Organic Syntheses

A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

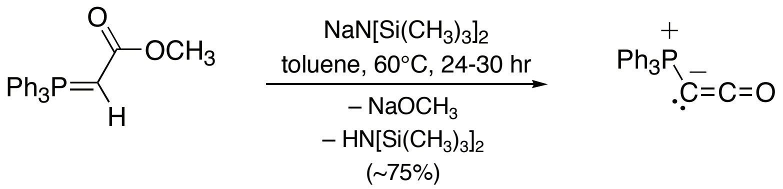
September 2014: The paragraphs above replace the section "Handling and Disposal of Hazardous Chemicals" in the originally published version of this article. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Copyright © 2005 Organic Syntheses, Inc. All Rights Reserved

DOI:10.15227/orgsyn.082.0140

Organic Syntheses, Vol. 82, p. 140-146 (2005); Coll. Vol. 11, p. 986-991 (2009).

PREPARATION OF (TRIPHENYLPHOSPHORANYLIDENE)-KETENE FROM (METHOXYCARBONYLMETHYLENE)-TRIPHENYLPHOSPHORANE



Submitted by Rainer Schobert.[1]
Checked by Robert K. Boeckman Jr. and Joseph E. Pero.

1. Procedure[2]

A 3-L, three-necked, round-bottomed flask, equipped with a mechanical stirrer and a lateral gas inlet is purged with dry argon (Note 1) and charged with sodium amide (19.5 g, 0.5 mol) (Note 2), toluene dried by passage through alumina (1300 mL) (Note 3), and bis(trimethylsilyl)amine (81 g, 105 mL, 0.5 mol) (Note 4). The flask is fitted with a reflux condenser, then flushed once more with argon, and immersed in an oil bath. The mixture is heated at 70-80 °C (bath temperature) until a clear and colorless solution of sodium hexamethyldisilazanide is obtained and the evolution of ammonia has ceased (2-4 h) (Notes 5, 6). The reaction mixture is cooled to room temperature and the condenser is removed briefly, with protection from air by a stream of argon, to allow the addition of (methoxycarbonylmethylene)-triphenylphosphorane (167 g, 0.5 mol) in several large portions (Note 7). The mixture is then heated again to ca. 60-70 °C (bath temperature) and stirring is continued for a further 24-30 h by which time the solution should take on a bright yellow hue (Note 8). While still hot and blanketed with a stream of argon, the reaction mixture is rapidly suction filtered using a 24/40 standard taper vacuum filtration adapter and a 350 mL fritted funnel (course porosity) open to the atmosphere through a 1 inch thick pad of Celite™ into a 2-L 24/40 single-necked round-bottomed flask (Notes 9 and 10).

Once filtration is complete, the receiving flask is flushed with argon and attached to a rotary evaporator (Note 11). The colorless filtrate is evaporated to dryness and the residue recrystallized from dry toluene (~1g / 5mL) by dissolution in hot toluene followed by cooling to -20 °C in a freezer overnight. While the mixture was cold, the resulting solids are collected by suction filtration using a 350 mL coarse fritted funnel and washed on the filter with three 100 mL portions of cold (0 °C) toluene affording the first crop of phosphorane (Note 3). The mother liquor is again concentrated to dryness under vacuum, redissolved in ~100 mL of hot dry toluene, and again cooled to -20 °C in a freezer overnight. The resulting solids are isolated and washed as above. The first and second crops of phosphorane are then combined and dried under high vacuum (ca 0.01 Torr) to a constant weight to afford 106.8-114.9 g (74-76%) (Note 12) of the phosphorane product as a very pale yellow, flaky powder having mp 173 °C (Note 13).

2. Notes

1. An atmosphere of dry argon is maintained throughout the entire process. While neither the starting nor the product ylide are particularly air- or moisture-sensitive in the solid state, hot solutions of the latter are sensitive.

2. Sodium amide should be of 95% purity. Powdery batches were found to react more readily than suspensions in mineral oil or pellets. Sodium amide can be purchased from Aldrich Chemical Company, Inc. The checkers employed sodium amide purchased from Acros Organics CAUTION: Sodium amide is highly flammable and corrosive and can cause severe burns.

3. The checkers employed toluene dried by passage through a column containing anhydrous alumina under nitrogen pressure. The submitters dried toluene by distillation from sodium metal. Attempts by the checkers to employ toluene dried by distillation from CaH_2 led to inferior results during attempts to form sodium hexamethyldisilazide (NaHMDS).

4. Bis(trimethylsilyl)amine (hexamethyldisilazane, HMDS), 99+%, was purchased from Aldrich Chemical Company, Inc. CAUTION: bis(trimethylsilyl)amine is harmful and corrosive.

5. Purging the set-up with argon every now and then cuts down reaction times considerably.

6. Commercially available sodium hexamethyldisilazide (e.g. Aldrich Chemical Company) can be used instead. However, it is costly and the reaction time and yields of product crucially depend on its age and quality.

7. (Methoxycarbonylmethylene)triphenylphosphorane can be bought

from Aldrich Chemical Company, Inc. The checkers employed Aldrich material as received. The phosphorane can also be readily prepared at low cost in two steps from triphenylphosphine and methyl bromoacetate according to a literature procedure.[3]

8. Monitoring reaction progress is possible by IR spectroscopy of aliquots of the reaction mixture measured as films on KBr plates. A strong product band at 2090 cm^{-1} of constant intensity and the disappearance of a starting ylide band at 1616 cm^{-1} are indicative of a complete reaction.

9. The submitters employed a funnel with a sintered frit (fine porosity) where the frit is covered with a 2 cm layer of basic alumina (III) and 1 cm of celite atop. Through side-arm stopcocks, the filter funnel is connected to an argon line and the receiving flask to a source of vacuum (water-jet or membrane pump). The whole set-up is positioned upright or slightly slanted and submitted to several cycles of evacuating and flushing with inert gas prior to use. During filtration occasional removal or resuspending of sedimented sodium methoxide from the surface of the celite/alumina plug by scraping with a long spatula may be necessary in order to maintain a continuous flow of filtrate.

10. The submitters filtered the reaction mixture by pouring through a tapered adaptor into a 2-L Schlenk-type filter funnel which is joined to the only neck of a round-bottomed 2-L receiving flask (Note 9). Filtration is then carried out by application of a slight overpressure from an argon line to the stoppered funnel and by gentle suction at the receiving flask (the stopcock to the vacuum source should be opened at regular intervals but only briefly at each time). During filtration which typically takes 30 to 60 min, the temperature of the reaction mixture in the filter funnel should be kept between 30 °C and 50 °C by means of a heating basket, mantle or tape, or at least insulating foil to avoid premature product crystallization.

11. The submitters concentrated the clear filtrate to 500 mL, flushed once more with argon and then placed in a refrigerator for 24 h. The faintly yellow precipitate (ca. 70-80 g) is collected on a second Schlenk-type filter funnel, washed with dry diethyl ether (300 mL) and dried on an oil pump at ca. 0.01 Torr. A second, darker crop of product (ca. 20-35 g) is obtained by concentrating the toluene mother liquor to ca. 250 mL, layering it with diethyl ether (50 mL) and cooling the mixture to 4 °C for 24 h. The resulting precipitate is collected, washed and dried like the first batch to which it is by then identical in color and all analytical data.

12. The submitters obtained 100-115g (66-75%) of pure phosphorane in two crops with identical mp and spectroscopic properties using the above described direct crystallization procedure (Note 11).

13. The product is pure by usual microanalytical standards; IR (KBr, ν): 2090 (s), 1625 (m), 1436 (m), 1110 (m) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz δ: 7.77-7.64 (m, 6H), 7.63-7.55 (m, 3H), 7.54-7.44 (m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz δ: 145.6 (d, $^2J_{PC}$ 43.0 Hz, C^β), 132.3 (s, C-*meta*), 132.2 (s, C-*para*), 129.6 (d, $^1J_{PC}$ 98.5 Hz, C-*ipso*), 128.8 (d, $^3J_{PC}$ 12.9 Hz, C-*ortho*), -10.5 (d, $^1J_{PC}$ 185.4 Hz, C^α); ^{31}P NMR ($CDCl_3$, 162 MHz δ: 6.0. Analysis performed on an unrecrystallized sample of the bulk material: Anal. Calcd for $C_{20}H_{15}OP$: C, 79.46; H, 5.00; P, 10.25. Found. C, 78.66; H, 5.30. Recrystallization of this sample from toluene and reanalysis gave: Anal. Calcd for $C_{20}H_{15}OP$: C, 79.46; H, 5.00; P, 10.25. Found. C, 79.60; H, 5.06. The only detectable impurities by ^1H NMR are the starting ester ylide and toluene (δ 3.60, s and 2.36, s). Based on this intergration, the purity of product is calculated to be ~99.97%. Prior analytical results have been reported.[4-6]

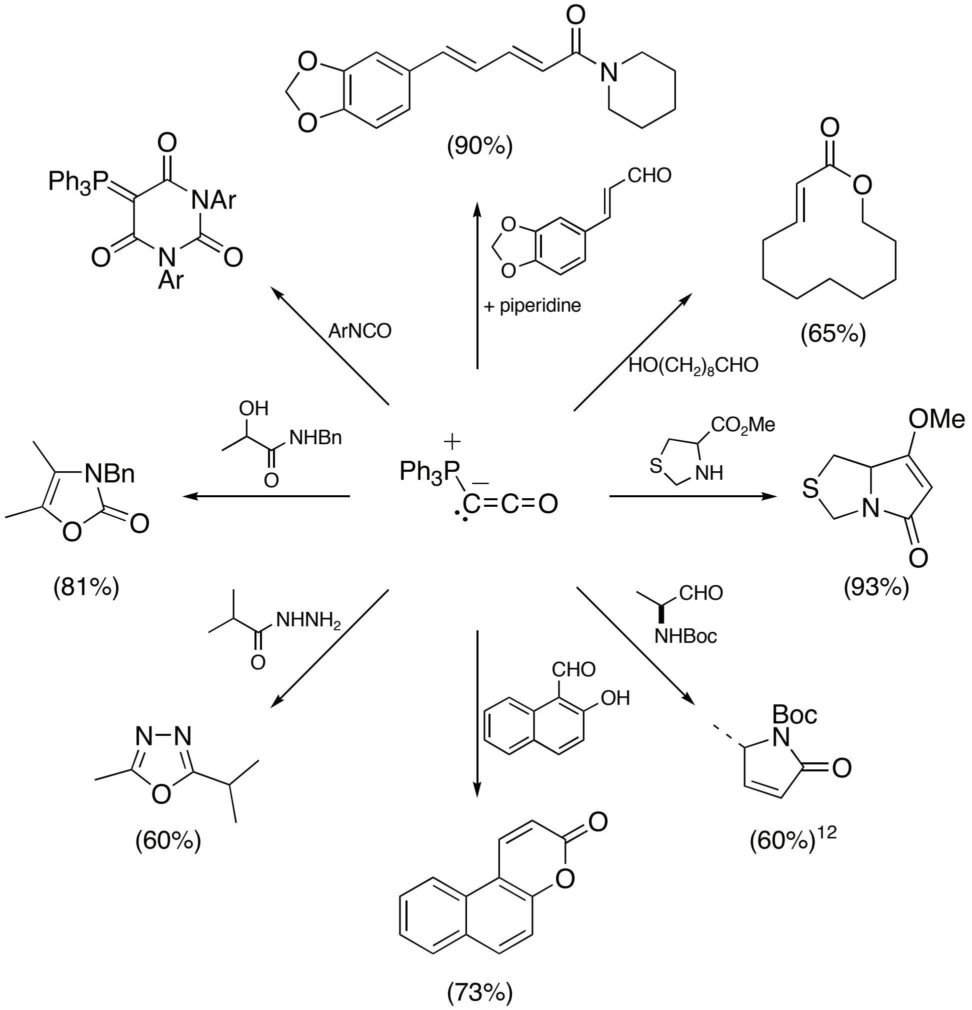
Waste Disposal Information

All toxic materials were disposed of in accordance with "Prudent Practices in the Laboratory"; National Academy Press; Washington, DC 1995.

3. Discussion

Alternative methods for the preparation of Ph_3PCCO: Strong bases other than sodium hexamethyldisilazanide (NaHMDS) have been employed for the elimination of methanol from (methoxycarbonylmethylene)triphenylphosphorane. With crystalline sodium amide, drastic reaction conditions (refluxing in benzene or toluene for several days) are required.[7] However, mixtures of sodium amide and catalytic quantities of HMDS react as readily as stoichiometric amounts of preformed NaHMDS.[8] Alkyllithium bases (e.g. *n*BuLi, PhLi) give low yields of Ph_3PCCO contaminated with various byproducts stemming from attack of the base on the phenyl rings.[9] The title ylide has also been prepared by pyrolysis of the disilylated ester ylide obtained from reaction of [1,1-bis(trimethylsilyl)methylene]triphenylphosphorane with carbon dioxide,[10] and by pyrolysis of the betaine obtained from the reaction of carbodiphosphorane, $Ph_3P{=}C{=}PPh_3$, with carbon dioxide.[6] However, neither protocol is suitable for large scale preparation.

Properties and reactions of Ph_3PCCO:[11] It is remarkably stable and solid samples can be stored for months at room temperature under an atmosphere of argon and handled even under ambient conditions without notable decomposition. This fact is due to its electronic structure featuring an orthogonal pair of filled π-systems ($\pi^4 \perp \pi^4$). Hence Ph_3PCCO shows little propensity to dimerize like the strongly electrophilic ketenes. It does not even enter readily into Wittig alkenation reactions which are so typical of common phosphorus ylides. It represents a nucleophilic-only C_2-building block reacting with a wide range of electrophiles in a variety of ways and undergoing cycloadditions both at the polar $P–C^{\alpha}$ and at the $C^{\alpha}{=}C^{\beta}$ bond. For example, acidic compounds, RXH, such as alcohols, thiols, amines, and CH-active 1,3-dicarbonyls add across the C=C bond of Ph_3PCCO to give the corresponding Wittig-active acyl ylides, $Ph_3P{=}CH–C(O)XR$. Multicomponent and domino reactions between the cumulated ylide, an

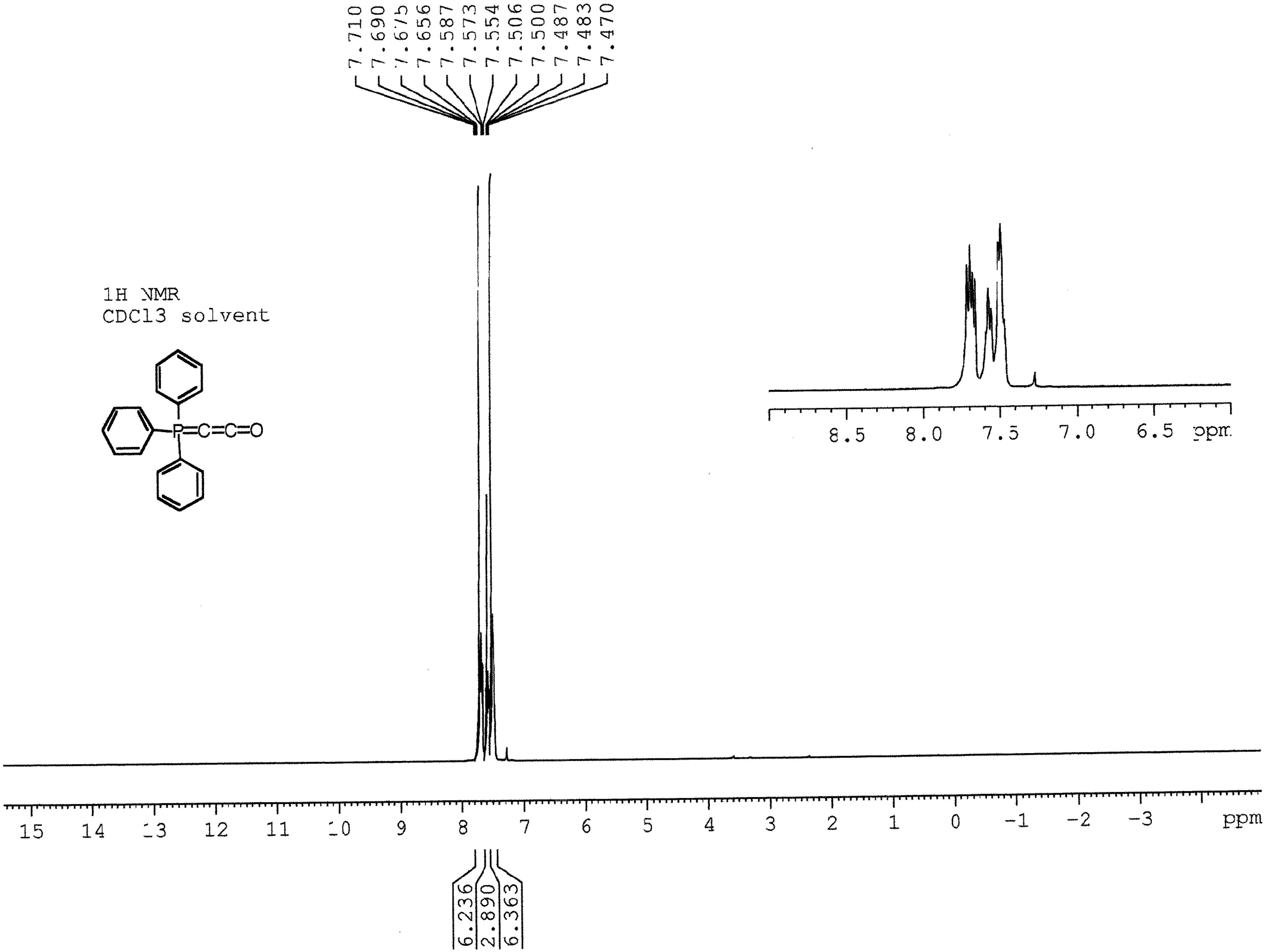


acidic compound, and a ketone or an aldehyde lead to various α,β-unsaturated carbonyl compounds. Intramolecular variants employing difunctional carbonyl derivatives, including esters and amides, bearing such acidic functionalities furnish (hetero)cyclic products with ring sizes ranging from five to twenty. Grignard compounds, RMgX, react with Ph_3PCCO to yield acyl ylides $Ph_3P{=}CHC(O)R$ upon hydrolytic work-up. Both [2+2]- and [2+4]-reactions are known of Ph_3PCCO, e.g. with ketenes to form cyclobutan-1,3-diones, and with iso(thio)cyanates to furnish six-membered pyrimidinetriones, or hexahydro-1,3-dithiazines, respectively.

1. Universität Bayreuth, Organisch-chemisches Laboratorium, Universitätsstrasse 30, D-95440 Bayreuth (Germany). E-mail: Rainer.Schobert@uni-bayreuth.de, Fax: +49 (0)921 552672.
2. Bestmann, H. J.; Sandmeier, D. *Angew. Chem.* **1975**, *87*, 630*; Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 634.
3. Isler, O.; Gutmann, H.; Montavon, M.; Ruegg, R.; Ryser, G.; Zeller, P. *Helv.Chim. Acta* **1957**, *40*, 1242-1249.
4. Daly, J. J.; Wheatley, P. J. *J. Chem. Soc. A* **1966**, 1703-1706.
5. Matthews, C. N.; Birum, G. H. *Chem. Ind. (London)* **1968**, 653.
6. (a) Matthews, C. N.; Birum, G. H. *Tetrahedron Lett.* **1966**, 5707-5710; (b) Matthews, C. N.; Birum, G. H. *Acc. Chem. Res.* **1969**, *2*, 373-379.
7. Bestmann, H. J.; Schmidt, M.; Schobert, R. *Synthesis* **1988**, 49-53.
8. Haas, W. *PhD Thesis*, University of Erlangen-Nürnberg, Germany **1992**, 20.
9. (a) Bestmann, H. J.; Besold, R.; Sandmeier, D. *Tetrahedron Lett.* **1975**, 2293-2294; (b) Buckle, J.; Harrison, P. G. *J. Organomet. Chem.* **1974**, *77*, C22-C24.
10. Bestmann, H. J.; Dostalek, R.; Zimmermann, R. *Chem. Ber.* **1992**, *125*, 2081-2084.
11. (a) Bestmann, H. J. *Angew. Chem.* **1977**, *89*, 361-376*; Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 349-364; (b) Schobert, R.; Gordon, G. J. *Science of Synthesis: Houben-Weyl Methods of Molecular Transformations*; Thieme: Stuttgart, **2004**, Vol. 27, p. 1042.
12. Andrus, M. B.; Li, W.; Keyes, R. F. *J. Org. Chem.* **1997**, *62*, 5542-5549.

Appendix
Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

(Triphenylphosphoranylidene)ketene: Phosphonium, triphenyl-, oxoethenylide (9); (73818-55-0) *and* Ethenone, (triphenylphosphoranylidene)- (9); (15596-07-3)
(Methoxycarbonylmethylene)triphenylphosphorane: Phosphonium, triphenyl-, 2-methoxy-2-oxoethylide (9); (21204-67-1)
Hexamethyldisilazane: Silanamine, 1,1,1-trimethyl-*N*-(trimethylsilyl)- (9); (999-97-3)
Sodium Amide (9); (7782-92-5)


7.710
7.690
7.675
7.656
7.587
7.573
7.554
7.506
7.500
7.487
7.483
7.470
1H NMR
CDCl3 solvent
P=C=C=O
8.5
8.0
7.5
7.0
6.5
ppm
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
−1
−2
−3
ppm
6.236
2.890
6.363