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THE ADDITION OF CUPRATES TO VINYLTRIPHENYLPHOSPHONIUM BROMIDE: A SYNTHESIS OF 1,5-DISUBSTITUTED Z,Z-PENTA-1,4-DIENES

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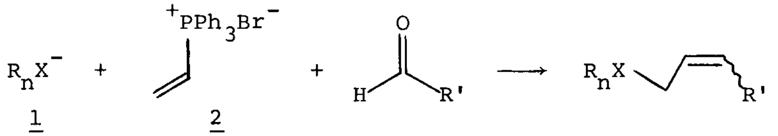
Abstract: *It is shown that alkyl, alkenyl and aryl cuprates add to vinyltriphenylphosphonium bromide to provide phosphoranes and that the Z:E ratio of their Wittig condensation products with benzaldehyde and hexanal are strongly influenced by the addition of hexamethylphosphoramide. This reaction is applied to the one-pot synthesis of the title compound.*

Whereas the reaction of vinyltriphenylphosphonium bromide 2 with anions 1 derived from alcohols, thiols and amines provides phosphoranes which are transformed to homoallylic ethers, thioethers and amines upon treatment with an aldehyde[1,2] (Eq. 1), the analogous reaction involving alkyl lithium reagents proceeds in poor yield only[3]. The main reason appears to be a competing elimination reaction transforming 2 to triphenylphosphine and acetylene, and in our hands, no olefins could be obtained by reaction of butyl, vinyl, or heptynyl lithium with 2 and benzaldehyde. When allyl magnesium bromide was used as nucleophile, some triphenylphosphine oxide was detected as product, indicating that the reaction may have proceeded, albeit to a small extent.

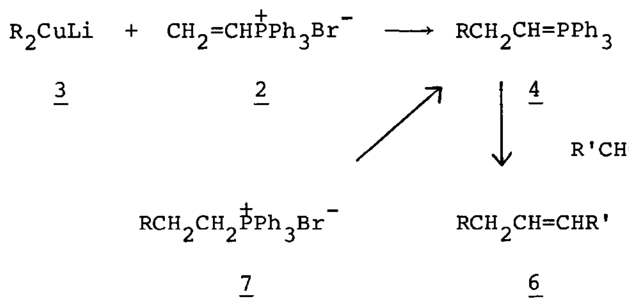


X = O,S,N
n = 1,2 (1)

However, when the less basic cuprates 3[4] were used as a source of carbanions, the desired addition took place readily, and the resulting phosphorane 4 could be transformed directly to olefin 6 by addition of aldehyde 5 (see Eq. 2)[5].

Yields and isomer ratios (Z:E) for this reaction are summarized in the following Table. Structures of products were proven by comparison with products obtained by reaction of the ylid derived from 7 and the appropriate aldehyde.

The yield of olefin could be significantly raised, based on aldehyde, by the simple expedient of changing the RLi/CuI/2/R'CHO ratio from 2/1/1/1



(2)

TABLE

TRIAL	R	R'	Yield of 6 from 3		Z/E Ratio from 3	Yield of 6 from 7	Z/E Ratio from 7	
1	vinyl	phenyl	35%[2]	6a	48/52	55%	50/50	6a
2	butyl	phenyl	20%[2]	6b	49/51	46%	59/41	6b
3	butyl	phenyl	82%[3]	6b	50/50			
4	butyl	phenyl	80%[3,4]	6b	97/3			
5	butyl	phenyl					91/9[4]	6b
6	butyl	pentyl	30%[1,2]	6c	77/23			
7	butyl	pentyl	58%[1,3,4]	6c	92/8			
8	phenyl	phenyl	25%[2]	6d	72/28			
9	phenyl	hexyl	25%[2]	6e	75/25			

All yields are based on aldehyde R'CHO 5.

[1] Z/E ratio established by ^{13}C NMR.

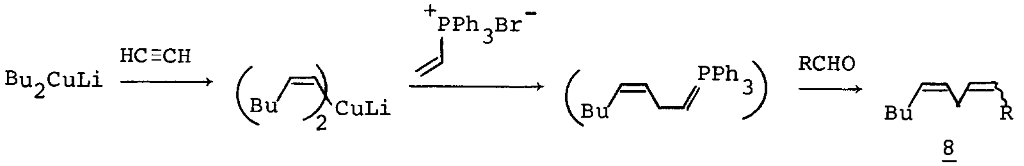
[2] Ratio of RLi/CuI/2/R'CHO = 2/1/1/1.

[3] Ratio of RLi/CuI/2/R'CHO = 4/2/2/1.

[4] 5 eq of HMPA added to cuprate or Wittig reagent.

to 4/2/2/1 (trial 3, 7). Interestingly, addition of hexamethylphosphoric triamide (HMPA) to the cuprate changed the Z/E isomer ratios of 6b and 6c from 49/51 to 97/3 (trial 4) and from 77/23 to 92/8 (trial 7), respectively. A very similar change of Z/E ratio was observed when HMPA was added to the normal Wittig reaction involving hexyltriphenylphosphonium bromide and benzaldehyde (trial 5).

In order to extend this reaction to the (one-pot) formation of 1,5-disubstituted Z,Z-1,4-pentadienes (Eq. 3), butyl cuprate was allowed to react with acetylene, using Normant's method[6], to form 1Z-hexenylcuprate, which upon treatment with vinyltriphenylphosphonium bromide and benzaldehyde or hexanal provided 8 in a yield of 50%[7].



(3)

R = phenyl, pentyl

The compatibility of these procedures with functional groups in the cuprate moiety is at present being explored, and will be described in due course.

EXPERIMENTAL

CuI[8] or CuBr·Me$_2$S[9] could be used to form the cuprate reagent. All reactions were carried out in an identical manner except as noted in footnotes 2, 3 and 4 in the Table.

1-Phenyl-1-heptene (trial 4)

To CuI (2.1 mmol, 427 mg) in dry THF (10 mL), under nitrogen, at -50°C was added 1.55 M n-butyllithium (4 mmol, 2.58 mL). The reaction mixture was stirred for 30 min, followed by addition of HMPA (10 mmol, 1.75 mL) and vinyltriphenylphosphonium bromide (2 mmol, 738 mg). Stirring was continued for 9 h at -50°C[10]. Benzaldehyde (1 mmol, 0.10 mL) was then added, and the mixture allowed to rise to 20°C (∿ 1 h), and stirring continued for 2-3 h. Pentane (50 mL) and 10% NH_4Cl (50 mL) were added, and the mixture filtered over Celite. The organic layer was washed with 10% NH_4OH (2 x 20 mL), H_2O (2 x 20 mL), dried over $MgSO_4$ and the solvents evaporated *in vacuo*. Purification by flash chromatography (petroleum ether-ethyl acetate 200:1) gave 1-phenyl-1-heptene in 80% yield.

G.C. separation (6% OV-101 on Chromosorb W) showed the product to be composed of a 97/3% mixture of *cis* and *trans* isomers.

Z-1-Phenyl-1-heptene (6b-Z): ^{1}H NMR ($CDCl_3$) δ: 0.88 (m, 3H, $CH_2C\underline{H}_3$), 1.32 (m, 6H), 2.31 (qxd, 2H, J = 7.4 x 1.5 Hz, $-C\underline{H}_2-CH=CH-$), 5.65 (ABX, sextet, 1H, C2, $J_{2,1}$ = 11.8 Hz, $J_{2,3}$ = 7.3 Hz), 6.39 (ABX, sextet, 1H, C1, $J_{1,2}$ = 11.6 Hz, $J_{1,3}$ = 1.8 Hz), 7.28 (s, 5H, $-C_6H_5$); ms (m/e 70eV): 174 ($M^{+\cdot}$, 15.01%).

E-1-Phenyl-1-heptene (6b-E): ^{1}H NMR ($CDCl_3$) δ: 0.88 (m, 3H, CH_2CH_3), 1.32 (m, 6H), 2.18 (q, 2H, J = 6.4 Hz, $-C\underline{H}_2CH=CH-$), 6.20 (ABX, sextet, 1H, C_2, $J_{2,1}$ = 17 Hz, $J_{2,3}$ = 6 Hz), 6.29 (ABX, sextet, 1H, C1, $J_{1,2}$ = 17 Hz, $J_{1,3}$ < 1 Hz), 7.28 (s, 5H, $-C_6H_5$); ms (m/e 70eV): 174 ($M^{+\cdot}$, 17.9%).

1-Phenyl-1,4-nonadiene (Eq. 3)

Acetylene (4 mmol, 96 mL) was bubbled into a stirred solution of butylcuprate (prepared as described for trial 4) at -50°C and stirring continued for an additional 30 min. The addition of HMPA, vinyltriphenylphosphonium bromide and benzaldehyde was done as in trial 4.

1-Phenyl-Z,Z-1,4-nonadiene: ^{1}H NMR ($CDCl_3$) δ: 0.88 (m, 3H, $CH_2C\underline{H}_3$), 1.32 (m, 4H), 2.00 (m, 2H, C6), 3.06 (m, 2H, C3), 5.43 (m, 2H, C4, C5), 5.66 (ABX, sextet, 1H, C2, $J_{2,1}$ = 11.8 Hz, $J_{2,3}$ = 7.4 Hz), 6.43 (ABX, sextet, 1H, C1, $J_{1,2}$ = 11.8 Hx, $J_{1,3}$ < 1 Hz), 7.29 (s, 5H, $-C_6H_5$); ms (m/e 70eV): 200 ($M^{+\cdot}$, 8.25%).

The *cis*-relation of protons at C4 and C5 could not be established by 200 NMR but other work done in this area has shown that alkyl cuprates add to acetylene forming exclusively (Z)-alkenyl cuprates[11].

ACKNOWLEDGEMENTS

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5. A few months ago, Nicotra *et al.* showed that diethyl vinylphosphonate underwent addition of vinylcopper complexes in a reaction analogous to the one described
   $R'RC{=}CHCuMgBr_2 + CH_2{=}CHPO(OEt)_2 \longrightarrow R'RC{=}CHCH_2CH_2PO(OEt)_2$
   F. Nicotra, L. Panya and G. Russo, J. Chem. Soc. Chem. Comm., 5 (1984).
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7. The reaction using benzaldehyde gave a 30% yield (unoptimized) with a Z/E ratio of 87/13, whereas that using hexanal gave a 50% yield (optimized) where C^{13} NMR seems to indicate an approximate Z/E ratio of 90/10.
8. G.B. Kauffman and L.A. Tater, Inorg. Synth., 7, 9 (1963).
9. H.O. House, Chia-Yeh Chu, J.M. Wilkins and M.J. Uman, J. Org. Chem., 40, 1460 (1975).
10. The reaction was kept at this temperature ± 2°C by using a Flexi-Cool apparatus (FTS Systems or in Canada from Spectrex LTD) and the yields were found to be the same whether the stirring was continued for 9 h or 21 h.
11. J.F. Normant, in *Modern Synthetic Methods*, Ed. R. Scheffold, Salle and Sauerlander, Frankfurt am Main, 1983, p. 161.

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