

Wittig Reaction by Using DBU as a Base

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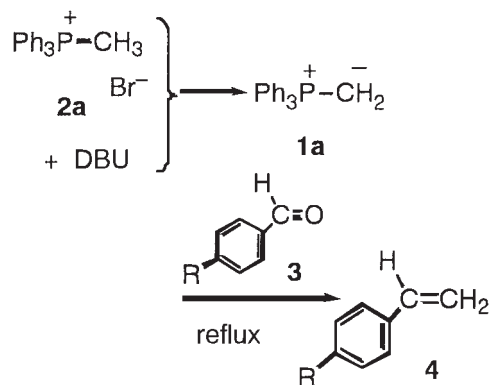
The reaction of methyltriphenylphosphonium bromide with DBU in refluxing dichloromethane or toluene afforded methylenetriphenylphosphorane, which further reacted with benzaldehydes to give styrenes in good yields. Semistabilized ylide, benzylidenetriphenylphosphorane was also synthesized by using DBU, which reacted with aldehydes to afford olefins in nearly quantitative yields.

Wittig reagents (**1**) form an important class of compounds because of their versatile synthetic utility.¹ Generally, nonstabilized ylides were formed by using strong bases, such as butyllithium, sodium hydride, LDA, and alkoxides.² The reaction was also carried out under phase-transfer conditions by using extremely concentrated aq. sodium hydroxide.³ Masamune et al. reported the Horner-Wadsworth-Emmons reaction in the presence of lithium chloride and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or ethyldiisopropylamine.⁴ However, there are few reports on the synthesis of phosphorus ylides by using amidine bases. The reported examples were the synthesis of stable phosphorus ylide by using 1,5-diazabicyclo[4.3.0]-5-nonene (DBN) as a base⁵ and the synthesis of indole derivatives by an intramolecular Wittig reaction using triethylamine and DBU as bases.⁶ Previously, we reported on an unusual formation of cyclopropylsulfoxonium salts from amino- or diaminosulfoxonium salts and aldehydes by using DBU as a base.⁷

Our desire to extend the scope of the method prompted us to examine the possibility of the formation of unstable or semistabilized phosphorus ylide by using DBU as a base. In this paper, we would like to describe the synthesis of olefins by the reaction of phosphonium salts with DBU.

Several amine bases (triethylamine, pyridine, DBN, and DBU) were tried for the synthesis of styrene by reactions with methyltriphenylphosphonium bromide (**2a**) and benzaldehyde (**3a**). When DBU was used as a base, styrene (**4a**) was obtained in 75%. Other bases did not afford **4a** in refluxing dichloromethane. Thus, the synthesis of other styrenes by using DBU as a base under several conditions was carried out. The treatment of **2a** with DBU in refluxing dichloromethane, followed by the addition of 4-chlorobenzaldehyde (**3c**), resulted in the formation of 4-chlorostyrene (**4c**) in 82% yield (Scheme 1). Other reactions were carried out in a similar manner (Table 1).

When the reaction of **1a** with aldehydes **3b** was carried out



Scheme 1.

Table 1. Reaction of **2a** with DBU, Followed by the Addition of Benzaldehydes **3**

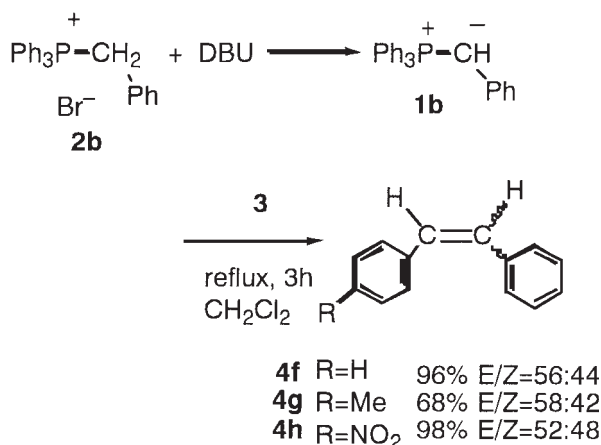
Entry	3	R	Solvent	Time/h	4	Yield/%
1	3a	H	CH ₃ CN	14	4a	75
2	3a		Toluene	14	4a	37
3	3b	Me	CH ₂ Cl ₂	14	4b	28
4	3b		Toluene	16	4b	81
5	3c	Cl	CH ₂ Cl ₂	5	4c	82
6	3d	NO ₂	CH ₂ Cl ₂	2	4d	98
7	3e	CF ₃	CH ₂ Cl ₂	2	4e	90

in dichloromethane, the yield was only 28%, even after refluxing for 14 h, whereas the yield was improved to 81% in refluxing toluene (entry 3, 4). Since the reaction of the ylide is nucleophilic in nature, electron-withdrawing substituents on the aldehydes should speed up the reaction, whereas on the salt they should slow down the reaction. Thus, electron-deficient aldehydes gave good yields, even in refluxing dichloromethane (entry 5, 6, 7). Since dichloromethane and toluene were almost insoluble in water, the reaction mixture was just washed with water to afford a clear mixture of olefin **4** and triphenylphosphine oxide. No other side products were obtained.

DBU is thought to be a relatively strong base, whose pK_a is 24 (conjugate acid).⁸ On the other hand, butyllithium is a stronger base than DBU. Butyllithium, LDA, and sodium hydride, which were used as bases for a Wittig reaction, are moisture sensitive and the reaction must be carried out under water free conditions. For this reason, very poor yields of the products were obtained in some cases, whereas the present reaction requires only the distilled solvent, and no further special treatment is required.

Benzylidenetriphenylphosphorane (**1b**), semistabilized ylide, was thought to be more stable than **1a**, we then tried the reaction of benzyltriphenylphosphonium bromide (**2b**) with DBU. When **2b** was treated with DBU in refluxing dichloromethane, followed by the addition of benzaldehyde **3a**, stilbene (**4f**) was obtained as a mixture of *E*- and *Z*-isomers in 95% yield (Scheme 2). Similarly, other benzaldehydes, **3b** and **3d**, gave the corresponding stilbenes in good yields. Thus, this method was found to be useful for the synthesis of olefins.

A Wittig reaction by using the amidine derivative was reported by Oediger et al.⁵ The reaction of methoxycarbonyl-



Scheme 2.

methyltriphenylphosphonium bromide with DBN resulted in the formation of methoxycarbonylmethylenetriphenylphosphorane, which further reacted with benzaldehyde to afford methyl cinnamate in 76% yield. However, this ylide is well known as an isolable stabilized ylide. They did not apply the formation of normal unstabilized ylides. Recently, Imamoto et al. reported on the synthesis of indoles by an intramolecular Wittig reaction by using triethylamine and DBU as bases.⁶ The present result is the first example on the formation of normal unstabilized or semistabilized ylides by using amidine derivatives. Nishizawa et al. reported the indirect synthesis of olefins via the isolation of 1,2-hydroxyphosphonium salts and subsequent treatment with DBU,⁹ whereas the present method does not require the isolation of 1,2-hydroxyphosphonium salts.

In conclusion, we have shown that the Wittig reaction by using DBU as a base in dichloromethane gave olefins in good yields.

Experimental

General. Flash chromatography was carried out by Merck Kieselgel 60 (230–400 mesh). Thin layer chromatography (TLC) was carried out on commercially available pre-coated aluminum plates (Merck silica Kieselgel 60F254). All solvents were distilled before use, and no further treatment was carried out. NMR spectra were measured on a JEOL GSX-400 (400 MHz for ^1H , 100 MHz for ^{13}C). The melting points were uncorrected.

Materials. Phosphonium salts **2a**, **b** and benzaldehydes **3a–e** were purchased from Wako. Styrenes **4a–e** and stilbenes **4f** were identified from authentic samples obtained from Aldrich (**4a**, **4b**, and **4e**) and TCI (**4c**, **4d**, and **4f**).

Reaction of Methyltriphenylphosphonium Bromide **2a with DBU Followed by the Addition of 4-Chlorobenzaldehyde (**3c**).** To a refluxing solution of **2a** (714 mg, 2 mmol) in dichloromethane (10 mL) was added DBU (339 mg, 2.2 mmol). After refluxing for 30 min, **3c** (141 mg, 1.0 mmol) in dichloromethane (3 mL) was added to this solution. After refluxing for 5 h, the reaction mixture was washed with water (5 mL $\times$ 3), dried over magnesium sulfate, filtered, and evaporated to afford a pale-yellow oil, which was

chromatographed over silica gel by elution from hexane and dichloromethane to give 4-chlorostyrene (**4c**) (114 mg, 0.82 mmol) and triphenylphosphine oxide (253 mg, 0.91 mmol). ^1H NMR (CDCl_3) δ 5.17 (d, 1H, $J = 11$ Hz, $=\text{CH}_2$), 5.62 (d, 1H, $J = 17$ Hz, $=\text{CH}_2$), 6.56 (dd, 1H, $J = 11$ and 17 Hz, $=\text{CH}$), 7.16–7.26 (m, 4H, Ar). ^{13}C NMR (CDCl_3) δ 114.64 ($=\text{CH}_2$), 127.63, 128.87, 133.64, 135.88 ($=\text{CH}$), 136.25.

Other reactions were carried out in a similar manner.

Reaction of Benzyltriphenylphosphonium Bromide (2b**) with DBU Followed by the Addition of Benzaldehyde.** To a refluxing solution of **2b** (520 mg, 1.2 mmol) in dichloromethane (10 mL) was added DBU (230 mg, 1.5 mmol). After refluxing for 30 min, **3a** (106 mg, 1.0 mmol) in dichloromethane (3 mL) was added to this solution. After refluxing for 2 h, the reaction mixture was washed with water (5 mL $\times$ 3), dried over magnesium sulfate, filtered, and evaporated to afford a pale-yellow oil, which was chromatographed over silica gel by elution from hexane and dichloromethane to give stilbene **4f** (167 mg, 0.93 mmol, $E/Z = 56/44$) and triphenylphosphine oxide (250 mg, 0.90 mmol). The mixture of stilbene was recrystallized from ethanol to give colorless crystals of *trans*-**4f**. mp 121–123 °C (lit.¹⁰ mp 124 °C).

Other reactions were carried out in a similar manner.

trans-4-Methylstilbene (**4g**): mp 116–118 °C (lit.¹⁰ mp 119 °C).

trans-4-Nitrostilbene (**4h**): mp 153–155 °C (lit.¹⁰ mp 155 °C).

^1H NMR (CDCl_3) δ 7.13 (d, 2H, $J = 16$ Hz, $=\text{CH}$), 7.26 (d, 2H, $J = 16$ Hz, $=\text{CH}$), 7.26–7.57 (m, 5H, Ph), 7.62 (br d, 2H, $J = 7$ Hz, Ar), 8.22 (br d, 2H, $J = 7$ Hz, Ar). ^{13}C NMR (CDCl_3) δ 124.34, 126.48, 127.05, 127.22, 129.04, 129.09, 133.51, 136.37, 144.05, 146.97.

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