5 September 1984)