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N-ALKYL-β-AMINOETHYLPHOSPHONIUM SALTS.

USEFUL REAGENTS FOR THE SYNTHESIS OF 2° ALLYLAMINES

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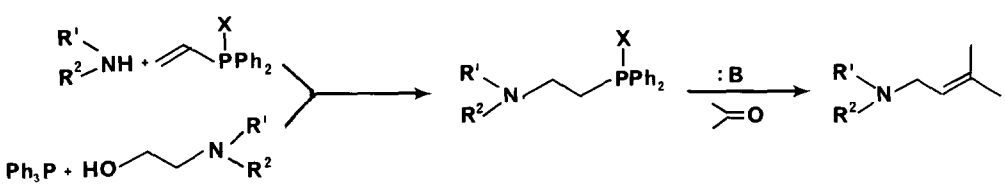
Summary: An improved procedure for the preparation of N-alkyl-β-aminoethylphosphonium salts, and the utilization of these functionalized salts in the preparation of secondary allylamines via the Wittig reaction is reported.

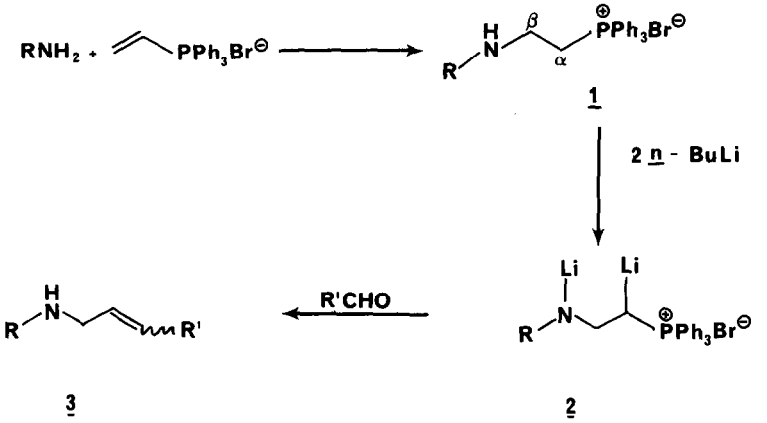
Recently there have been a number of reports describing the preparation of N,N-disubstituted allyl amines via the Wittig route involving N,N-disubstituted-β-aminoethylphosphonium salts[1] or vinylphosphine oxides[2] (Scheme 1). We reported[3] the addition of phthalimido anions to vinylphosphonium salts and carbonyl compounds to generate primary allyl amines with considerable E,Z-selectivity.

Scheme 1



R', R² = Alkyl (ref. 1,2) X = O, Ph (ref. 1,2)
R', R² = Phthaloyl (ref. 3) X = Ph (ref. 3)

We now describe an improved procedure for the preparation of N-alkyl-β-aminoethylphosphonium salts 1, and demonstrate that the di-lithio derivatives 2 are suitable precursors for generating secondary allyl amines 3 via the Wittig reaction, a process previously reported[1a] as being problematic. In addition, the allyl amine products obtained from aromatic or unsaturated aldehydes show a marked preference for the trans olefin, an unexpected result for reactions of non-stabilized ylides[4].



The monoalkyl-β-aminoethylphosphonium salts 1 were smoothly prepared by heating to reflux (12 h) an equimolar quantity of a primary amine and vinyltriphenylphosphonium bromide (Aldrich) in acetonitrile. Evaporation of the solvent and recrystallization from acetonitrile or acetone gave the salts 1 in >90% yield (Table 1). These salts tend to be hygroscopic and will decompose at or near their melting point. When stored under Argon, the salts are stable for several days and may be utilized in synthesis if rapid transfers are employed. Attempted preparation of 1 using the lithium salt of primary amines gave only polymeric products when added to the vinylphosphonium salt[5]. This procedure differs markedly from that of Marxer[1a] or Evans[1b] in that high temperatures (120°-150°C) and strongly acidic conditions, as well as the

TABLE 1. N-Alkyl-β-Aminoethylphosphonium Salts 1

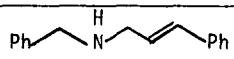
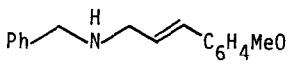
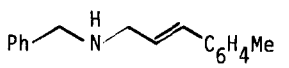
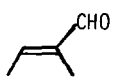
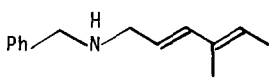
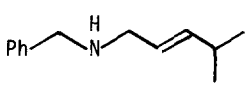
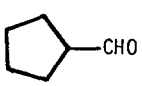
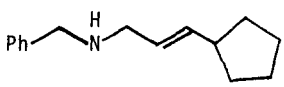
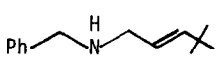
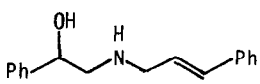
RNH_2	1(%)	H'-nmr ($CDCl_3$)				^{13}C-nmr ($CDCl_3$)[h]		
		α[f]	β	$J_{PH}(\alpha)$	$J_{PH}(\beta)$	α	β	ipso
$PhCH_2$	95[a]	3.00	4.00	17.71	11.71	23.49	41.99	118.78
p-$FC_6H_4CH_2$	97[b]	2.96	3.98	17.71	11.71	24.69	42.52	118.89
p-$ClC_6H_4CH_2$	95[c]	2.98	4.04	17.71	11.71	24.57	42.52	118.83
Cyclohexyl	96[d]	3.00	4.02	18.21	11.78	24.28	39.60	118.25
Ph-CHCH$_2$- (OSiMe$_2$Bu^t)	90[e]	2.93	g	20.57	--	24.80	43.55	119.18

a) Mp 178-179°; b) Mp 195-197°; c) Mp 186-189°; d) Mp 147-149°; e) Mp 68-71°; f) $J_{H\alpha H\beta}$ for all salts are 6-6.3 Hz; g) The β-H is masked by other signals; h) J_{PC} for all salts ranged: J_{PC_α} 50-55 Hz; J_{PC_β} 4.4-5.8 Hz; $J_{PC_{ipso}}$ 86.45 Hz.

limitations due to the availability of β-ethanolamines are avoided. For example, the preparation of the silyloxy substituted phosphonium salt (Table 1, entry 5) would not be feasible via the previously reported[1a] procedure. The generality of the present method was also demonstrated by the preparation of N,N-dibutyl-β-aminoethylphosphonium bromide (95%, mp 138°-140°C; lit.[1a] mp 142°-144°C).

When a suspension of the N-alkyl-β-aminoethylphosphonium salt in THF was treated with 2 equivalents of nBuLi (hexane) at RT (rapid addition), the dianion 2 formed as a deep red, clear solution. After stirring 30 min., the aldehyde (1.0 equiv.) was added (RT), and the resulting yellow suspension was stirred 12-14 h at ambient temperature followed by hydrolysis with 5% HCl (aq. soln.). Ether extraction removed the non-basic material, and subsequent basification and ether extraction of the aqueous phase provided the secondary allyl amine product 3 (Table 2). Marxer[1a] reported a 6% yield when he attempted to use a primary amine in this process.

TABLE 2. N-Alkyl Allylamines 3.

Aldehyde	Solvent	Allylamines	% Yield	E:Z[a]
PhCHO	THF		73	71:29
p-$MeOC_6H_4CHO$	Et_2O		73	82:18
p-MeC_6H_4CHO	Et_2O		40	68:32
	THF		90	67:33[b]
	Et_2O		69	92:8
Me_2CHCHO	THF		81	37:63
	Et_2O		57	20:80
	Et_2O		51	46:54
t-BuCHO	Et_2O		88	82:18
PhCHO	THF		40[c]	78:22

a) Determined by integration of the allylic CH_2 protons; E protons were upfield in all cases from Z isomer. b) This ratio was transformed into 92:8 by heating in toluene with 0.25% iodine. Other ratios changed only slightly under equilibration. c) Silyl group was cleaved during acidic quench.

The E,Z-selectivity of the reaction is worthy of some comment. There have been some reports of trans-selective Wittig olefination reactions with non-stabilized ylides possessing a distal oxido or carboxyl group[6]. Trans-olefin selectivity was exhibited for aromatic, but not aliphatic aldehydes. The results we have obtained with the β-amino functionalized ylide reagents are entirely analogous. We feel that the presence of an internal nucleophile serves to increase electron density at phosphorus[7], a phenomenon known to increase the ratio of E olefin product[4]. Although the E:Z ratios are not highly favorable, the fact remains that functionalized primary amines can be employed in this homologation sequence. The unique trans selectivity observed provides another example of internal nucleophilic group induced stereoselectivity.

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REFERENCES

1. a) A. Marxer and T. Leutert, Helv. Chim. Acta, 61, 1708 (1978); b) D. J. Hart, P. A. Cain, D. A. Evans, J. Am. Chem. Soc., 100, 1548 (1978); c)E. Cereda, M. Attolini, E. Bellora, A. Donetti, Tetrahedron Letters, 23, 2219 (1982); d) E. E. Schweizer, L. D. Smucker, R. J. Votrol, J. Org. Chem., 31, 467 (1966).

2. D. Cavella and S. Warren, Tetrahedron Letters, 23, 4505 (1982); ibid, 24, 295 (1983).

3. A. I. Meyers, J. P. Lawson, and D. R. Carver, J. Org. Chem., 46, 3119 (1981).

4. I. Gosney and A. G. Rowley, in "Organophosphorus Reagents in Organic Synthesis," J.I.G. Cadogan, Ed., Academic Press, New York, 1979, p. 17-153; M. Schlosser, Top. Stereochem. 5,1 (1970).

5. When the lithium salt of benzylamine was added to vinyltriphenylphosphonium bromide (THF, 0°-25°C, 16 h) in the presence of isobutyraldehyde, the allyl amine product was not isolated. However, a nearly quantitative yield of $PhCH_2\overset{H}{N}CH_2CH_2POPh_2$ was obtained (mp 115°-117°C). Thus, the aldehyde provided a proton source (as did similar reactions in the presence of other proton sources) and, after aqueous quench and stirring for 3 h in 15% NaOH, gave the phosphine oxide (S. Trippett, Chem. Comm. 2813 (1964)).

6. B. E. Maryanoff and B. A. Duhl-Emswiler, Tetrahedron Letters, 22, 4185 (1981) and references therein.

7. The possibility of an internal deprotonation to form a β-oxidoylide (the Schlosser modification[8]) has not been ruled out at this time.

8. M. Schlosser and K. F. Christmann, Angew. Chem. Intl. Ed., 5, 126 (1966).

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