

Z-Selective Horner–Wadsworth–Emmons-type Reaction Using a 10-P-5 Phosphorane Bearing Bidentates Derived from 1-Naphthol

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A Horner–Wadsworth–Emmons-type 10-P-5 phosphorane reagent bearing bidentate ligands from 1-naphthol was prepared and examined in the olefination of aldehydes. Z-Selectivity was generally high except for the case of 3-phenylpropanal, and acetophenone was also found to react with relatively high selectivity.

The Wittig reaction and its phosphoryl variant, the Horner–Wadsworth–Emmons (HWE) reaction are valuable methods for introducing double bonds with carbon–carbon bond formation.¹ For disubstituted alkenes conjugated with an electron-withdrawing group such as a carbonyl or a cyano group, in order to prepare the thermodynamically less stable Z-olefin with high selectivity, the Still reagent² and the Ando reagent³ have emerged as highly versatile reagents. Useful variants⁴ based upon the Ando reagent along with highly selective Peterson-type reagents⁵ have also been disclosed. We⁶ and Evans⁷ have independently found that 10-P-5 phosphoranes **1** and **2**, respectively, could also function as HWE reagents, although they are already pentacoordinated (Figure 1). This is interesting in light of the fact that in the ordinary HWE reaction the tetracoordinated reagent has to increase its valency to a pentacoordinated state in order to yield the olefinic product. With our system, which utilizes the Martin ligand, it was also found that olefins could be obtained with almost exclusive Z-selectivity when the reagent bore an ester^{6a} or an amide moiety,^{6b} and moderate selectivity was observed when it had a cyano group.^{6b} Although the reagents showed high selectivity, a drawback was that the reactivity of the reagents was rather low and the reaction temperature could not be lowered below 0 °C for ester and amide systems. We attributed this low reactivity to the presence of the bulky trifluoromethyl groups in the bidentate Martin ligand. Thus, to increase reactivity we decided to examine a 10-P-5 phosphorane reagent bearing a flat bidentate generated from 1-naphthol, of which the parent **3** has found utility in the preparation of unique transition-metal complexes.⁸

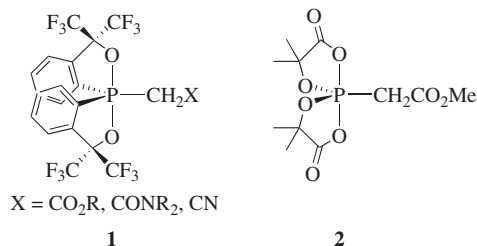
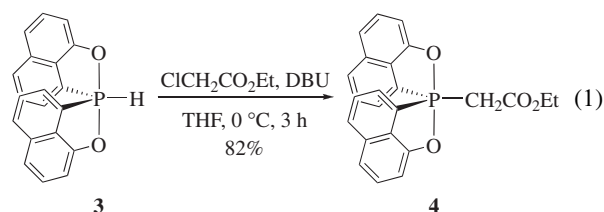


Figure 1.

Preparation of the 10-P-5 HWE reagent **4** was carried out by reacting the known P–H phosphorane **3**⁸ with ClCH₂CO₂Et in the presence of DBU. The spectroscopic data of **4** was in accord with expectations for a 10-P-5 compound.⁹

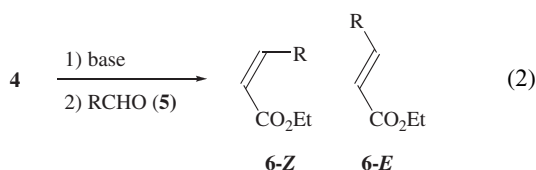


The reaction of **4** with *n*-BuLi at 0 °C followed by benzaldehyde proceeded to give an olefinic product with 93:7 selectivity in favor of the Z-olefin (Table 1). This reaction was found to proceed even at –78 °C with an increased selectivity of 98:2, although more sluggishly, as the reaction was not complete after 3 h at this temperature. Nonetheless, it was evident that the reaction proceeded faster than that of phosphorane **1**. With phosphorane **1**, a counter cation effect was observed, and selectivity was in the order of K⁺ > Na⁺ > Li⁺. Thus, we next examined the reaction of benzaldehyde using *t*-BuOK and NaH as bases. The reaction using *t*-BuOK turned out to be somewhat messy, and thus NaH was the optimum base among the three examined, giving the product with selectivity up to 96:4 at 0 °C.¹⁰

Table 1. Reactions of **4** with various aldehydes

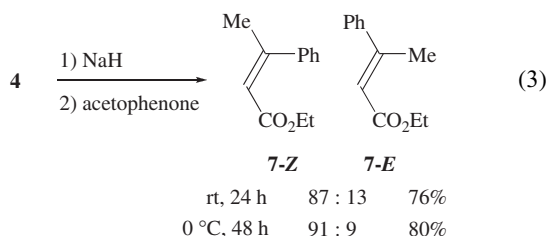
Entry	RCHO	Base	Conditions ^a	Z:E	Yield/%
1	PhCHO (5a)	<i>n</i> -BuLi	–78 °C, 3 h	98:2	53
2		<i>n</i> -BuLi	–78 to 0 °C, 3 h	97:3	73
3		<i>n</i> -BuLi	0 °C, 3 h	93:7	73
4		NaH	0 °C, 3 h	96:4	83
5		<i>t</i> -BuOK	0 °C, 3 h	95:5	61
6	<i>o</i> -MeOC ₆ H ₄ CHO (5b)	NaH	0 °C, 3 h	97:3	66
7		NaH	–40 °C, 6 h	99:1	64
8	<i>m</i> -MeOC ₆ H ₄ CHO (5c)	NaH	0 °C, 3 h	95:5	70
9		NaH	–40 °C, 6 h	97:3	68
10	<i>p</i> -MeOC ₆ H ₄ CHO (5d)	NaH	0 °C, 3 h	96:4	58
11		NaH	–40 °C, 6 h	97:3	89
12	PhCH ₂ CH ₂ CHO (5e)	NaH	0 °C, 3 h	85:15	70
13		NaH	–78 °C, 12 h	86:14	75
14	PhMeCHCHO (5f)	NaH	0 °C, 3 h	97:3	68
15		NaH	–78 °C, 12 h	99:1	70
16	PhMe ₂ CCHO (5g)	NaH	0 °C, 6 h	99:1	72

^aAll reactions were carried out in THF.



To determine the scope of the reaction, *o*-, *m*- and *p*-MeO-substituted benzaldehydes were reacted similarly with NaH as the base at 0 °C, and it was found that high *Z*-selectivity could be attained regardless of the position of the substituent. Carrying out the reaction at –40 °C led to a slight increase in selectivity for all three substrates. Noteworthy is that nearly complete control could be observed for the most sterically hindered *o*-substituted substrate. As for aliphatic aldehydes, 3-phenylpropanal, 2-phenylpropanal, and 2-methyl-2-phenylpropanal were examined. High selectivity was observed for the two α -branched aldehydes, whereas selectivity was moderate for unbranched 3-phenylpropanal. Lowering the temperature led to nearly complete control for 2-phenylpropanal. However, practically no improvement was observed for 3-phenylpropanal.

In addition to the fact that the reactions could be carried out at –78 °C, the increased reactivity of phosphorane 4 compared with 1 could be demonstrated by the reaction with acetophenone. Thus, the reaction proceeded at 0 °C to give the olefinic product with the relatively high selectivity of 91:9, in favor of the *Z*-product. The reaction required less time when it was carried out at rt, albeit with somewhat lower selectivity. Unfortunately, bulkier ketones such as alkyl phenyl ketones with higher alkyl groups were reluctant to react.



In conclusion, we have found that the novel 10-P-5 phosphorane HWE reagent 4 could be utilized as an efficient reagent for the preparation of *Z*-olefins from aldehydes and that acetophenone also reacts with relatively high selectivity. These results provide valuable insight for the designing of other 10-P-5 type HWE reagents that might be of higher utility.

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- 4: Mp 117 °C; ¹H NMR (500 MHz, CDCl₃): δ 8.30 (dd, *J* = 12.2, 7.0 Hz, 2H), 7.99 (dd, *J* = 7.9, 2.7 Hz, 2H), 7.62 (dd, *J* = 13.7, 6.7 Hz, 2H), 7.47 (dd, *J* = 8.2, 7.6 Hz, 2H), 7.33 (dd, *J* = 8.2, 2.2 Hz, 2H), 6.90 (d, *J* = 7.6 Hz, 2H), 3.92 (dq, *J* = 10.4, 6.7 Hz, 1H), 3.80 (dq, *J* = 10.4, 6.7 Hz, 1H), 3.76 (dd, *J* = 22.7, 14.3 Hz, 1H), 3.72 (dd, *J* = 22.2, 14.3 Hz, 1H), 0.74 (t, *J* = 7.3 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ 166.6 (*J* = 7 Hz), 155.9 (*J* = 2 Hz), 134.3 (*J* = 8 Hz), 131.9 (*J* = 14 Hz), 131.4 (*J* = 4 Hz), 129.3 (*J* = 26 Hz), 129.1, 128.2 (*J* = 17 Hz), 124.4 (*J* = 161 Hz), 116.1, 104.0 (*J* = 2 Hz), 61.0, 43.4 (*J* = 117 Hz), 13.4; ³¹P NMR (202 MHz, CDCl₃): δ –37.5; HRMS(EI+) *m/z*: calcd for C₂₄H₁₉O₄P 402.1021, found 402.1001.
- Representative procedure: To a solution of phosphorane 4 (71.1 mg, 0.177 mmol) in THF (1.0 mL) was added a suspension of NaH (60% in oil, 7.2 mg, 0.18 mmol) in THF (1.0 mL) at 0 °C under nitrogen. After stirring for 1 h, PhCHO (14.9 mg, 0.140 mmol) in THF (1.0 mL) was added, and the resulting solution was stirred for another 3 h. The reaction mixture was quenched with aq. NH₄Cl, extracted with Et₂O, and the combined organic layer was washed with water then brine, dried with MgSO₄, and then concentrated. The crude mixture was purified by PTLC (benzene) to give PhCH=CHCO₂Et (20.5 mg, 83%, *Z*:*E* = 96:4).