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REGIOSPECIFIC AND STEREOSELECTIVE SYNTHESIS OF E OR Z-N-ALLYL PYRROLES VIA VINYLPHOSPHONIUM SALTS

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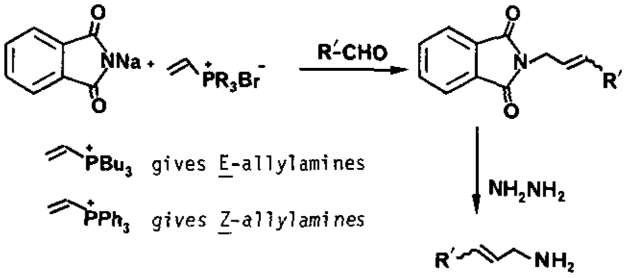
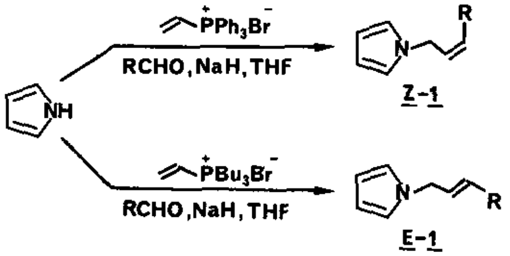
Abstract - Reaction of N-sodiopyrrole with vinyltriphenyl phosphonium bromide and various aldehydes gives only N-allylpyrroles with generally very high Z-geometry. The same reaction using vinyltri-n-butylphosphonium bromide furnished N-allylpyrroles with moderate to high E-geometry.

Considerable literature exists[1] on pyrrole alkylation (N vs C) and of the various experimental parameters which favor regioselective alkylations. In particular, N-allylation vs C-allylation of pyrroles has also been studied recently by Papadopoulus and Vanderwerf[2].
We now describe an extension of our earlier work[3] involving amide addition to vinyl phosphonium salts with in situ trapping by aldehydes to give allylamines (eq. 1) as applied to N-sodiopyrrole (Schweizer reaction[4]). When sodium hydride (1.5 mmol) was added to a suspension of pyrrole (1.1 mmol), vinylphosphonium bromide (1.1 mmol) and an aldehyde (1.0 mmol) in THF at room temperature and the mixture allowed to stir for 8 h, the N-allylpyrrole product was obtained in good yield after chromatography (eq. 2). If vinyltributylphosphonium bromide is utilized, the product is, in general, the E isomer 1. However, if vinyltriphenylphosphonium bromide is employed, the Z isomer 1 predominates. No trace of a C-allylated positional isomer could be detected in the crude reaction mixture. The extent of the stereoselectivity for the reaction can be seen in Table 1.

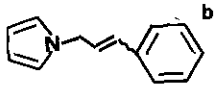
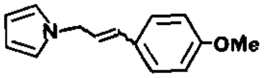
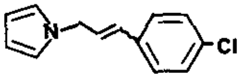
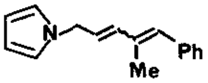
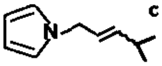
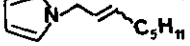


(1)



(2)

TABLE 1. (E and Z)-N-Allylpyrroles, 1

Product[a]	$CH_2=CH\overset{\oplus}{P}R_3\overset{\ominus}{Br}$	E:Z[e]	Yield[g] (%)		Chem. Shift Allylic $CH_2(\delta)$[h]
 [b]	Ph	10:90	72	E	4.62, J=4.5Hz
	Bu	91:9	98	Z	4.72, J=6.80, 1.90Hz
	Ph	9:91	46	E	4.55, J=5.37Hz
	Bu	86:14	91	Z	4.72, J=6.71, 1.83Hz
	Bu	95:5	90	E	4.60, J=4.50Hz
				Z	4.70, J=6.00, 1.75Hz
	Ph	22:78	60	E	4.58, J=5.71Hz
	Bu	99:1	81	Z	4.75, J=6.00Hz
 [c]	Ph	1:99	44	E	4.35, J=5.00Hz
	Bu	50:50[f]	27	Z	4.52, J=5.61Hz
 [d]	Ph	3:97	65	E	4.38, J=5.00Hz
	Bu	43:57	55	Z	4.48, J=5.50Hz

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a) Products were determined by usual spectroscopic means. M/e were determined. b) M^+, 183. c) M^+, 149. d) M^+, 177. e) There was no change in the E/Z ratio before and after chromatography. Ratios were determined by ^1H-NMR integration and/or gas chromatography (capillary column, SE-52, 2%, 100-200°C programmed at 2°/min). f) Accurate ratio could not be determined due to peak overlap, ±10%. g) Yields are not optimized in all cases. h) $CDCl_3$ soln.

As noted earlier[3], changing the ligand on phosphorus from electron withdrawing (phenyl) to electron donating (butyl) results in a dramatic change in the olefin stereochemistry. It is interesting to note that these ylides are prepared under "salt-free" conditions, and are of the non-stabilized type. These factors should lead predominantly to the formation of cis olefinic products via decomposition of the initially formed oxaphosphetane intermediate[5]. Indeed, this result is observed for the triphenylphosphonium ylide which produces the kinetically favored Z olefin. In contrast, the tri-n-butyl ylide results in selective E olefin formation, the more thermodynamically favored isomer. Since the reaction conditions are identical for each vinylphosphonium salt, the observed stereochemical results herein are controlled solely by the electronic nature of the group attached to phosphorus[6]. The electron donating butyl groups on phosphorus apparently act to stabilize the transition state, thereby allowing equilibration of the betaine intermediate[7]. Decreasing the electron density at the aldehydic carbon should also serve to facilitate this process by polarization of the oxaphosphetane C-C bond. This is the case for the aldehydes studied, the degree of E selectivity increases in proportion to the electron withdrawing ability of the substituent; $C(CH_3)C(H)Ph > pClC_6H_4 > C_6H_4 > pMeOC_6H_4$. Electron donating substituents, alkyl aldehydes, result in a decreased E selectivity.

A typical experimental procedure follows: Pyrrole (1.1 mmol), vinyltributylphosphonium or vinyltriphenylphosphonium bromide (1.1 mmol), and the aldehyde (1.0 mmol) were suspended in 20 ml dry THF under a nitrogen or argon atmosphere. Sodium hydride (60% oil dispersion, 1.5 mmol) was then added and the heterogeneous mixture was stirred at 23-25°C for 8 h. The mixture was poured into 50 ml water and 50 ml ether and the layers separated. The aqueous phase was extracted with ether (2x50 ml) and the combined ethereal extracts were washed with brine (1x25 ml), dried (K_2CO_3) and concentrated. The residue was chromatographed on silica gel (200-400 mesh) using 20% ethyl acetate-hexane as eluent.

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