Table I. Conversion $R_1R_2C{=}O \rightarrow R_1R_2C{=}CH_2$ *via* Methylphosphonic Acid Bis(dimethylamide) Adducts

Carbonyl compd	Yield of adduct, %	Yield of olefin, %[a]
Benzophenone	95	93
4-*t*-Butylcyclohexanone	98	65[b]
2-Cyclohexenone	96	78[c, d]
Benzaldehyde	95	53[c]
Δ^3-Cyclohexenecarboxaldehyde	95	67[c]
Dodecanal	89	70[c]

[a] Yields given refer to reaction in benzene at reflux for 12 hr. [b] Yield of isolated product. [c] Yield as determined by vpc or nmr analysis. [d] Elimination carried out without silica gel and in the presence of triethylamine to prevent isomerization of the olefinic product.

Table II. Conversion $R_1R_2CO \rightarrow R_1R_2C{=}CHCH_3$ *via* Ethylphosphonic Acid Bis(dimethylamide) Adducts

Carbonyl compd	Yield of adduct, %	Yield of olefin, %
Benzophenone	97	90
4-*t*-Butylcyclohexanone	92	80
Benzaldehyde	98	90[a,b]
Δ^3-Cyclohexenecarboxaldehyde	96	79[a]

[a] For stereochemistry see E. J. Corey and G. T. Kwiatkowski, *J. Am. Chem. Soc.*, **88**, 5653 (1966). [b] Yield for reaction in toluene at reflux for 12 hr; all other yields for reaction in benzene at reflux for 12 hr.

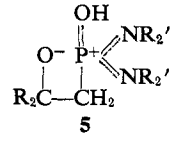
to β-alkoxy phosphonium (Wittig) betaines, do not undergo olefin-forming elimination under normal conditions. Results for a variety of carbonyl components are summarized in Tables I and II.

The phosphonic amide route to olefins is general in the sense that it can be applied to the formation of mono-, di-, tri-, and tetrasubstituted ethylenic systems. Table II shows the yields of adducts and olefins obtained from aldehydes and ketones using as reagent the α-lithio derivative of ethylphosphonic acid bis(dimethylamide), prepared by metalation with butyllithium as described above. The α-lithio derivative of isopropylphosphonic acid dimethylamide, similarly available, also is useful; for example, with benzophenone the β-hydroxy phosphonic acid amide **3** ($R_1 = R_2 = C_6H_5$; $R_3 = R_4 = CH_3$; $R = CH_3$) is obtained in 94% yield, and 1,1-diphenyl-2-methylpropene is formed in 92% yield.[6]

A wide variety of phosphonic acid chlorides and amides are readily available by known procedures.[2] In addition, it has been found that lithio derivatives of type **1** can be alkylated with alkyl iodides and bromides which are not excessively prone to elimination. Thus, reaction of the lithio derivative **1** ($R_3 = R_4 = H$; $R = CH_3$) with 1 equiv of methyl iodide, followed by sequential addition of 1 equiv of *n*-butyllithium and 1 equiv of benzophenone, produces the β-hydroxy phosphonic amide **3** ($R_1 = R_2 = C_6H_5$; $R_3 = CH_3$, $R_4 = H$, $R = CH_3$) in 96% yield; the analogous sequence using *n*-butyl bromide in the alkylation affords the adduct **3** ($R_1 = R_2 = C_6H_5$; $R_3 = n\text{-}C_4H_9$; $R_4 = H$; $R = CH_3$) in 96% yield.

These findings open up a host of interesting synthetic possibilities and a number of questions. The phosphonamide and the sulfinamide[1] routes to olefins are now available as alternatives to the Wittig reaction with phosphonium ylides,[7] as well as the somewhat less general, but often very useful, Horner–Emmons reaction with certain stabilized carbanions derived from phosphonate esters and phosphine oxides,[8,9] and the newer variation which employs carbanions derived from thiophosphonate esters.[10] Several general advantages of the phosphonamide route to olefins compared to the Wittig reaction are apparent; these include (1) the absence of reaction products, such as triphenylphosphine oxide in the case of the Wittig reaction, which can complicate the isolation of olefin; (2) the ready availability and potential low cost (especially on a molar basis) of the phosphonamide reagents; (3) the possibility of purification at the stage of the intermediate β-hydroxy phosphonic amide;[11] (4) the relatively greater opportunity to control the stereochemistry of the intermediate β-hydroxy phosphonic amide and, hence, of the olefin;[12] and (5) the availability of phosphonamide reagents by routes involving alkylation on carbon (usually impractical with phosphonium ylides).

This investigation is being continued along a broad front to determine the full range of utility in synthesis of the new reagents reported here and to clarify the underlying reaction mechanisms. In regard to the mechanism of olefin formation from β-hydroxy phosphonic amides, it seems attractive to consider oxygen attack on phosphorus from a dipolar intermediate **5** followed by *cis* cycloelimination, although this is speculative at present.[13]



5

(6) In general, the rate of elimination from the adducts of type **3** to form olefin increases with the number of carbon substituents at the ethylenic function; yields also appear to improve with substitution.

(7) For a review see A. Maercher, *Org. Reactions*, **14**, 270 (1965).
(8) L. Horner, H. Hoffman, W. Klink, H. Ertel, and V. G. Toscano, *Ber.*, **95**, 581 (1962).
(9) W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, **83**, 1733 (1961).
(10) E. J. Corey and G. T. Kwiatkowski, *ibid.*, **88**, 5654 (1966).
(11) These substances have been found uniformly to be nicely crystalline substances which are readily and efficiently purified by a single recrystallization.
(12) See Table II, footnote *a*.
(13) We thank the National Institutes of Health for generous financial aid in the form of a research grant and postdoctoral fellowship.

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The Synthesis of *cis* and *trans* Olefins *via* β-Keto and β-Hydroxy Phosphonamides

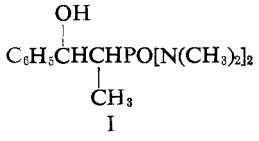
Sir:

The Wittig synthesis of olefins combines the extension of carbon skeleton with the feature of position-specific introduction of an ethylenic unit and in consequence has proved to be tremendously useful.[1] One serious limitation, however, arises from the frequent difficulty of synthesizing a particular geometrical form of an

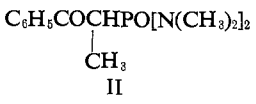
(1) For a recent review see A. W. Johnson, "Ylid Chemistry," Academic Press Inc., New York, N. Y., 1966.

olefin which can exist in *cis* or *trans* arrangements.[2] In this note the application of the phosphonamide route to olefins[3] to this problem is described.

One advantage of the phosphonamide method derives from the fact that the intermediate β-hydroxy phosphonamides are isolable (usually crystalline) substances which can be subjected to purification and which undergo stereospecific (probably *cis*[3]) elimination to form olefins. Even if adduct formation with a carbonyl compound is not stereospecific, separation of diastereomers and subsequent elimination serves to produce the pure isomeric olefins. The synthesis of pure *cis*-1-phenylpropene is illustrative. Reaction of benzaldehyde with the α-lithio derivative of ethylphosphonic acid bis(dimethylamide) in tetrahydrofuran–toluene (1:4) at −78° afforded in essentially quantitative yield the β-hydroxy phosphonamide I as a mixture of two diastereomers, IA and IB, in a ratio of 3.5:1.



I

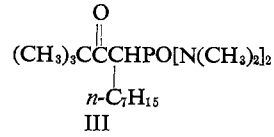


II

The major isomer[4] was separated by recrystallization (ether–pentane) and converted in excellent yield to *cis*-1-phenylpropene[5] by heating at reflux in toluene.

Pure *trans*-1-phenylpropene was synthesized stereospecifically by utilizing another route which is generally available for the preparation of β-hydroxy phosphonamides. Reaction of the α-lithio derivative of ethylphosphonic acid bis(dimethylamide) (2 equiv) with methyl benzoate led to the oily β-keto phosphonamide II in high yield. Reduction of II with sodium borohydride in methanol (0°) produced in 80% yield and with 98% stereospecificity the β-hydroxy phosphonamide IB, which was further converted to *trans*-1-phenylpropene[5] by heating at reflux in toluene. The β-keto phosphonamide II can also be made efficiently by oxidation of the corresponding hydroxy compounds IA and IB by active manganese dioxide in chloroform at reflux. Thus, the use of intermediate β-keto phosphonamides amplifies the advantage of the phosphonamide method.[6]

The phosphonamide method can serve as an excellent complement to the Wittig synthesis in some cases. Reaction of pivalaldehyde with Wittig reagents of the type $(C_6H_5)_3PCHR$ produces *cis* olefins in heavy predominance; in fact, in dimethyl sulfoxide the product from the ylide with R = n-C_7H_{15} is a mixture of 98.5% *cis*- and 1.5% *trans*-1-*t*-butyl-1-nonene.[7] In contrast to the Wittig reaction, the phosphonamide method can be made to afford pure *trans*-1-*t*-butyl-1-alkenes readily. Treatment of methyl pivalate with the α-lithio derivative of *n*-octylphosphonic acid bis(dimethylamide) (2 equiv) afforded the β-keto phosphonamide III in 97% yield. Reduction of III with lithium alumi-



III

num hydride–aluminum chloride with alkoxide equilibration[8,9] led mainly to one β-hydroxy phosphonamide (92–94% of the diastereomeric mixture), thermal decomposition of which in benzene at reflux for 1.75 hr produced pure *trans*-1-*t*-butyl-1-nonene in 71% yield.[10,11]

The attainment of predictable and complete control of stereochemistry in the synthesis of β-hydroxy phosphonamides by the various routes will require much more information than is now available. The stereochemical results obtained thus far encourage the belief that progress can be made in this direction and reinforce the view[3] that the phosphonamide route to olefins is a widely useful method.[12]

(2) Moderate progress has been made in altering the proportion of isomers from the Wittig reaction by the variation of reaction conditions; see M. M. Shemyakin in "Organo-phosphorus Compounds," Butterworth & Co. (Publishers) Ltd., London, 1964, p 271.

(3) E. J. Corey and G. T. Kwiatkowski, *J. Am. Chem. Soc.*, 88, 5652 (1966).

(4) The major isomer IA (mp 80.5–82°) shows nmr peaks due to C-methyl (doublet of doublets) centered at δ 0.94 (J_{HH} = 7.5, J_{HP} = 17), whereas for the minor isomer IB the corresponding values are δ 0.75 (J_{HH} = 7.5, J_{HP} = 17). All intermediates reported here have been characterized by nmr and infrared, elemental, or mass spectral analysis and by conversion to known olefins.

(5) R. Y. Mixer, R. F. Heck, S. Winstein, and W. G. Young, *J. Am. Chem. Soc.*, 75, 4094 (1953).

(6) The following reagents have been used successfully for the reduction of β-keto phosphonamides to β-hydroxy phosphonamides: sodium or lithium borohydride, lithium aluminum hydride or lithium alkoxyaluminum hydrides, hydrogen–Raney nickel, aluminum amalgam–tetrahydrofuran–water, diborane, and diisoamylborane. It is our experience that with the proper choice of these reagents either diastereomeric β-hydroxy phosphonamide can usually be produced stereoselectively.

(7) E. Hamanaka and E. J. Corey, unpublished results; see also ref 2.

(8) Method of E. L. Eliel and M. N. Rerick, *J. Am. Chem. Soc.*, 82, 1367 (1960).

(9) The ketone III is not reduced by sodium borohydride under a variety of conditions, apparently because of the considerable steric hindrance.

(10) The rate of decomposition of the diastereomeric β-hydroxy phosphonamide leading to *trans*-1-*t*-butyl-1-nonene is much faster than that of the diastereomer which gives the *cis* olefin. Therefore, it is possible to obtain pure *trans* olefin, even though the β-hydroxy phosphonamide used is contaminated with *ca.* 6% of the unwanted diastereomer, simply by limiting the reaction time; this is another useful feature of the phosphonamide method.

(11) The reaction of α-lithio-*n*-octylphosphonic acid bis(dimethylamide) with pivalaldehyde at −78° in tetrahydrofuran affords a mixture of diastereomeric adducts which after total conversion to olefin gives rise to a mixture of *trans*- and *cis*-1-*t*-butyl-1-nonene in a ratio of 3:1.

(12) We are indebted to the National Institutes of Health for financial support of this work in the form of a postdoctoral fellowship and a research grant.

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The Synthesis of Olefins from O,O′-Dialkyl α-Lithioalkylphosphonothioate Esters

Sir:

Anions derived from phosphonate esters which possess a charge-stabilizing electron-withdrawing substituent, *e.g.*, **1**, X = cyano, carbonyl, or aryl, are extremely useful in the synthesis of certain olefins from aldehydes and ketones.[1-3] Anions of type **1** with X = H or alkyl (or other nonstabilizing substituents) have not previously been generated, despite attempts[1]

(1) W. S. Wadsworth and W. D. Emmons, *J. Am. Chem. Soc.*, 83, 1733 (1961).

(2) L. Horner, H. Hoffmann, and H. G. Wippel, *Ber.*, 91, 61 (1958).

(3) L. Horner, H. Hoffmann, W. Klink, H. Ertel, and V. G. Toscano, *ibid.*, 95, 581 (1962).