Facile One-Pot Syntheses of 1-Allenylpyrroles

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A number of pyrroles have been *N*-allenylated in reasonable to good yields by treatment with anhydrous potassium hydroxide and propargyl chloride, 2,3-dichloro-1-propene or 1,2,3-trichloropropane in anhydrous dimethyl sulfoxide.

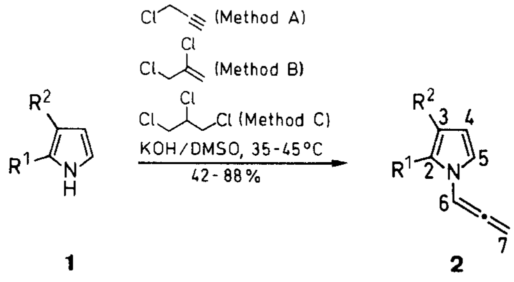
Compounds with the system $NCH{=}C{=}CH_2$ are usually obtained by base-catalyzed isomerization of the corresponding *N*-propargylic compounds using tertiary alkoxides[1-3] in dimethyl sulfoxide, hexamethylphosphoric triamide (HMPT) or sodium amide on alumina.[4] The requisite starting compounds are accessible by reaction of aliphatic secondary amines,[3] or – when the nitrogen atom is incorporated in an heteroaromatic ring – of the *N*-metalated heterocyclic compound and propargyl bromide. In the latter cases yields of the *N*-propargyl compounds are from low to moderate.[1,4]

The ratio of the three compounds occuring in the base-catalyzed reaction, in general, strongly depends upon the nature of the substituents, the time of interaction, and the base–solvent system used.

$$NCH_2C{\equiv}CH \leftrightarrows NCH{=}C{=}CH_2 \leftrightarrows NC{\equiv}CCH_3$$

As a consequence, only a few compounds with the allenyl system have been obtained in satisfactory yields and purity.[1-4]

We report here three efficient procedures for the preparation of 1-allenylpyrroles, making these compounds available in sizable amounts. In method A the pyrrole **1** is reacted with propargyl chloride in anhydrous dimethyl sulfoxide in the presence of potassium hydroxide.



Presumably the *N*-propargylpyrrole derivative is formed first. The isomerization to the allene occurs under the influence of the excess of potassium hydroxide, which in dimethyl sulfoxide exhibits as a strongly basic reagent, comparable with tertiary alkoxides (cf. Ref. 3). It should be noted that similar good results are obtainable when using 2,3-dichloro-1-propene (Method B) and 1,2,3-trichloropropane (Method C) as allenylating reagents. These three allenylations of pyrroles were only briefly announced by us[5-7] without experimental details. The latter two variants, however, require the use of a much larger excess of potassium hydroxide, that has been freed from water by heating at 500 °C. We have not investigated whether in the formation of the allenes in these cases, the first step involves reaction of the pyrrole anion with propargyl chloride (formed from the polychloro compounds by dehydrochlorination) or nucleophilic substitution of a terminal chlorine atom by the pyrrole anion.

Table. *N*-Allenylpyrroles **2** Prepared

Product[a]	R^1	R^2	Method	Yield (%)	n_D^{20}	Molecular Formula[b] or Lit. bp (°C)/Torr	^1H NMR ($CDCl_3$/HMDS), δ[c]				
							H-3	H-4	H-5(2)	H-6	H-7
2a	H	H	A C	63[d] 50	1.5590	30/0.5[1]	6.18	6.18	6.70	6.77	5.40
2b	Me	H	A	68	1.5520	C_8H_9N (119.7)	5.88	6.10	6.73	6.83	5.45
2c	Me	Me	A	49	1.5568	$C_9H_{11}N$ (133.2)	–	5.98	6.64	6.81	5.42
2d	$(CH_2)_4$		A B	88 42	1.5790	$C_{11}H_{13}N$ (159.2)	–	5.97	6.62	6.76	5.42
2e	$(CH)_4$[e]		A	45	–	$C_{11}H_9N$ (155.2)	–	6.55	7.54	7.14	5.56
2f	Ph	H	A B C	67 70 62	1.6370	$C_{13}H_{11}N$ (181.2)	6.26	6.26	6.94	6.94	5.43

[a] All allenylpyrroles show the characteristic C=C=C vibration at $\nu = 1950-1960\ cm^{-1}$ in the IR spectra.
[b] Satisfactory microanalytical data for C, H and N (deviation from calculated values < 0.3%) were obtained.
[c] Measured at 100 MHz.
[d] Bp 27°C/1 Torr.
[e] Abbreviation for 1-propadienylindole.

The 1-allenylpyrrole **2** ($R^1 = R^2 = H$) is a colourless liquid, the other derivatives are yellow-orange liquids rapidly darkening upon exposure to air at 20 °C. At low temperatures (– 20 to – 70 °C) and under argon, their quality can be maintained for several weeks.

Allenylation of Pyrroles 1; General Procedures:

Method A, with Propargyl Chloride: A mixture of the pyrrole **1** (0.025 mol), KOH pellets (15% water content, 5.6 g, 0.10 mol) and DMSO (water content < 0.2%) (50 mL) was stirred at r.t. for 45 min. Subsequently, freshly distilled propargyl chloride (3.73 g, 0.05 mol) was added over 10 min, while keeping the internal temperature between 28 and 30 °C (exothermic reaction). A further amount of KOH (16.8 g, 0.30 mol, obtained by treating the commercially available pellets for 4 h at 500 °C) was added, while heating between 35 and 40 °C for 20 min and then the reaction mixture was poured into H_2O (100 mL) under efficient stirring. The mixture was extracted with Et_2O (3 × 50 mL). The Et_2O extract was washed with H_2O until the aqueous layer had become neutral, and subsequently dried ($MgSO_4$). The liquid remaining after evaporation of the solvent in vacuo was chromatographed over alumina, using a mixture of Et_2O and hexane (1 : 3) as eluent. Evaporation of the solvent in vacuo (the last traces at < 0.5 Torr) gave the *N*-allenylpyrroles **2** (Table).

Method B, with 2,3-Dichloro-1-propene: To a stirred mixture of the pyrrole **1** (0.025 mol), and KOH (8.4 g, 0.15 mol) (calcined for 4 h at 500 °C) in DMSO (< 0.2% H_2O) (50 mL) was added from a dropping funnel over 10 min 2,3-dichloro-1-propene (4.16 g, 0.0375 mol). The temperature of the mixture rose within 10 to 15 min to 40–45 °C. After warming for an additional 20 min at 40 °C (internal temperature), the mixture was poured into water (100 mL) with vigorous stirring. Isolation of the compounds **2** was carried out as described above (Table).

Method C, with 1,2,3-Trichloropropane: The allenylation of **1** with 1,2,3-trichloropropane was carried out in a way similar to the reaction with 2,3-dichloropropene, using **1** (0.025 mol), KOH (11.2 g, 0.2 mol, heated for 4 h at 500 °C), DMSO (50 mL, water content < 0.2%) and 1,2,3-trichloropropane (5.53 g, 0.38 mol) (Table).

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