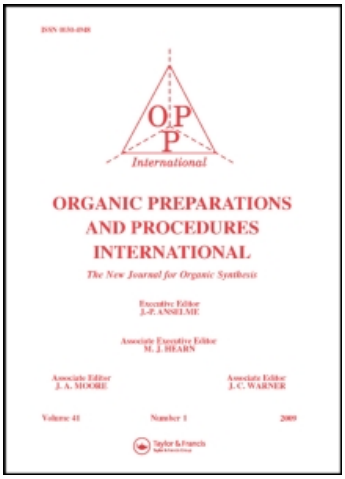

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A CONVENIENT SYNTHESIS OF 2-AMINOALKYL ALLYL ETHERS

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A CONVENIENT SYNTHESIS OF 2-AMINOALKYL ALLYL ETHERS

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(04/24/92)

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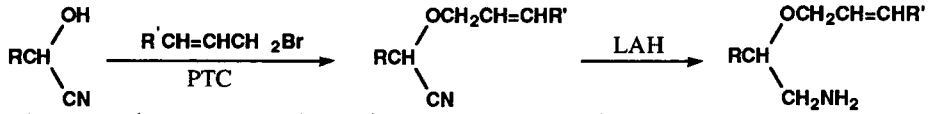
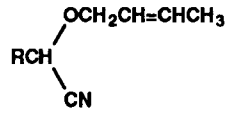
In the course of our investigations on the synthesis of morpholines, we needed a useful method for the synthesis of differently substituted 2-aminoalkyl allyl ethers. We recently reported a route for the preparation of 2-benzylaminoalkylallyl ethers by allylation of the corresponding benzylideneamino alcohols and followed by reduction with sodium borohydride.[1] However, direct allylation of 2-aminoalcohols[2] occurred exclusively at nitrogen regardless of different reaction conditions tried. Retrosynthetic analysis suggested the use of suitably substituted O-allylcyanohydrins (**2**) as intermediates which could then be reduced to the desired compounds **3** according to the scheme shown.

The cyanohydrins **2** were prepared by direct one-pot synthesis from aldehydes and allyl bromide under PTC conditions.[3] Our attempts to obtain O-allylated cyanohydrin with 3-chloro-2-methylpropene failed.



a) R = Et, R' = H; b) R = *n*-C_3H_7, R' = H; c) R = *n*-C_3H_7, R' = CH_3; d) R = *i*-C_3H_7, R' = H; e) R = *i* -C_3H_7, R' = CH_3; f) R = *i*-C_3H_7, R' = C_6H_5; g) R = *n*-C_4H_9, R' = H; h) R= *t*-C_4H_9, R' = H; i) R = C_6H_5, R' = H; j) R= *c*-C_6H_{11}, R' = H

As would be expected,[4] in some cases we obtained a mixture of the desired allylated cyanohydrin **4** and its rearranged isomer, the 1-methyl-2-propenyl ether **5**. The ^1H NMR spectra of the



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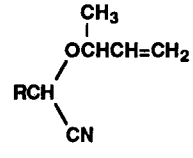

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reaction product (mixture of both isomers) displayed sharp signals for the CH_3CH= group at δ 1.68-1.76 as well as the characteristic doublet for a CH_3CH- group at δ 1.11-1.15 in a ratio 60:40 with the allylated cyanohydrins **4** predominanting; the isomers were not separated. However, allylation with cinnamyl bromide gave predominantly the expected product **2f** (61%) along with a small amount of the rearranged isomer.

As was demonstrated by McIntosh,[3] the synthesis of allyl ethers starting from ketones failed under conditions used with the aldehydes. Our attempts under different reaction conditions (solid potassium cyanide without solvent)[5] also were unsuccessful.

TABLE 1. O-(2-Alkenyl)aldehyde Cyanohydrins **2**

	Yield (%)	bp. (°C/torr) (lit. bp.)	Analysis Calcd. (Found) C	H	N
2a	21	69-71/20	67.16 (66.90)	8.85 (8.71)	11.19 (10.97)
2b	42	70-72/2 (64-65/7.4)[3]			
2c	41	87-88/14	70.59 (70.81)	9.87 (9.71)	9.15 (9.04)
2d	54	80-82/25 (58-60/8.5)			
2e	58	92-93/21	70.59 (70.41)	9.87 (10.02)	9.15 (9.26)
2f	61	162-164/3 (142-144/1.7)[3]			
2g	60	84-85/11	70.59 (70.32)	9.87 (9.65)	9.15 (8.89)
2h	50	73-75/13	70.59 (70.33)	9.87 (9.93)	9.15 (9.28)
2i	35	119-121/10 (132-134/16)[3]			
2j	71	118-120/12 (86-88/1.9)[3]			

IR spectra (liquid). 1050-1070, 1090-1100 (COC), 2220-2230 (CN) cm^{-1}.

The O-allyl ethers **2** were reduced smoothly in good yields (Table 2) by $LiAlH_4$ in ether. The structure of the desired 2-aminoalkyl allyl ethers **3** was confirmed by their IR and ^1H NMR spectra (characteristic bands for NH_2 group in the region 3350-3400 cm^{-1} and typical multiplets for allylic groups at δ 5.05-5.25 and 5.70-5.90).

EXPERIMENTAL SECTION

All starting compounds were available commercially. The IR spectra ($CHCl_3$) were obtained on a Specord IR 75 spectrophotometer, Zeiss (Germany). ^1H NMR spectra were recorded on a Brucker AM-250 WB spectrometer (250 MHz) in deuteriochloroform with TMS as internal standard.

Synthesis of O-Allyl Cyanohydrins 2. General Procedure.- To a mixture made up of a solution of 20 g (0.3 mol) of KCN in 50 mL water, 100 mL dichloromethane and 2.5 g triethylbenzylammonium chloride (TEBA) was added with continuous stirring a mixture of 0.25 mole of the corresponding aldehyde and 0.25 mole 2-alkenyl bromide. After being stirred 24 hrs at room temperature, the

organic layer was separated and washed with 100 mL of water. The solvent was removed and 250 mL ether was added to induce the precipitation of TEBA. The solution was then dried over Na_2SO_4 and after the removal of the solvent, the residue was distilled at reduced pressure. The analytical data of the products obtained are summarized in Table 1.

Synthesis of 2-Aminoalkyl Allyl Ethers 3.- To a suspension of 3.04 g $LiAlH_4$ in 300 mL anh. ether, a solution of 0.05 mole of the corresponding O-allylcyanohydrin **2** in 50 mL anh. ether was added. The mixture was refluxed 20 hrs and after cooling 200 mL ether was added. The unreacted $LiAlH_4$ was decomposed by addition of 25-30 mL 30% aqueous NaOH.[6] The organic layer was separated, dried over Na_2SO_4, and after removal of the ether, the residue was distilled at reduced pressure.

TABLE 2. 2-Aminoalkyl (2-alkenyl) Ethers **3**

	Yield (%)	bp. (°C/torr)	Analysis Calcd. (Found) C	H	N
3a	79	76-78/20	65.11 (65.34)	11.71 (11.53)	10.84 (10.71)
3b	65	72-74/9	67.12 (67.18)	11.97 (12.15)	9.78 (9.57)
3c	83	82-83/12	68.78 (69.03)	12.19 (12.05)	8.91 (8.84)
3d	63	67-68/10	67.12 (66.41)	11.97 (12.21)	9.78 (9.88)
3e	88	88-89/16	68.78 (68.63)	12.19 (12.26)	8.91 (8.75)
3f	72	148-150/8	78.09 (78.35)	10.53 (10.41)	6.51 (6.25)
3g	82	82-83/8	68.78 (69.03)	12.19 (11.95)	8.91 (9.04)
3h	68	122-124/55	68.78 (69.01)	12.19 (11.85)	8.91 (9.01)
3i	76	128-129/10	74.52 (74.30)	8.53 (8.42)	7.90 (8.02)
3j	86	130-131/12	72.09 (71.81)	11.55 (11.80)	7.64 (7.42)

IR spectra (liquid): 1050-1070, 1090-1100 (COC), 3350-3400 (NH_2) cm^{-1}

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6. For the synthesis of **2i** the aqueous layer was acidified with HCl (1:1) and then the neutral compounds were extracted with ether. The desired product was obtained by ether extraction of the basified aqueous layer.

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PREPARATION OF LOW MOLECULAR WEIGHT, OPTICALLY ACTIVE ALLYLIC ALCOHOLS FROM (*S*)-(-)-ETHYL LACTATE

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(07/27/92)

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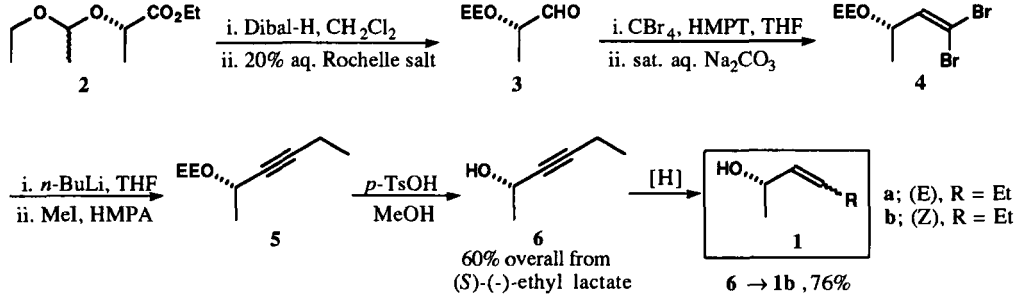
In conjunction with various [2,3]sigmatropic,[1] enolate Claisen,[2] and aza-Claisen[3] rearrangement studies ongoing in our laboratories, we required ready access to a variety of enantiomerically pure secondary allylic alcohols of general structure **1**. Optically enriched crotyl alcohols (i.e., **1** where



R = Me) are available by Sharpless kinetic resolution,[4] but optical purities are only modest (≈ 91% ee) and α,β-ynone reduction protocols[5] are problematic in purifying the volatile product from the chiral