

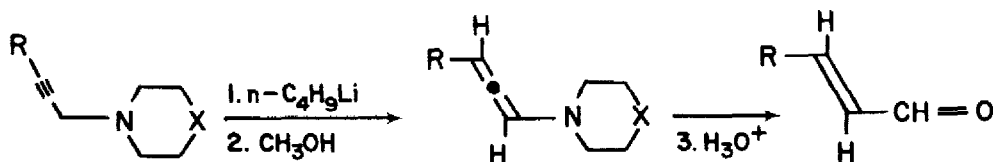
SYNTHESIS OF α,β -UNSATURATED ALDEHYDES
VIA 1-AMINOPROPA-1,2-DIENES: MECHANISTIC STUDIES

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Summary: A facile prototropic rearrangement of N-(prop-2-ynyl)amines to 1-aminopropa-1,2-dienes, followed by acid hydrolysis, affords a novel synthesis of α,β -unsaturated aldehydes. The mechanism of the reaction has been examined by deuterium labeling.

Heterosubstituted allenes are of interest as synthetic precursors to α,β -unsaturated aldehydes, and acid hydrolysis of alkoxyallenes has been reported¹ to produce the desired ethylenic carbonyl compounds. We have examined a number of the corresponding allenic enamines 2 (Scheme 1) obtained from the tertiary N-(prop-2-ynyl)amines 1² (Table 1) by metallation with n-butyl lithium at -76°C followed by protonation with methanol at 0°C .



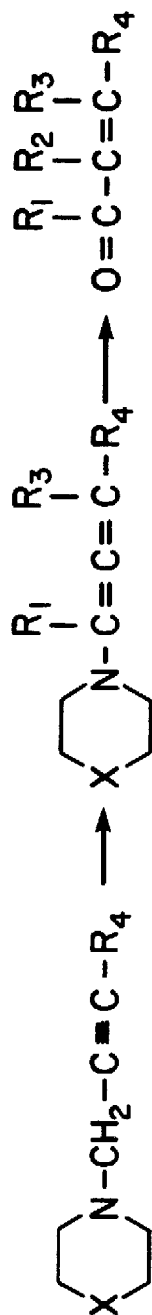
Scheme 1

The allenic structures 2 were confirmed by their ir (1950 cm^{-1} , HC = C = CH), nmr (two downfield doublets with $J = 6\text{ Hz}$ due to two vinylic protons) and mass spectra.³ We found that hydrolysis of the enamines 2 with aqueous acetic acid (Scheme 1) proceeded quantitatively to give the pure α,β -unsaturated aldehydes 3 in high overall yield⁴ (Table 1). The mechanism of the hydrolysis was examined using deuterium labeling (Table 1).

Hydrolysis of the allenic enamine 2a with acetic acid - 0-d_1 in D_2O gave (Table 1) cinnamaldehyde - 2-d_1 (3b). The fact that the aldehyde proton appeared as a singlet (9.72 ppm) indicated that labeling of C-2 with deuterium was complete. Protonation of the lithio-derivative (from 1a)⁵ with methanol - 0-d_1 led to the allenic enamine 2b containing only the vinylic proton at C-1. Hydrolysis of 2b using aqueous acetic acid afforded cinnamaldehyde- 3-d_1 (3c) showing the aldehydic proton as a doublet, while reaction of 2b with acetic acid- 0-d_1 in D_2O yielded cinnamaldehyde- $2,3\text{-d}_2$ (3d), with the aldehyde proton appearing as a singlet.

Similar results were obtained using N-(3-phenylprop-2-ynyl)morpholine (1b) or N-(hept-2-ynyl)piperidine (1c) as starting materials (Table 1). Alkylation of the lithio-derivative from 1b

Table 1



N-(Prop-2-ynyl) amine <u>1</u>		1-Aminopropa-1,2-diene <u>2</u>		α, β -Unsaturated Aldehyde <u>3</u>		
Compound	X R ₄	Reagents Used	Compound	R ₁ R ₃	R ₁ R ₂	Overall Yield (%)
<u>1a</u> ⁵	CH ₂ C ₆ H ₅	a, b	<u>2a</u>	H H	H H	88
<u>1a</u>	CH ₂ C ₆ H ₅	a, b	<u>2a</u>	H H	H D	88
<u>1a</u>	CH ₂ C ₆ H ₅	a, d	<u>2b</u>	H D	H* H**	88
<u>1a</u>	CH ₂ C ₆ H ₅	a, d	<u>2b</u>	H D	H* D	88
<u>1b</u> ⁵	0 C ₆ H ₅	a, b	<u>2c</u>	H H	H H	88
<u>1c</u> ⁶	CH ₂ n-C ₄ H ₉	a, b	<u>2d</u>	H H	H H	68
<u>1b</u>	0 C ₆ H ₅	a, c	<u>2e</u>	H CH ₃	H H	86
<u>1b</u>	0 C ₆ H ₅	a, c then a, d	<u>2f</u>	D CH ₃	D D	86

Reagents used: a, n-C₄H₉Li/hexane; b, CH₃OH; c, (CH₃)₂SO₄; d, CH₃OD; e, CH₃COOH/H₂O; f, CH₃COOD/D₂O;

** 0.3 D

* 0.4 D

with dimethyl sulfate at -76°C gave the allenic enamine N-(3-phenylbuta-1,2-dienyl)morpholine (2e), converted by acetic acid hydrolysis into 3-methylcinnamaldehyde (3g). Metallation of 2e followed by deuteration with methanol- O-d_1 gave N-(3-phenylbuta-1,2-dienyl)morpholine-1- d_1 (2f), hydrolysis of which with acetic acid- O-d_1 in D_2O afforded 3-methylcinnamaldehyde-1,2- d_2 (3h), shown by nmr analysis to be completely deuterated at C-1 and C-2.

The results of the deuterium labeling experiment shown in Table 1 support the mechanism summarized in Scheme 2 for the hydrolysis of the allenic enamines. The observed occurrence of 0.3 D at C-2 in the product 3c (Table 1) is explained by partial exchange of acetic acid with methanol- O-d_1 still present in the solution from the previous step. The finding of 0.4 D at the aldehydic proton (C-1) in both 3c and 3d (Table 1) suggests that the allenic enamine 2b undergoes partial metallation at C-1 by the lithium methoxide produced in the previous step (1 + 2) and is then rapidly deuterated by excess methanol- O-d_1 .

In addition to the preparative ease and high yield of the method, the possibility of specifically introducing label into the C-2 and C-3 positions of the product has synthetic utility.

References and Notes

1. (a) Y. Leroux and R. Mantione, *Tetrahedron Lett.*, 591 (1971); (b) E. J. Corey and S. Terashima, *Tetrahedron Lett.*, 1815 (1972).
2. Readily obtained from the corresponding commercially available propargyl alcohols via their bromo-derivatives by reaction with piperidine or morpholine.
3. All compounds gave ir, nmr and mass spectra in full agreement with proposed structures.
4. Some of the original N-(prop-2-ynyl)amine 1 was present and was readily removed by washing with dilute acid. All yields refer to the pure aldehyde.
5. H. J. Reich and S.K. Shah, *J. Amer. Chem. Soc.*, 99, 263 (1977).
6. S. Shatzmiller and A. Eschenmoser, *Helv. Chim. Acta*, 56, 2975 (1973).
7. The p-nitrophenylhydrazone had m.p. and mixed m.p. $190-191^{\circ}$; J.M. Lalancette, G. Rollin and A. P. Dumas, *Can. J. Chem.*, 50, 3058 (1972).
8. The p-nitrophenylhydrazone had m.p. and mixed m.p. $150-152^{\circ}$; P. Gyax, T.K. DasGupta and A. Eschenmoser, *Helv. Chim. Acta*, 55, 2205 (1972).
9. The 2,4-dinitrophenylhydrazone had m.p. and mixed m.p. $210-212^{\circ}$; R.C. Cookson and N.W. Hughes, *J. Chem. Soc. Perkin I*, 2738 (1973).

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