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Use of Silver Carbonate in the Wittig Reaction

Lukas Jedinak[†], LaToya Rush[†], Mijoon Lee, Dusan Heseck, Jed F. Fisher, Bill Boggess, Bruce C. Noll, and Shahriar Mobashery

Department of Chemistry and Biochemistry, University of Notre Dame, Notre Dame, Indiana 46556

Shahriar Mobashery: mobashery@nd.edu

Abstract

An efficient synthesis of olefins by the coupling of stabilized, semi-stabilized, and non-stabilized phosphorus ylides with various carbonyl compounds in the presence of silver carbonate is reported. Wittig olefination of aromatic, heteroaromatic, and aliphatic aldehydes (yields > 63%) and a ketone (yield 42%) are demonstrated. These reactions proceed overnight at room temperature, under weakly basic conditions, and as such extend the applicability of the Wittig reaction to base-sensitive reactants.

The Wittig reaction is a standard methodology for the synthesis of the alkene, due to its specificity of bond placement and its use of relatively mild conditions. The classic method generates the requisite phosphorus ylide, using a base of appropriate basicity, which then reacts with an aldehyde or ketone to yield the corresponding alkene.¹ Under the classical conditions, the Wittig reaction has certain limitations with base-sensitive compounds, such as self-condensation of the carbonyl, disproportionation of the carbonyl via the Cannizzaro reaction, and epimerization of adjacent stereocenters.² Modifications to the Wittig conditions to accommodate these limitations include Masamune's and Roush's use of LiCl with DBU,³ and the use by Blasdel et al. of lithium 1,1,1,3,3,3-hexafluoroisopropoxide.⁴ Other bases that have been found effective^{5,6} include tertiary amines,^{7,8} LiOH,⁹ KH,¹⁰ and KOSiMe₃.¹¹ Though Wittig and Horner-Wadsworth-Emmons reactions using mild bases have been described, most examples are limited to stabilized ylides or to Horner-Wadsworth-Emmons phosphonates bearing an electron-withdrawing group at the α-carbon, thus enabling deprotonation of the phosphonium salt (or phosphonate) using a weaker base.^{12–15} Attempts to form a non-stabilized ylide, by alkylphosphonium halide deprotonation with a mild base, have failed.¹⁶ The first Wittig olefination of non-stabilized ylide promoted by weak carbonate base (K₂CO₃) was achieved in solid state under ball milling conditions.¹⁷ In solution phase chemistry, potassium carbonate¹⁸ or sodium

Correspondence to: Shahriar Mobashery, mobashery@nd.edu.

[†]Both authors contributed equally to this work.

Supporting Information Available. MS data for **8a–8m**; the chromatograms used to determine the enantiomeric ratios for **8i–8m**; the ¹H and ¹³C NMR spectra for compounds **4**, **5**, **8a–8m**; and the crystallographic information file (CIF) for compound **5**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

bicarbonate^{14,19} were used, but the reactions required elevated temperatures and were conducted only with stabilized or semi-stabilized ylides. The Wittig reaction was successfully applied to the synthesis of unsaturated amino acids^{20,21} without loss of stereochemical integrity, using K_3PO_4 as a strong base under phase transfer conditions at elevated temperature (90 °C).²⁰ However, a general method for the mild, room temperature olefination of base-sensitive and α -epimerizable aldehydes is lacking.⁴

During the synthesis of *meso*-diaminopimelate (an amino acid found in the cell wall of Gram-negative bacteria) we sought a means to generate ylide **2a** so as to enable a synthetic route based on the Wittig reaction as the key synthetic connection (Scheme 1). As both the ylide and the aldehyde counterparts contain acidic α -carbons, this system had the potential for erosion of stereochemical integrity in both reagents. As a possible solution to this dilemma, we chose to evaluate silver carbonate (Ag_2CO_3) as the base. While Ag_2CO_3 has a recognized ability to exert basicity in reactions that exploit its halophilic character,^{22–24} to our knowledge this ability has not been explored previously in the context of the Wittig reaction. Our first efforts appeared unpromising. Treatment of a mixture of phosphonium iodide **4** and aldehyde **1** with Ag_2CO_3 gave a complex mixture. Nonetheless, a significant constituent of this mixture was purified. Single-crystal X-ray analysis revealed its structure as that shown as compound **5**. We contemplated that **5** was formed from ylide **2b** by intramolecular reaction with the ester. Notwithstanding the failure to give the desired product en route to *meso*-diaminopimelate, the reaction implicated Ag_2CO_3 as a capable reagent for ylide formation.

This implication prompted the further exploration of silver carbonate as a mild base for ylide formation (stabilized, semi-stabilized and non-stabilized ylides) for the Wittig reaction. As outlined in the general Scheme 2, we generated the ylide by reaction of a triphenylphosphonium salt with Ag_2CO_3 in acetonitrile. After 1 h, the resulting ylide was then treated with an aldehyde, in expectation of alkene formation.

We used (carbomethoxymethyl)triphenylphosphonium chloride **7a** as the ylide precursor, Ag_2CO_3 in acetonitrile at room temperature as the reaction condition, and *p*-anisaldehyde **6a** as the carbonyl acceptor. We compared the outcome of this reaction to one using commercial methyl (triphenylphosphoranylidene)acetate without Ag_2CO_3 . Both reactions gave the desired product **8a**. Encouraged by this result, we set up several Wittig reactions using various phosphonium halides, including aromatic **7b**, heterocyclic **7c** and aliphatic **7d** examples (Table 1), in reaction with *p*-anisaldehyde. Styrene derivatives **8a–d** were obtained in 63–97% yields. The poorest yield, seen for styrene **8d** (Entry 4), is likely due to the poorer acidity of ethyl triphenylphosphonium bromide **7d**. The diastereoselectivity of the reaction leading to **8a** and **8c** strongly favored the *E* isomer, as expected for stabilized ylides (**7a** and **7c**).

The *E/Z* selectivity decreased for semi-stabilized and nonstabilized ylides (**7b** and **7d**) leading to **8b**, **8d** and **8e**, respectively. It is remarkable that even the aliphatic alkylphosphonium halides **7d** could be deprotonated using Ag_2CO_3 in acetonitrile at room temperature (entries 4 and 5) to form the nonstabilized ylide under mild conditions. We evaluated Ag_2O and $AgOAc$ as alternative sources of $Ag(I)$ in the reaction of aldehyde **6b** with **7d**. The yield of olefin **8e** was poorer (28% in the case of $AgOAc$ and 68% in the case of Ag_2O).

Silver carbonate is an affordable (approximate cost of \$1 per mmol) reagent for smaller scale reactions. We evaluated the possibility that the combination of the inexpensive base K_2CO_3 with Ag_2CO_3 might mitigate reagent cost. Reaction of the phosphonium salt **7d** with 4-chlorobenzaldehyde **6b** under the standard reaction conditions (1 equiv Ag_2CO_3) gave

alkene **8e** in 50% yield (Table 1, entry 5). Using a mixture of 0.5 equiv K_2CO_3 and 0.5 equiv Ag_2CO_3 in this same reaction gave an essentially identical (46%) yield. The yield for the reaction of *p*-chlorobenzaldehyde **6b** with K_2CO_3 alone as the base was poor (7%). Use of 2 equiv Ag_2CO_3 and 2 equiv of the phosphonium salt improved the yield from 50% to 72%, without change in the dr of the product. These results emphasize the halide affinity of the Ag(I) cation as a driving force for ylide formation. Verkade et al.¹⁶ described an analogous Wadsworth-Emmons-Horner reaction promoted by a mild triaminophosphine base, but in their case *p*-chlorobenzaldehyde **6b** did not react with alkylphosphonate, presumably because the weaker base was unable to deprotonate less acidic alkylphosphonate. This outcome highlights the ability of silver carbonate to deprotonate even a less acidic alkylphosphonium halide under mild conditions.¹⁶

For another example of the use of Ag_2CO_3 , we chose 2-furaldehyde **6c** as a commercially available, heterocyclic aldehyde. Wittig reaction of **6c** with **7b** yielded olefin **8g** in a yield of 85%. The reaction was complete in 2 h, and thus was a much faster reaction compared to the reaction with compounds **6a** and **6b**. When 2-furylaldehyde **6c** was coupled with phosphonium salt **7a**, compound **8f** was obtained in 87% yield.

Ketones are less reactive in the Wittig olefination compared to aldehydes. We chose cyclohexanone as a representative ketone to couple with reagent **7a**. As expected, the reaction was sluggish and required heating (60 °C, overnight in acetonitrile). Unsaturated ester **8h** was obtained in 42% yield (entry 8). This yield is less than the reported yields for this same reaction (98%) using sodium methoxide as the base.²⁵ On the other hand, when cyclohexanone **6d** was reacted with **7a** using K_2CO_3 as base, only trace quantities (less than 1% detected by 1H NMR) of the ester product **8h** was formed. This result emphasizes the beneficial effect of silver cation for the Wittig reaction and demonstrates the profound effect of the silver ion over the potassium ion.

Aldehyde **6e** was an example of an aliphatic aldehyde as a useful synthetic reagent. This aldehyde is derived from D-aspartate, and is a precursor to unsaturated amino acids.²¹ The reaction of **6e** with benzyltriphenylphosphonium chloride **7b** gave compound **8j** in 60% yield. The yield was improved to 83% by using freshly prepared aldehyde **6e**, as obtained by DIBAL-H reduction of the corresponding methyl ester,²¹ prior the Wittig reaction. The analogous reactions of **6e** with the Wittig reagents **7a** and with **7c** gave **8i** (82% yield) and **8k** (97% yield), respectively. Moreover, olefins **8i**, **8j** and **8k** each were obtained with high enantiomeric ratio (er > 95:5 as assessed by chiral support HPLC analysis, as shown in the Supporting Information). No evidence for loss of stereochemical integrity by the Ag_2CO_3 base was seen. Again, we compared Ag_2CO_3 with other bases (entries 9 and 10). While Wittig olefination using K_2CO_3 gave the product **8i** in 69% yield (82% with Ag_2CO_3), the reaction with the less acidic phosphonium salt **7b** gave a much poorer yield (8%). Using the strong base *t*BuOK for the olefination of the base-sensitive aliphatic aldehyde **6e** primarily caused self-reactions of the starting aldehyde. The olefin product was detected in small amounts in the crude mixture (yield of less than 1% as determined by 1H NMR, entry 9). Epimerizable aldehydes⁴ **6f** and **6g** having an α -stereogenic carbon were condensed with phosphonium salt **7a** in THF at 0 °C yielding olefins **8l** and **8m** in high yield and remarkably high E/Z ratio (>95 % *E* isomer). Both olefins **8l** and **8m** were obtained without observable epimerization as determined by 1H NMR of the crude mixture (entry 12 and 13) To explore potential of the reaction to be scale up, we conducted Wittig olefination of aldehyde **6e** with phosphonium salt **7a** at 10-mmol scale. We obtained a comparable result to the 1-mmol scale reaction (92 % yield, dr 95:5).

Silver carbonate is a reagent with substantial promise for the convenient (as an out-of-the bottle reagent added to reagent-quality solvent) Wittig reaction of stabilized and semi-

stabilized ylides with base-sensitive aldehydes, and for the Wittig reaction of non-stabilized ylides with enolizable aldehydes, with good to excellent (63–97 %) yields.

EXPERIMENTAL SECTION

General methods

All organic reagents were purchased from commercial suppliers and used without further purification. Solvents were HPLC grade (THF and acetonitrile used directly from the bottle, without additional drying). Reactions were monitored by thin-layer chromatography using UV light, or ninhydrin or phosphomolybdic acid staining, for visualization. Flash chromatography was carried out with 230–400 mesh silica gel 60. ^1H , ^{13}C , H,H-COSY, H,C-HSQC and H,C-HMBC NMR spectra were recorded on 300, 400 and 500 MHz spectrometers. ^1H and ^{13}C chemical shifts were referenced to residual solvent. NMR assignments for new compounds were made on the basis of H-H COSY, H-C HSQC, and H-C HMBC correlations. High-resolution mass spectra were obtained via FAB or ESI ionization with TOF detection, or EI ionization with orthogonal acceleration TOF detection. Chiral phase HPLC analyses were performed on (S,S) Whelk-O1 (25 cm $\times$ 4.6 mm i.d.), using hexanes/isopropanol or hexanes/isopropanol/diethylamine as the mobile phase. Reactions were carried out at room temperature under a nitrogen atmosphere, and were run overnight (18 h) unless otherwise noted.

Reagents and known products

Aldehydes **6e**,²¹ **6f**,⁴ and **6g**⁴ were prepared according to the literature procedures. Silver carbonate was purchased from commercial suppliers or was freshly prepared from silver nitrate.²⁶ Both reagents gave comparable results. Compounds **8a**,^{14,27} **8b**,^{28,29} **8c**,³⁰ **8d**,^{31,32} **8e**,³³ **8f**,³⁴ **8g**,^{35,36} **8h**,²⁵ **8i**,²¹ and **8l**⁴ are known. Their NMR spectra were identical to the referenced values. The synthesis of methyl 4-methoxycinnamate **8a** is given as representative example.

Phosphonium, 1-methyl-1-[(3S)-3-[[[(1,1-dimethylethoxy)carbonyl]amino]-4-oxo-4-[(4-methoxyphenyl)methoxy]butyl]-1-diphenyl, iodide (1:1): (**4**)

Methyldiphenylphosphonium iodide (**4**) was prepared by refluxing *N*-Boc-2-amino-4-iodobutanoate 4-methoxyphenylmethyl ester and methyldiphenylphosphine in benzene. **4**: ^1H NMR (500 MHz, CDCl_3) δ 1.36 (s, 9H), 2.15 (s, 2H), 2.76 (d, J = 13.4 Hz, 3H), 3.29 (m, 2H), 3.75 (s, 3H), 4.37 (m, 1H), 5.08, 5.14 (AB, J = 12.0 Hz, 2H), 5.98 (d, J = 5.4 Hz, 1H), 6.81 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.4 Hz, 2H), 7.58–7.90 (m, 11H); ^{13}C NMR (126 MHz, CDCl_3) δ 8.8 (d, J = 55.1 Hz), 19.9 (d, J = 53.5 Hz), 24.2, 28.3, 53.4, 55.4, 67.5, 114.0, 118.5 (d, J = 36.2 Hz), 119.2 (d, J = 36.2 Hz), 127.5, 130.4, 130.4, 130.5, 130.6, 132.5, 132.6, 135.0 (d, J = 3.3 Hz), 135.1 (d, J = 3.3 Hz), 155.8 (m), 159.8, 170.8; MS (ESI-TOF) m/z $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{30}\text{H}_{38}\text{NO}_5\text{P}$ 523.2482, found 523.2502.

($\pm$)-4-[[[(1,1-Dimethylethoxy)carbonyl]amino]-3-oxo-1,1-diphenylphosphorinanium, 2-ylide (**5**)

An acetonitrile solution of **4** (0.71 g, 1.1 mmol) was stirred with Ag_2CO_3 (0.28 g, 1.0 mmol) for 1 h at room temperature. The reaction mixture was filtered through a layer of Celite. Evaporation of volatiles followed by column chromatography gave **5** as a crystalline solid. The structure of **5** was determined by X-ray crystallography (Supporting Information). **5**: ^1H NMR (500 MHz, CDCl_3) δ 1.42 (s, 9H), 1.83 (m, 1H), 2.53–2.71 (m, 2H), 2.75–2.92 (m, 1H), 3.68 (d, J = 12.0 Hz, 1H), 3.93 (d, J = 11.2 Hz, 1H), 6.22 (br s, 1H), 7.48–7.70 (m, 10H); ^{13}C NMR (126 MHz, CDCl_3) δ 21.2 (d, J = 55.1 Hz), 26.5, 28.6, 48.9 (d, J = 101.2

(Hz), 54.7, 79.2, 129.3, 129.4, 129.5, 131.5 (m), 131.6, 131.9, 132.0, 132.9, 156.8, 185.4; MS (ESI-TOF) m/z $[M+H]^+$ calcd for $C_{22}H_{27}NO_3P$ 384.1723, found 384.1746.

Methyl 4-methoxycinnamate (8a)

(Carbomethoxymethyl)triphenylphosphonium chloride (0.82 g, 2.2 mmol) was added to a suspension of Ag_2CO_3 (0.55 g, 2.0 mmol) in acetonitrile (5 mL). After 1 h, *p*-anisaldehyde (0.27 g, 2.0 mmol) was added. The reaction mixture was stirred overnight. The dark brown mixture was filtered through a layer of Celite. The Celite pad was washed with EtOAc. The combined filtrate was concentrated under reduced pressure, and the crude product was purified by chromatography on silica gel (6:1 hexanes/EtOAc) to yield compound **8a** as a colorless oil (0.38 g, 97%). For NMR analysis, the *E* and *Z* isomers were separated by a second chromatography. The 1H NMR spectrum of both isomers matched the reported values.^{14,27} *E*-**8a**: 1H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H), 3.80 (s, 3H), 6.29 (d, J = 16.0 Hz, 1H), 6.88 (d, J = 8.8 Hz, 2H), 7.44 (d, J = 8.8 Hz, 2H), 7.63 (d, J = 16.0 Hz, 1H). *Z*-**8a**: 1H NMR (500 MHz, $CDCl_3$) δ 3.73 (s, 3H), 3.83 (s, 3H), 5.84 (d, J = 12.6 Hz, 1H), 6.86 (d, J = 12.6 Hz, 1H), 6.88 (d, J = 9.0 Hz, 2H), 7.70 (d, J = 9.0 Hz, 2H).

Methyl (2*R*)-3-(bis(*tert*-butyloxycarbonyl)amino)-5-phenylpent-4-enoate (8j)

Compound **8j** was prepared following the representative procedure. Compound **8j** was obtained at 1 mmol scale as a colorless oil (0.34 g, 83%), and by 1H NMR was a 1:1 *E/Z* mixture: 1H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 1.45 (s, 9H), 2.80–2.89 (m, 1H), 2.98–3.14 (m, 3H), 3.71 (s, 3H), 3.75 (s, 3H), 5.02–5.09 (m, 2H), 5.65 (ddd, J = 11.6, 8.8, 6.0 Hz, 1H, $PhCH=CH$, *Z*), 6.17 (ddd, J = 15.7, 9.0, 6.1 Hz, 1H, $PhCH=CH$, *E*), 6.43 (d, J = 15.7 Hz, 1H, $PhCH=CH$, *E*), 6.55 (d, J = 11.6 Hz, 1H, $PhCH=CH$, *Z*), 7.17–7.24 (m, 1H), 7.25–7.35 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.099, 28.08, 29.3, 33.9, 52.3, 52.4, 58.0, 58.2, 125.8, 126.3, 126.9, 127.3, 127.6, 128.3, 128.5, 128.9, 131.8, 133.2, 137.1, 137.4, 152.0, 152.1, 170.9, 171.0; MS (ESI-TOF) m/z $[M+Na]^+$ calcd for $C_{22}H_{31}NNaO_6$ 428.2044, found 428.2025; er > 95:5 for both *E/Z* isomers determined by chiral support HPLC analysis.

Methyl (2*R*)-3-(bis(*tert*-butyloxycarbonyl)amino)-5-(pyridin-2-yl)pent-4-enoate (8k)

Compound **8k** was prepared following the representative procedure, with the exception that triphenyl(pyridin-2-ylmethyl)phosphonium chloride hydrochloride **7c** was used as the ylide precursor. Title compound was obtained at 1 mmol scale as a pale yellow oil (0.39 g, 97%), as a 6:1 *E/Z* mixture. The *E* and *Z* isomers were subsequently separated for NMR analysis by a second chromatography. *E*-**8k**: 1H NMR (500 MHz, $CDCl_3$) δ 1.44 (s, 18H), 2.90 (dddd, J = 14.5, 9.8, 8.7, 1.0 Hz, 1H), 3.09 (dddd, J = 14.5, 6.4, 5.1, 1.2 Hz, 1H), 3.74 (s, 3H), 5.08 (dd, J = 9.8, 5.1 Hz, 1H), 6.57 (d, J = 15.6 Hz, 1H), 6.70 (ddd, J = 15.6, 8.7, 6.4 Hz, 1H), 7.12 (dd, J = 6.9, 4.9 Hz, 1H), 7.29 (d, J = 7.8 Hz, 1H), 7.62 (ddd, J = 7.8, 6.9, 1.2 Hz, 1H), 8.52 (dd, J = 4.9, 1.2 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.9, 33.7, 52.2, 57.7, 83.2, 121.0, 121.9, 131.2, 132.6, 136.6, 148.9, 151.9, 155.3, 170.6. *Z*-**8k**: 1H NMR (500 MHz, $CDCl_3$) δ 1.42 (s, 9H), 1.43 (s, 9H), 3.35–3.40 (m, 2H), 3.73 (s, 3H), 5.18 (dd, J = 8.6, 6.6 Hz, 1H), 5.90 (ddd, J = 11.8, 7.8, 7.3 Hz, 1H), 6.57 (d, J = 11.8 Hz, 1H), 7.13 (dd, J = 7.1, 5.1 Hz, 1H), 7.28 (d, J = 6.9 Hz, 1H), 7.66 (ddd, J = 7.1, 6.9, 1.5 Hz, 1H), 8.60 (d, J = 4.4 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.0, 29.7, 52.3, 58.3, 83.2, 121.5, 124.2, 130.8, 132.1, 136.3, 149.3, 152.1, 156.3, 171.2; MS (ESI-TOF) m/z : $[M+H]^+$ calcd for $C_{21}H_{31}N_2O_6$ 407.2177, found 407.2170; er > 95:5 determined for *E* isomer by chiral support HPLC analysis.

Methyl (2*E*,4*S*)-4-[[[(2*S*)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-3-phenylpropyl]amino]pent-2-enoate (8l)

Compound **8l** was prepared from aldehyde **6f** and Wittig reagent **7a** following the representative procedure, except THF was used as a solvent and the reaction was performed at 0 °C for 18 h. A 1 mmol scale reaction gave **8l** (0.31 g, 82%) as a white powder. Its ¹H and ¹³C NMR spectra matched the reported values.⁴ ¹H NMR (400 MHz, CD₃OD) δ 1.23 (d, *J* = 6.9 Hz, 3H), 1.39 (s, 9H), 2.86 (dd, *J* = 13.5, 8.1 Hz, 1H), 3.01 (dd, *J* = 13.5, 7.1 Hz, 1H), 3.72 (s, 3H), 4.24–4.30 (m, 1H), 4.52–4.59 (m, 1H), 5.68 (d, *J* = 15.7 Hz, 1H), 6.72 (dd, *J* = 15.7, 5.3 Hz, 1H), 7.19 – 7.29 (m, 5H); ¹³C NMR (126 MHz, CD₃OD) δ 19.9, 28.8, 39.7, 47.1, 52.2, 57.7, 80.8, 121.0, 128.0, 129.6, 130.6, 138.4, 150.4, 157.6, 168.5, 173.6; dr > 95:5 determined by ¹H NMR.

Methyl (2*E*,4*R*)-4-[[[(2*S*)-2-[[[(1,1-dimethylethoxy)carbonyl]amino]-1-oxo-3-phenylpropyl]amino]pent-2-enoate (8m)

Compound **8m** was prepared from aldehyde **6g** and Wittig reagent **7a** following the representative procedure, except THF was used as a solvent and the reaction was performed at 0 °C for 16 h. A 1 mmol scale reaction gave **8m** (0.34 g, 90%) as a white powder: ¹H NMR (400 MHz, CD₃OD) δ 1.09 (d, *J* = 7.1 Hz, 3H), 1.40 (s, 9H), 2.88 (dd, *J* = 13.4, 7.9 Hz, 1H), 2.99 (dd, *J* = 13.4, 7.2 Hz, 1H), 3.70 (s, 3H), 4.25 (dd, *J* = 7.9, 7.2 Hz, 1H), 4.45–4.54 (m, 1H), 5.94 (d, *J* = 15.7 Hz, 1H), 6.84 (dd, *J* = 15.7, 5.1 Hz, 1H), 7.19–7.30 (m, 5H); ¹³C NMR (126 MHz, CD₃OD) δ 19.6, 28.8, 39.4, 47.2, 52.2, 57.8, 80.8, 121.0, 127.9, 129.6, 130.6, 138.6, 150.4, 157.7, 168.6, 173.8; MS (ESI-TOF) *m/z*: [M+H]⁺ calcd for C₂₀H₂₉N₂O₅ 377.2071, found 377.2065; [M+Na]⁺ calcd for C₂₀H₂₈N₂NaO₅ 399.1890, found 399.1869; dr 95:5 determined by ¹H NMR.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Scheme 1.

Scheme 2.

Table 1

Wittig reactions of phosphonium salts **7a–d** with carbonyl compounds **6a–g**

Entry	Aldehyde	Wittig reagent	Product ^a	Yield (%)	<i>E:Z</i> ^b
1				97	18:1
2				75	1:2
3				75	10:1
4				63	3:2
5				50 (72) ^c 46 ^d 7 ^{e,f}	2:1
6				87	12:1

Entry	Aldehyde	Wittig reagent	Product ^d	Yield (%)	<i>E:Z</i> ^b
7	6c	7b		85	2:3
8		7a	8g	42 ^g <1 ^e	
9	6d	7a		82 69 ^e <1 ⁱ	10:1
10	6e	7b	8l(<i>er</i> > 95:5) ^h	83 8 ^e	1:1
11	6e	7c	8j(<i>er</i> > 95:5) ^h	97	6:1
12		7a	8k(<i>er</i> > 95:5) ^h	82 ^{k,l}	>19:1

Entry	Aldehyde	Wittig reagent	Product ^d	Yield (%)	<i>E:Z</i> ^b
13	<p>6f (<i>dr</i> > 95:5)</p> <p>6g (<i>dr</i> = 95:5)</p>	7a	<p>8l (<i>dr</i> > 95:5) ^j</p> <p>8m (<i>dr</i> 95:5) ^j</p>	90 ^{k,l}	>19:1

^a Structures are of the major product.

^b *E:Z* ratio was determined from ¹H NMR spectra of the crude product.

^c 2 equivalent of Ag₂CO₃ and 2 equivalent **7d** were used.

^d 0.5 equivalent Ag₂CO₃ and 0.5 equivalent K₂CO₃ were used.

^e K₂CO₃ was used instead of Ag₂CO₃.

^f In the analogous example aldehyde **6b** and diethyl ethylphosphonate gave no Wittig reaction when promoted by the weak base bicyclic triaminophosphine (reference 16) in THF.

^g Reaction mixture was heated at 60 °C.

^h Enantiomeric ratio determined by chiral support HPLC analysis.

ⁱ tBuOK was used instead of Ag₂CO₃.

^j Diastereoisomeric ratio determined by ¹H NMR of crude sample.

^k Reaction was performed in THF because of the poorer solubility of the carbonyl compound in MeCN.

^l Reaction was performed at 0 °C.