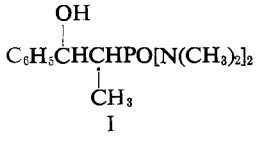
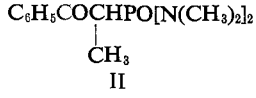
olefin which can exist in *cis* or *trans* arrangements.[2] In this note the application of the phosphonamide route to olefins[3] to this problem is described.

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

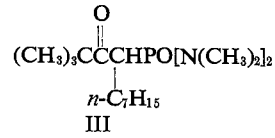


II

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:*

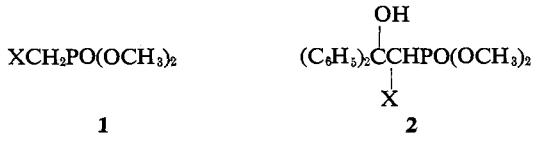
Anions derived from phosphonate esters which possess a charge-stabilizing electron-withdrawing substituent, *e.g.*, **1**, X = cyano, carbonyl, or aryl, are extremely useful in the synthesis of certain olefins from aldehydes and ketones.[1-3] Anions of type **1** with X = H or alkyl (or other nonstabilizing 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).

using methods which suffice for the more stabilized varieties, and, consequently, their use in synthesis has remained unclear. We now report that such anions as **1**, X = H and $CH_3$, can be formed as lithio derivatives efficiently and conveniently by the action of 1 equiv of *n*-butyllithium in tetrahydrofuran at −78° for 5 min, as shown by reaction with benzophenone to produce the adducts **2**, X = H and $CH_3$, in high yield. (All operations with organometallic reagents described herein were conducted using a nitrogen atmosphere.) These intermediates do not appear to



**1** **2**

be *directly* applicable to olefin synthesis, however, since neither **2**, X = H or $CH_3$, nor the conjugate bases undergo efficient or facile cycloelimination to form an ethylenic bond under a wide range of conditions.[4-6] *In contrast*, the α-lithio derivatives of alkylphosphonothioates **3**, $R_1R_2$ = H or alkyl, which can be prepared by metalation with *n*-butyllithium and which react rapidly with

**3** **4**

aldehydes and ketones to form adducts of type **4**, *can* be used as reagents for the synthesis of 1,1-disubstituted, trisubstituted, and tetrasubstituted olefins.

The following O,O′-dialkyl phosphonothioate esters were metalated by *n*-butyllithium in tetrahydrofuran under nitrogen to give *ca.* 0.5 *M* solutions of the corresponding α-lithio derivatives: dimethyl methylphosphonothioate (**3**, $R_1 = R_2 = H$) (−78°, 5 min), dimethyl ethylphosphonothioate (**3**, $R_1 = H$, $R_2 = CH_3$) (−78°, 20 min), dimethyl *n*-butylphosphonothioate (**3**, $R_1 = H$, $R_2 = n\text{-}C_3H_7$) (−78°, 30 min), and dimethyl isopropylphosphonothioate (**3**, $R_1 = R_2 = CH_3$) (−50°, 1.5 hr).[7] These lithio reagents were allowed to react with a variety of carbonyl compounds, including benzophenone, 4-*t*-butylcyclohexanone, 2-cyclohexenone, and $\Delta^3$-cyclohexenecarboxaldehyde, at low temperatures (−78 to 0°) to form carbonyl addition products, and the adducts were further decomposed at room temperature or above *in situ* to give olefins; Table I summarizes the results for a number of olefin syntheses. It should be noted that the temperatures required for elimination were higher than 25° in certain cases, generally those in which the starting carbonyl component was a nonconjugated ketone or an aldehyde. Although carbonyl adducts were easily obtained from aldehydes and the lithio derivatives of dimethyl methylphosphonothioate and dimethyl *n*-alkyphosphonothioates, these did not afford olefins under normal and even drastic conditions involving the lithium or potassium alkoxides in tetrahydrofuran or dimethoxyethane.

**Table I.** Synthesis of Olefins from Carbonyl Compounds and Dimethyl α-Lithiophosphonothioates in Tetrahydrofuran

| Olefinic product | Elimination conditions: time, hr (temp, °C) | Yield, % |
|---|---|---|
| 1,1-Diphenylethylene[a] | 21 (25) | 81 |
| 4-*t*-Butylmethylenecyclohexane[a] | 24 (65) | 52 |
| 3-Methylenecyclohexene[a] | 5 (25) | 31 |
| 1,1-Diphenyl-2-methylethylene[b] | 6 (25) | 93 |
| 4-*t*-Butylethylidenecyclohexane[b] | 20 (65) | 75 |
| 1,2-Dimethylphenylethylene[b] | 16 (25) | 53[e] |
| 1,1-Diphenyl-2-*n*-propylethylene[c] | 3 (25) | 88 |
| 1,1,2-Tri-*n*-propylethylene[c] | 20(65) | 69 |
| 3-Butylidenecyclohexene[c] | 1 (65) | 61[f] |
| 1,1-Diphenyl-2,2-dimethylethylene[d] | 1 (25) | 80 |
| 4-*t*-Butylisopropylidenecyclohexane[d] | 4 (50) | 71 |
| 1,1-Dimethyl-$\Delta^3$-cyclohexenylethylene[d] | 36 (65) | 68 |

[a] Reagent: dimethyl methylphosphonothioate. [b] Reagent: dimethyl ethylphosphonothioate. [c] Reagent: dimethyl *n*-butylphosphonothioate. [d] Reagent: dimethyl isopropylphosphonothioate. [e] *trans*:*cis* = 0.43. [f] *trans*:*cis* = 2.4.

O,O′-Dialkyl α-lithioalkylphosphonothioates have been found to undergo smooth alkylation, *e.g.*, with methyl iodide or *n*-butyl bromide. Thus, O,O′-dimethyl ethylphosphonothioate and O,O′-dimethyl isopropylphosphonothioate[7] have been obtained efficiently by sequential methylation of O,O′-dimethyl methylphosphonothioate. Further, in one flask starting with O,O′-dimethyl methylphosphonothioate, 1,1-diphenyl-1-hexene has been obtained in 84% over-all yield by the following sequential operations: (1) addition of *n*-butyllithium at −78°, (2) reaction with *n*-butyl bromide at −78 to 25°, (3) addition of *n*-butyllithium at −78°, (4) addition of benzophenone, and (5) storage at 25° for 6 hr to effect elimination.

Finally, we report the discovery of a unique silver(I)-catalyzed olefin-forming elimination from β-hydroxy phosphonothioate esters. For example, the adduct from 4-*t*-butylcyclohexanone and O,O′-dimethyl methylphosphonothioate, when treated with silver nitrate in methanol at 25° for a few hours, afforded 4-*t*-butylmethylenecyclohexane (40% yield). This interesting catalytic effect appears to be quite specific, since other metal ions with an affinity for sulfur, *e.g.*, mercury(II) and copper(II), are without activity. Further study of this catalytic elimination is planned. It is attractive to suppose that the catalyzed process involves coordination of silver(I) with sulfur in the β-hydroxy phosphonothioate system with consequent

(4) For example, the anion of **2**, X = H, in tetrahydrofuran was heated to ~60° in the presence of potassium *t*-butoxide, tertiary amines, dimethylformamide, dimethyl sulfoxide, hexamethylphosphoramide, or lithium chloride, and, at best, only a 30% yield of 1,1-diphenylethylene was obtained, together with benzophenone, unsaturated phosphonate, and acidic materials. The slowness of elimination from the anion of **2**, X = H, relative to **2**, X = electron-withdrawing group, appears to indicate that considerable negative charge accumulates at the carbon α to phosphorus in the transition state for olefin formation; cycloelimination from a four-membered cyclic structure may *not* be completely concerted.

(5) The adduct of benzophenone and α-lithioisopropylphosphonate, a particularly favorable case for elimination of phosphate monoanion, affords only 65% yield of 1,1-diphenyl-2,2-dimethylethylene.

(6) Anions derived from **1** (X = H or alkyl) *are* of value in the synthesis of keto phosphonates **1** (X = RCO) by reaction with esters. The preparation of these intermediates, which are of value in olefin synthesis [see H. Takahashi, K. Fujiwara, and M. Ohta, *Bull. Chem. Soc. Japan*, **35**, 1498 (1962)], is usually impractical by the Michaelis–Arbusov reaction.

(7) The methyl-, ethyl-, and butylphosphonothioate esters were obtained as described by F. W. Hoffmann, D. H. Wadsworth, and H. D. Weiss, *J. Am. Chem. Soc.*, **80**, 3945 (1958). Dimethyl isopropylphosphonothioate was synthesized by reaction of dimethyl α-lithioethylphosphonothioate with methyl iodide. *Anal.* Found: C, 35.47; H, 7.83. All compounds reported here were adequately characterized by infrared and nmr spectroscopy.

labilization of phosphorus to nucleophilic attack by the β-oxygen function.[8]

(8) 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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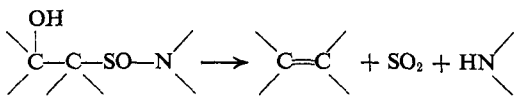
## The Synthesis of Olefins and Ketones from Carbonyl Compounds and Sulfinamides

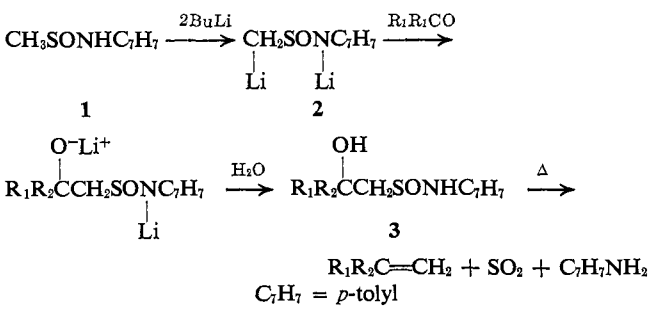
*Sir:*

A number of considerations led to the hypothesis that olefins might be produced from β-hydroxy sulfinic acid amides by an elimination of the form



We now report the observation of such reactions and a method of synthesis of the β-hydroxy sulfinyl system from carbonyl compounds and lithium salts of sulfinamides; together, these reactions constitute a new synthesis of olefins. Lithium salts of sulfinamides also react with carboxylic esters to form ketones in a one-step process.

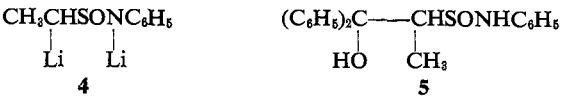
Reaction of N-methanesulfinyl-*p*-toluidine (**1**)[1] in tetrahydrofuran at −78° with 2 equiv of *n*-butyllithium afforded a dilithio derivative (**2**)[2] in less than 20 min, as determined by deuteration with $D_2O$ and nmr analysis. Treatment of the dilithio derivative **2** with 1 equiv of benzophenone afforded after hydrolysis the carbonyl addition product **3**, $R_1 = R_2 = C_6H_5$, in 97% yield.[3] The adduct **3**, $R_1 = R_2 = C_6H_5$, decomposes cleanly when heated alone at 137–139° (melting point) or at reflux in dry benzene (5 hr) to form 1,1-diphenylethylene (99%), *p*-toluidine (96%), and sulfur dioxide.



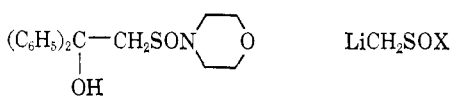
The dilithio derivative **2** adds similarly to 4-*t*-butylcyclohexanone to give an adduct (94% based on reacted ketone) which undergoes elimination at reflux in benzene to 4-*t*-butylmethylenecyclohexane (84%) and *p*-toluidine (92%). However, the reaction of this ketone with **2** is accompanied significantly (*ca.* 40%) by proton transfer to give an enolate which affords after work-up the starting ketone, 4-*t*-butylcyclohexanone; this is easily separated from the β-hydroxy sulfinamide by treatment with pentane, in which the latter is insoluble. Similarly, the adducts from **2** and cyclohexanone and cyclopentanone upon heating in benzene furnished methylenecyclohexane and methylenecyclopentane in *ca.* 90% yield.

The conversion of aldehydes to olefins has also been demonstrated. Thus, benzaldehyde, Δ³-cyclohexenecarboxaldehyde, and dodecanal react with the reagent **2** to form β-hydroxy sulfinamides in 98, 73, and 68% yield, respectively; these adducts are decomposed by heating in *dry* toluene at reflux for 5 hr to afford, respectively, styrene (76%), 4-vinylcyclohexene (90%), and 1-tridecene (83%).[4]

Treating N-ethanesulfinylaniline with 2 equiv of *n*-butyllithium at −40 to −45° for 30 min afforded the dilithium salt **4**, as evidenced by reaction with benzophenone to give the β-hydroxy sulfinamide **5** in 55% yield. Thermal decomposition of the adduct **5** at reflux in benzene for 5 hr produced 1,1-diphenylpropene in >98% yield. Similarly, 1-phenyl-1-propene was obtained as a mixture of *trans* and *cis* isomers (ratio 1.6:1) in two steps from **4** and benzaldehyde.



Adducts from N,N-disubstituted sulfinamides and aldehydes or ketones, *e.g.*, the morpholide **6**, decompose cleanly to olefins at 80° in dry benzene (96% 1,1-diphenylethylene from **6**). However, the generation of



α-lithio N,N-disubstituted sulfinylamides is complicated by the tendency of these intermediates to decompose to sulfines. Thus, reaction of methanesulfinylmorpholine with *t*-butyllithium[5] (added rapidly) at −78° in tetrahydrofuran led to the formation of the desired reagent **7**, X = morpholide, and the undesirable by-product **7**, X = *t*-butyl (presumably from $H_2C{=}SO$ and *t*-butyllithium), in a ratio of *ca.* 8:1 and a total yield of only *ca.* 50%, as determined by isolation of the corresponding adducts with benzophenone. As expected from this result, the α-lithio derivatives of alkanesulfinic acid esters are too unstable to be prepared by the techniques described here.[6] The presence of electron-withdrawing groups at $C_\alpha$ should facilitate the generation of α-anions from sulfinic acid N,N-disubstituted amides and esters; however, this has not been studied as yet.

With regard to the mechanism of formation of olefins from β-hydroxy sulfinamides, it is attractive to suppose that elimination occurs *via* intermediates of type **8** and **9**, the former being easily accessible because of the

(1) Prepared from *p*-toluidine and methanesulfinyl chloride; the acid chloride was obtained by the procedure of I. B. Douglass, B. S. Farah, and E. G. Thomas, *J. Org. Chem.*, **26**, 1996 (1961).

(2) See R. L. Gay, S. Boatman, and C. R. Hauser, *Chem. Ind.* (London), 1789 (1965), for an analogous metalation of acetanilide.

(3) The new compounds reported herein have been characterized satisfactorily by elemental analysis and/or spectroscopic (nmr, infrared) measurement.

(4) The rates of elimination of the β-hydroxy sulfinamides from **2** and aldehydes are considerably slower than those for the adducts from ketones and, consequently, the higher boiling solvent toluene is more suitable for the formation of olefins derived from aldehydes. In addition, in these cases it is important that no water be present, since this leads to side reactions which diminish the yield of olefin.

(5) This is a more satisfactory reagent than *n*-butyllithium in this case.

(6) In contrast, the α-lithio derivative of methyl methanesulfonate ($LiCH_2SO_2OCH_3$) is formed cleanly with *n*-butyllithium in tetrahydrofuran at −78°, as shown by the isolation of adducts with benzophenone (91%) and cyclohexanone (76%).