or acetone (79–82 kcal).[13] Moreover, the reaction was not quenched by 1,3-pentadiene (59 kcal; 0.1 M). These results indicate that the photoreaction occurs from the singlet state. This is quite unusual because, to our best knowledge, hydrogen abstraction of olefins from the singlet states has not been reported. The quantum yield of the reaction of **1c** was 0.04_9 (consumption of **1c**) and was much higher than that of 1,5-hydrogen transfer reaction of an α-alkylstyrene from the triplet state ($\Phi = 0.0005$).[4] The isotope effects were measured by using **1c**-d_2.[14] The value, $\Phi_H/\Phi_D = 2.0$, is considerably smaller than that of the triplet-state reaction of the alkylstyrene ($\Phi_H/\Phi_D \simeq 5$).[4] In view of these results, it is conceivable that the photocyclization of **1c** involves sequential electron–proton transfer[15] rather than one-step hydrogen atom transfer, although electron transfer from amides to excited olefins has not been reported. The scope and further mechanistic studies of the photocyclization are being studied.

Registry No. **1a**, 76916-92-2; **1b**, 76916-93-3; **1c**, 76916-94-4; **1d**, 76916-95-5; **2c**, 76916-96-6; **2c'**, 76916-97-7; **2d**, 76916-98-8; **2d'**, 76916-99-9; *N,N*-diethyl-2,2-dimethyl-3-oxo-3-phenylpropionamide, 76917-00-5; *N,N*-diisopropyl-2,2-dimethyl-3-oxo-3-phenylpropionamide, 76917-01-6; *N,N*-dibenzyl-2,2-dimethyl-3-oxo-3-phenylpropionamide, 61845-93-0; *N,N*-diallyl-2,2-dimethyl-3-oxo-3-phenylpropionamide, 76917-02-7; methyl iodide, 74-88-4.

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(14) A similar measurement of isotope effects has been reported: Padwa, A.; Eisenhardt, W.; Gruber, R.; Pashayan, D. *J. Am. Chem. Soc.* **1971**, *93*, 6998.
(15) (a) Padwa, A.; Gruber, R. *J. Am. Chem. Soc.* **1970**, *92*, 107. (b) Wagner, P. J.; Kemppainen, A. E.; Jellinek, T. *Ibid.* **1972**, *94*, 7512; (c) Arnold, D. R.; Maloulis, A. *Ibid.* **1977**, *99*, 7355.

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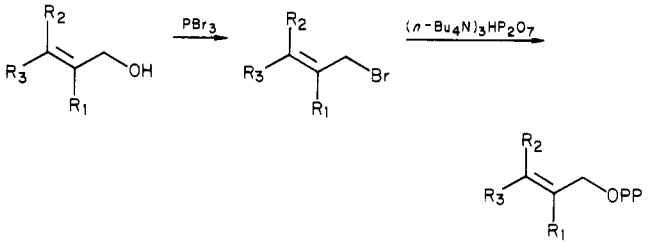
Tris(tetra-*n*-butylammonium) Hydrogen Pyrophosphate. A New Reagent for the Preparation of Allylic Pyrophosphate Esters

Summary: Tris(tetra-*n*-butylammonium) hydrogen pyrophosphate was used to prepare dimethylallyl pyrophosphate (**1**-OPP), 7-methylocta-2,6-dien-1-yl pyrophosphate (**2**-OPP), geranyl pyrophosphate (**3**-OPP), 2-fluorogeranyl pyrophosphate (**4**-OPP), and farnesyl pyrophosphate (**5**-OPP) from the corresponding alcohols in moderate yields by a two-step sequence via the corresponding primary, allylic bromides.

Sir: Pyrophosphate esters of allylic alcohols are important intermediates in terpene metabolism.[1] Since the pyrophosphate group is introduced very early in the pathway,[2] most biological syntheses of the allylic substrates begin with acetate or mevalonate and lack flexibility for the preparation of analogues. Although terpene allylic pyrophosphates were discovered in the late 1950's[3,4] few chemical syntheses from the corresponding alcohols have been reported. The lack of success in this area is undoubtedly due to two reinforcing factors—the 3,3-dialkyl allylic moiety typically found in the substrates is highly reactive,[5] and phosphate and pyrophosphate residues are superb leaving groups when they bear little or no negative charge.[6] The only procedure routinely used to synthesize allylic pyrophosphates was first reported in 1959[7] and has not been significantly altered since then.[8,9] This one-pot sequence involves treating the alcohol with inorganic phosphate and trichloroacetonitrile. The desired product must then be isolated from a complex mixture of organic and inorganic mono-, di-, and triphosphates by ion-exchange chromatography. Yields are sometimes as high as 30% but are often less. In addition, the procedure is difficult to manage if more than ca. 50 mg of product is desired.

It occurred to us that many of the problems presented by the highly reactive terpene system could be circumvented if the carbon–oxygen bond were introduced in a final step by utilizing a salt of inorganic pyrophosphate in a direct displacement. We now report a two-step procedure for synthesis of primary allylic pyrophosphate esters from the corresponding alcohols via the bromides as illustrated below. Moderate (i.e., 46–54%) yields were obtained for dimethylallyl alcohol (**1**-OH, $R_1 = H$; $R_2 = R_3 = CH_3$),[10] 7-methyl-2,6-octadien-1-ol (**2**-OH, $R_1 = R_2 = H$; $R_3 = C_6H_{11}$),[11] geraniol (**3**-OH, $R_1 = H$; $R_2 = CH_3$; $R_3 = C_6H_{11}$),[10] 2-fluorogeraniol (**4**-OH, $R_1 = F$; $R_2 = CH_3$; $R_3 = C_6H_{11}$),[12] and farnesol (**5**-OH, $R_1 = H$; $R_2 = CH_3$; $R_3 = C_{11}H_{19}$).[13]



Tris(tetra-*n*-butylammonium) hydrogen pyrophosphate is a white, hygroscopic solid which is soluble in acetonitrile and dimethyl sulfoxide. The material was prepared by passing a solution of disodium dihydrogen pyrophosphate (Stauffer) through a column of Dowex 50W-X8 (H^+ form) cation-exchange resin and titration of the acidic eluant to pH 7.0 with tetra-*n*-butylammonium hydroxide (Aldrich). Water was removed by lyophilization, and the powdery residue was stored over phosphorus pentoxide until used.

All of the primary allylic bromides used in the study were prepared from the corresponding alcohols by treatment with phosphorus tribromide.[15,16] Because of their

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(8) Cramer, W. D.; Weiman, G. *Chem. Ind. (London)* **1960**, 46.
(9) Cornforth, R. H.; Popjak, G. *Methods Enzymol.* **1969**, *15*, 359–390.
(10) Obtained from Aldrich.
(11) The synthesis of **2**-OH, including spectral data and combustion analyses for all new compounds, will be presented elsewhere.
(12) Poulter, C. D.; Argyle, J. C.; Mash, E. A. *J. Biol. Chem.* **1978**, *253*, 7227–7233.
(13) Prepared by reduction of methyl farnesate[14] with diisobutylaluminum hydride.
(14) Sum, F. W.; Weiler, L. *J. Am. Chem. Soc.* **1979**, *101*, 4401–4403.
(15) Coates, R. M.; Ley, D. A.; Cavender, P. L. *J. Org. Chem.* **1978**, *43*, 4915–4922.

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Table I. Yields and NMR Spectral Data of Allylic Pyrophosphates

compd	% yield	^{1}H NMR (D_2O),[a] δ	^{31}P NMR (D_2O),[b] δ
1-OPP	54[c]	1.65 (6, br s, allylic CH_3), 4.5 (2, t, J = 7.0 Hz, H at C(1)), 5.45 (1, m, H at C(2))	6.2 (d, J = 21 Hz, P_β), 10.1 (d, J = 21 Hz, P_α)
2-OPP	50[c]	1.60 and 1.67 (6, 2 s, allylic CH_3), 2.08 (4, br s, H at C(4) and C(5)), 4.40 (2, m, H at C(1)), 5.50 (3, m, H at C(2), C(3), and C(6))	5.4 (d, J = 21 Hz, P_β), 9.5 (d, J = 21 Hz, P_α)
3-OPP	46[c]	1.65 (9, br s, allylic CH_3), 2.05 (4, br s, H at C(4) and C(5)), 4.45 (2, t, J = 7.0 Hz, H at C(1)), 5.40 (2, m, H at C(2) and C(6))	6.3 (d, J = 21 Hz, P_β), 10.0 (d, J = 21 Hz, P_α)
4-OPP	48[d]	1.60, 1.65, and 1.75 (9, 3 s, allylic CH_3), 2.15 (4, m, H at C(4) and C(5)), 4.25 (2, m, H at C(1)), 5.40 (1, m, H at C(6))	7.7 (d, J = 22 Hz, P_β), 11.7 (d, J = 22 Hz, P_α)
5-OPP	49[d]	1.65 (12, br s, allylic CH_3), 2.1 (8, br s, H at C(4), C(5), C(8), and C(9)), 4.50 (2, m, H at C(1)), 5.3 (3, m, H at C(2), C(6), and C(10))	6.2 (d, J = 21 Hz, P_β), 10.4 (d, J = 21 Hz, P_α)

[a] Chemical shifts relative to internal DSS. [b] ^{1}H decoupled; chemical shifts at pH 8.0, relative to external 85% phosphoric acid. [c] Starting with 1.0 mmol of alcohol. [d] Starting with 0.5 mmol of alcohol.

reactivity, the bromides were checked by IR and ^{1}H NMR spectroscopy following removal of solvent and then used immediately, without purification. Displacements with Tris(tetra-*n*-butylammonium) hydrogen pyrophosphate were carried out in acetonitrile at room temperature with a 0.5 molar excess of the salt. The products were purified by chromatography.

A typical procedure is given for geranyl pyrophosphate (**3**-OPP). Phosphorus tribromide (80 μL, 0.5 mmol) was added to a well-stirred solution of 154 mg (1.0 mmol) of geraniol (**3**-OH) in 10 mL of dry pentane at 0 °C. After 10 min, 4–5 drops of methanol was added with vigorous stirring. The resulting mixture was then washed with water and 10% sodium bicarbonate, dried over anhydrous magnesium sulfate, and concentrated under vacuum. The residue was dissolved in 6 mL of anhydrous acetonitrile, 1.375 g (1.5 mmol) of tris(tetra-*n*-ammonium) hydrogen pyrophosphate was added, and the resulting slightly turbid solution was allowed to stir at room temperature for 24 h under nitrogen.

Two different procedures were used to purify **3**-OPP. In the first, the ammonium salt was isolated by batch elution from Dowex AG 1-X8 (200–400 mesh, formate form). A 1 × 13 cm column was equilibrated with 30 mL of 50 mM ammonium formate in methanol–water–ammonium hydroxide (95:5:0.5). Acetonitrile was removed from the reaction mixture at reduced pressure, the residue was dissolved in 0.5 mL of methanol–water (3:1), and the resulting solution was loaded onto the column. The column was washed with 150 mL of the solvent used for equilibration, and **3**-OPP was eluted with 300 mL of 0.6 M ammonium formate. Fractions (4 mL each) were collected, and all of the tubes were placed in the refrigerator overnight, whereupon **3**-OPP crystallized as a fluffly white precipitate (fractions 15–35).

Although pure material can be recovered at this point, somewhat higher yields are obtained by the following treatment. The fractions containing **3**-OPP were combined, methanol was removed at reduced pressure, and the residue was freeze-dried. The white residue was then washed thoroughly with 15 mL of cold methanol and pelleted by centrifugation. After a second treatment, the remaining solid was dissolved in water and freeze-dried to yield 168 mg (48% based on the triammonium salt) of a white powder judged to be homogeneous.[17] That portion not designated for immediate use was stored in 1-mL portions as a 20 mM solution at −80 °C. It is our experience that significant decomposition occurs upon prelonged storage at −10 °C or upon repeated freezing and thawing.

In the second precedure, the tetra-*n*-butylammonium salt of **3**-OPP was isolated by ion-paired chromatography on silica gel 60. The mixture obtained by treating 61 mg (0.28 mmol) of **3**-Br with 380 mg (0.42 mmol) of tris(tetra-*n*-butylammonium) hydrogen pyrophosphate was loaded onto a 1.5 × 85 cm column which had been previously equilibrated with *n*-propanol–ammonium hydroxide (12:3) and was then eluted with a convex gradiant formed from 200 mL of *n*-propanol–ammonium hydroxide–water (6:3:1), as described by Gafni and Shechter.[18] The progress of the chromatography was recorded by measuring the UV absorption of the eluant at 206 nm. Fractions (4 mL each) were collected, and those containing **3**-OPP (66–88) were combined. Solvent was removed under reduced pressure, and the resulting residue was dissolved in 30 mL of deionized water. Freeze-drying yielded 109 mg (48% based on the ammonium bis(tetra-*n*-butylammonium) salt) of an off-white viscous oil[19] which gave a single spot after thin-layer chromatography on silica gel, R_f 0.53 (2-propanol–2-butanol–ammonium hydroxide–water, 4:2:0.1:3.9).[20] Yields and NMR spectral data for the allylic pyrophosphates are given in Table I.

In summary, tris(tetra-*n*-butylammonium) hydrogen pyrophosphate can be used to prepare pyrophosphate

(16) The bromides should be checked by NMR because the reaction is sometimes accompanied by rearrangement to the allylic and double bond isomers. The material we used always contained less than 10% of the allylic isomer and less than 5% (none detected) of the C(2)–C(3) double bond isomer.

(17) Following this procedure 1-OPP–5-OPP gave single spots ($0.3 \leq R_f \leq 0.4$) on silica gel H plates buffered with $(NH_4)_2HPO_4$ when developed with $CHCl_3$–MeOH–H_2O (10:10:3) and visualized with iodine. Contamination by ammonium pyrophosphate could be detected by ^{31}P NMR since the signal for the inorganic salt appears as a singlet between the AB doublets of the monoester. Ammonium formate can be detected by ^{1}H NMR as a singlet at 8.54 ppm. Contamination by ammonium bromide can be revealed by treating a small portion of the sample with a few drops of 6 M H_2SO_4 and adding 1 mM $KMnO_4$ dropwise until the purple color persists. This procedure oxidized bromide to bromine, and upon shaking with CCl_4, bromine is extracted into the organic layer. As little as 5% of a contaminating ammonium salt could have been detected. ^{1}H NMR spectra of the pyrophosphates indicated less than 5% (none was detected) of allylically rearranged or double bond isomers. Presumably, the small amounts of rearranged bromides formed during bromination did not react with the pyrophosphate anion or reacted by an S_N2' displacement to give the desired double bond isomer.

(18) Gafni, Y.; Shechter I. *Anal. Biochem.* **1979**, *92*, 248–252.

(19) ^{1}H NMR ($CDCl_3$, Me_4Si internal standard) δ 1.0 (24, m, methyls on butyl group), 1.6 (41, m, H at C(2) and C(3) of butyl groups and methyls at C(3) and C(7)), 2.04 (4, m, H at C(4) and C(5)), 3.39 (16, m, H at C(1) of butyl groups), 4.60 (2, t, J = 5.3 Hz (apparent t with similar couplings to H at C(2) and Pα), H at C(1)), 5.21 (1, t, J = 6.0 Hz, H at C(6)), 5.52 (1, t, J = 4.8 Hz, H at C(2)), 6.15 (4, br s, NH_4).

(20) Benedict, C. R.; Kett, J. *Arch. Biochem. Biophys.* **1965**, *110*, 611–621.

esters of highly reactive allylic terpene alcohols. Preliminary results indicate that the displacement method is also successful for the less reactive homoallylic isopentenyl system. Experiments are now underway to explore the scope of the reaction with other primary alcohols and phosphorus-containing nucleophiles.[21]

Acknowledgment. We are grateful for support of this work by the Institute of General Medical Sciences (Grants GM-25521 and GM-21328). We also thank Mr. Richard Griffey for obtaining the ^{31}P NMR spectra and Dr. Eugene Mash for suggesting use of the tetra-*n*-butylammonium cation.

Registry No. 1-OH, 556-82-1; 1-Br, 870-63-3; 1-OPP, 358-72-5; 2-OH, 76985-83-6; 2-Br, 76946-99-1; 2-OPP, 76947-00-7; 3-OH, 106-24-1; 3-Br, 6138-90-5; 3-OPP, 763-10-0; 4-OH, 2284-91-5; 4-Br, 76947-01-8; 4-OPP, 76963-02-5; 5-OH, 4602-84-0; 5-Br, 6874-67-5; 5-OPP, 13058-04-3; tris(tetrabutylammonium) hydrogen pyrophosphate, 76947-02-9.

(21) Recently Zwierzak and Kluba[22] reported the syntheses of a variety of monophosphates from the corresponding bromides using tetra-*n*-butyl di-*tert*-butyl phosphate in a displacement reaction, followed by treatment with trifluoroacetic acid to remove the *tert*-butyl groups. Although the procedure can be used to prepare allyl phosphate, it is not applicable to the more acid-sensitive terpene phosphates.

(22) Zwierzak, A.; Kluba, M. *Synthesis* **1978**, 770–771.

(23) National Institutes of Health Postdoctoral Fellow, GM 06775.
(24) Research Career Development Awardee, 1975–1980, HL 00084.

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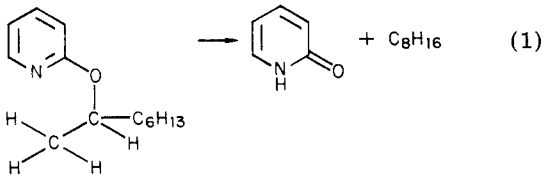
Pyrolysis of Alkyl Pyridyl Ethers[1]

Summary: A study of the mechanism of the pyrolysis of a series of alkyl pyridyl ethers has revealed the absence of any 1,3 alkyl shift and a linear correlation between olefin regiochemistry and pyridine leaving group ability in a thermal elimination reaction.

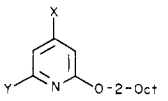
Sir: The pyrolysis of 2-octyl 2-pyridyl ether (eq 1) affords



(1)

a mixture of isomeric octenes and 2-pyridone.[2] If understood as a cyclic pyrolytic elimination, this is a rare example of such an elimination involving the formal disruption of an aromatic system.[3] Moreover, it involves a substrate wherein the electronic and steric features of the leaving group can be varied in a systematic and uncoupled fashion by appropriate substitution on the pyridine ring.

Table I. Product Distributions and Basicities for 2-Octyl Pyridyl Ethers[2,6]



	% 1-octene[a]	% *trans*-2-octene[a]	% *cis*-2-octene[a]	basicity,[b] kcal/mol
1, X = Y = Br	40	42	18	205.0
2, X = H; Y = Br	45	41	14	207.8
3, X = Y = H	50	36	13	212.6
4, X = Y = CH_3	57	33	11	219.1
5, X = H; Y = $SiMe_3$	61	31	8	219.7
6, X = H; Y = *t*-Bu	64	29	7	218.6

[a] Product distributions are ±1%. [b] Basicity values are ±1 kcal/mol.

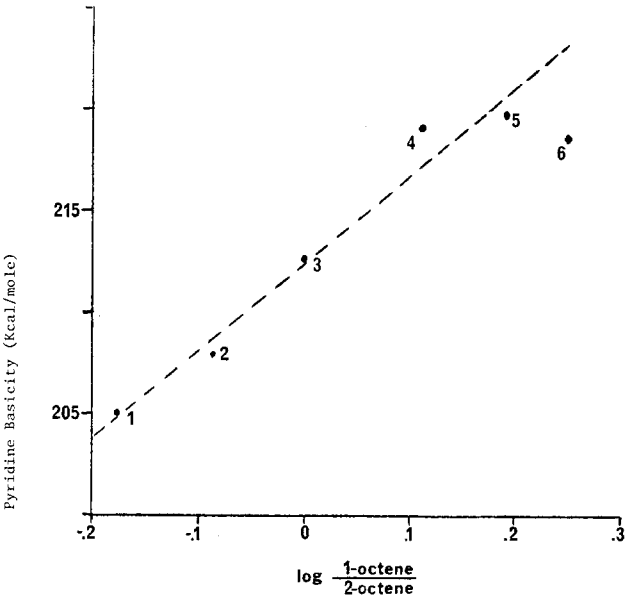
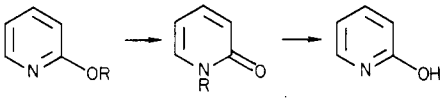


Figure 1.

The studies we report herein have yielded both a description of the transition state of this reaction and an interesting relationship between pyridyl leaving group ability and product regiochemistry.

We considered two general mechanisms. The obvious possibility suggested by eq 1 is a cyclic process using the pyridine lone pair as an internal base.[4] Alternatively, initial rearrangement of the pyridine ether to an *N*-alkylpyridone followed by elimination, as shown in eq 2,



(2)

would yield the same result.[5] Independent synthesis of *N*-(2-octyl)pyridone and its pyrolysis revealed that under conditions where the pyridine ether gave a 6–8% yield of olefin, the *N*-alkylpyridone yielded little or no (<1%) olefin products. Moreover, no conversion of pyridine ether

(1) Portions of this work were reported at the ACS Central Regional Meeting, May 7–10, 1979, Columbus, OH.

(2) All pyrolyses were done in an atmospheric pressure flow system, using N_2 carrier gas at 400–500 °C. Products were analyzed by calibrated GLC analysis.

(3) The discovery of the pyrolytic conversion of 2-ethoxypyridine to ethylene and pyridone and its kinetics were reported by Taylor while this work was in progress: Taylor, R. *J. Chem. Soc., Chem. Commun.* **1978**, 732.

(4) The analogous conversion of imidates to olefin and amide has been reported: Marullo, N. P.; Smith, C. D.; Terapane, J. F. *Tetrahedron Lett.* **1966**, 6279.

(5) The thermal conversions of 2-methoxypyridine to *N*-methylpyridone and of imidates to amides are known: (a) Wiberg, K. B.; Shryne, T. M.; Kintner, R. R. *J. Am. Chem. Soc.* **1957**, *79*, 3160; (b) Wislicenus, W.; Goldschmidt, M. *Chem. Ber.* **1900**, *33*, 1470. Also see: Newkome, G. R.; Kohli, D. K.; Kawato, T.; *J. Org. Chem.* **1980**, *45*, 4508 and references therein.

0022-3263/81/1946-1969$01.25/0