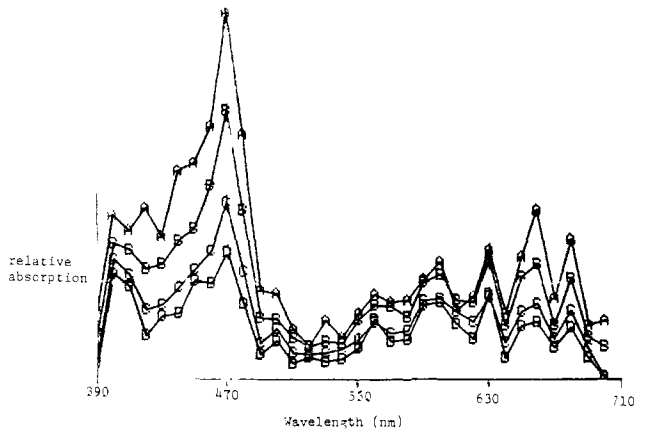

Figure 1. Transient production of the *trans*-stilbene radical cation sensitized by colloidal TiO_2 (λ excitation = 355 nm, 0.01 M *trans*-stilbene in colloidal TiO_2 suspended in 0.1 M perchloric acid in acetonitrile). Times after flash (μs): A, 13; B, 52; C, 95; D, 126.

the quantum yield of radical cation formation (relative to that reported for the triplet yield of benzophenone[7]) is 0.005.[8] The yield of the stilbene radical cation did not appear to be affected by the addition of methyl viologen as might have been expected if the stilbene oxidation efficiency were limited by competition with electron-hole recombination. Possible contributory factors to the low yield include the presence of isopropanol from our colloid preparation and/or the presence of adsorbed oxygen at the particle surface, which may lead to rapid chemical reactions that consume the cation radical.

Although no evidence for the formation of the stilbene radical anion (λ_{max} 490 nm[9]) could be obtained, reduction could be observed upon analogous excitation of colloidal TiO_2 in the presence of methyl viologen (Figure 2). Here the transient produced agrees well with that reported for the singly reduced radical cation.[10] One significant difference in the formation of this reduction product and the oxidation product from *trans*-stilbene is that not all of the production of the methyl viologen cation radical is prompt. With 10^{-4} M solutions, about half of the transient absorption attributable to the one-electron reduction occurs with the laser flash, with the remainder developing over a period of 15–20 μs. Since methyl viologen dication absorbs weakly at 355 nm, the prompt fluorescence may be due entirely to direct excitation, the slower formation being derived from TiO_2 sensitization. The time scale for such slower electron transfer corresponds, perhaps coincidentally, to that observed in laser coulostatic flash experiments for redox systems at the surface of TiO_2 single crystals in aqueous[11] and nonaqueous[12] electrolytes.

Although previous work has demonstrated the formation of oxidized and reduced species at metal oxide powders[13] or colloids[14] in aqueous suspensions (where hydroxy radical is throught to be a major oxidant[15]), these results represent direct observations of organic radical ions in nonaqueous solvents at colloidal TiO_2 and provide important mechanistic insight into the general problem

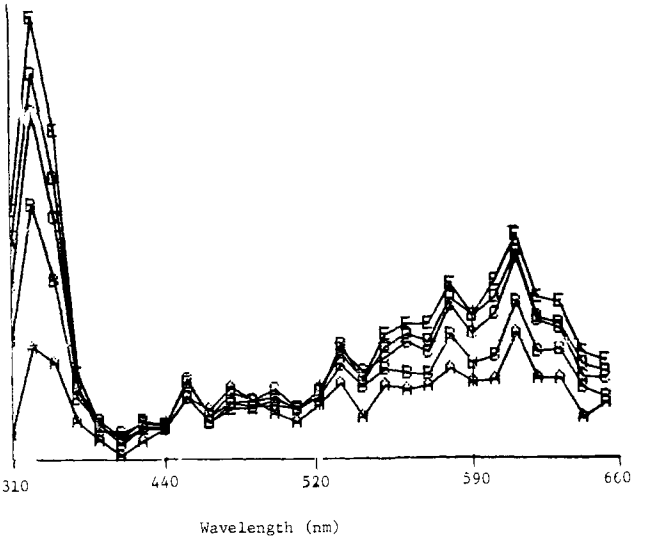

Figure 2. Growth of the absorption spectrum of methyl viologen$^{+\cdot}$ sensitized by colloidal TiO_2 (λ excitation = 355 mm, 1×10^{-1} M methyl viologen^{2+} in colloidal TiO_2 suspended in 0.1 M perchloric acid in acetonitrile). Times after flash (μs): A, 0.4; B, 1; C, 2.2; D, 4.4; E, 10.

of organic transformations occurring upon photocatalysis at heterogeneous surfaces.[3,16,17]

Acknowledgment. Generous support of this research by the U.S. Department of Energy, Fundamental Interactions Branch, is acknowledged. M.A.F. is grateful for support as an Alfred P. Sloan Research Fellow and as a Camille and Henry Dreyfus Teacher–Scholar. This work was conducted at the Center for Fast Kinetics Research, a facility funded by the National Institutes of Health and by the University of Texas at Austin.

Registry No. TiO_2, 13463-67-7; acetonitrile, 75-05-8; *trans*-stilbene, 103-30-0; methyl viologen, 1910-42-5; *trans*-stilbene radical cation, 59532-48-8; oxygen, 7782-44-7; methyl viologen radical cation, 25239-55-8.

(7) Birks, J. B. "Photophysics of Aromatic Molecules"; Wiley: New York, 1970.
(8) This value is corrected for fractional TiO_2 absorption of the incident pulse. Whether this low value is caused by rapid chemical reaction of the photoinduced radical ion pair or by low concentrations of radicals derived from small quantities of water or isopropyl alcohol is at present unknown.
(9) Zabolotny, E. R.; Garst, J. F. *J. Am. Chem. Soc.* **1964**, *86*, 1645.
(10) For example, see: Kalyanasundaram, K.; Dung, D. *J. Phys. Chem.* **1980**, *84*, 2551.
(11) Richardson, J. H.; Perone, S. P.; Deutscher, S. B. *J. Phys. Chem.* **1981**, *85*, 341.
(12) Kamat, P. V.; Fox, M. A., submitted for publication in *J. Phys. Chem.*
(13) Kraeutler, B.; Jaeger, C. D.; Bard, A. J. *J. Am. Chem. Soc.* **1978**, *100*, 4903.
(14) Henglein, A., private communication.
(15) Izumi, I.; Dunn, W. W.; Wilbourn, K. O.; Fan, F.-R.; Bard, A. J. *J. Phys. Chem.* **1980**, *84*, 3207.
(16) Pavlik, J. W.; Tantayanon, S. *J. Am. Chem. Soc.* **1981**, *103*, 6755.
(17) Kanno, T.; Oguchi, T.; Sakuragi, H.; Tokumaru, K. *Tetrahedron Lett.* **1980**, 467.

Carbon–Carbon Bond Formation via the Reaction of Trialkylallylstannanes with Organic Halides

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Received May 3, 1982

In connection with ongoing synthetic studies in our laboratories, we required a method for the replacement of halogen by an allyl moiety in substrates such as bromolactone **1** (Table I). Very few methods compatible with such substrates are known, since conversion of **1** to an organometallic derivative, or reaction of such substrates with organometallic derivatives, is frustrated by an obviously facile reductive elimination possibility. Palladium-catalyzed processes have been employed for this type of conversion but are in general limited to substrates without aliphatic β hydrogens.[2] We have found the reaction of allyltri-*n*-butylstannane with halides or other precursors to carbon-centered radicals to

(1) Fellow of the Alfred P. Sloan Foundation, 1981–1983.
(2) For recent reviews of palladium-catalyzed C–C bond forming reactions, note: Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146. Trost, B. M. *Tetrahedron* **1977**, *33*, 2615.

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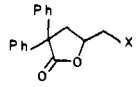
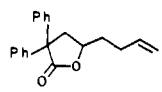
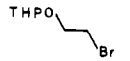
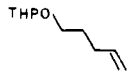
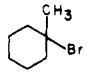
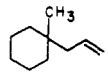
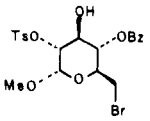
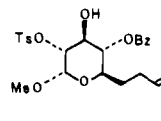
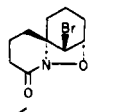
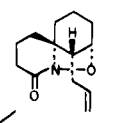
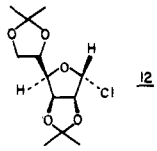
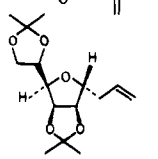
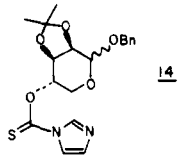
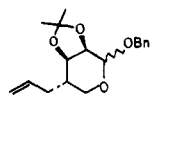
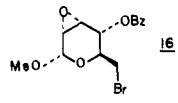
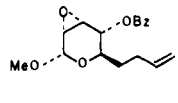
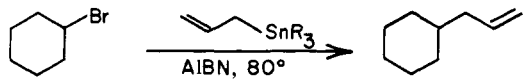
Table I

SUBSTRATE	METHOD[a]	PRODUCT	YIELD[b]
 1 X=Br 3 X=SePh	A A	 2	88 84
	B B		82 75
 4	A	 5	(98)
 6	A	 7	(90)
 8	A	 9	74
	B		60
 10	A	 11	93
	B		88
 12	A	 13	79
	B		68
 14	A	 15	27
	B		68
 16	A	 17	76

[a] Method A: 2.0 equiv of allyltri-*n*-butylstannane with 1.0 equiv of substrate, in degassed toluene solution (1 mL/mmol of substrate) containing 0.15 equiv of AIBN, at 80 °C for 8 h. Method B: 2.0 equiv of allyltri-*n*-butylstannane with 1.0 equiv of substrate in degassed toluene (1 mL/mmol of substrate) photoinitiated for 5 h at 25 °C.[6] [b] Yields in parentheses are VPC yields calibrated to internal standards prepared by usual methods. All others are isolated yields of chromatographically homogeneous materials that yielded spectral data and C, H combustion analyses and/or high-resolution mass spectra in accord with the assigned structures.

provide a general solution to this problem which promises to be of broad utility.[3]

The overall reaction process is summarized by eq 1. Thus,



(1)

reaction of 2.0 equiv of allyltri-*n*-butylstannane with 1.0 equiv of cyclohexyl bromide, in degassed toluene solution (1 mL/mmol of bromide) containing 0.15 equiv of azobis(isobutyronitrile) (AIBN) at 80 °C for 8 h, afforded allylcyclohexane as the sole product in 88% yield. Unreacted cyclohexyl bromide accounted for the remaining material.

It should be noted that such a reaction sequence is not without precedent. Examples of such processes were recorded independently in 1973 by Kosugi and by Grignon,[4] who found that pyrolysis of simple organic halides such as CCl_4 with allyltri-*n*-butylstannane afforded coupled products, generally in poor yields. In contrast, we find that good to excellent yields are easily achieved (by using the conditions outlined above) with a wide variety of substrates. Moreover, our studies have revealed that several other functional groups may be utilized for such a coupling process and that, with the exception of those few functional groups that undergo the reaction, almost all other functionality is compatible with the very mild and specific conditions utilized for the allylation reaction. Representative results are shown in Table I.[5]

It is noteworthy that the reaction, even though radical in nature, tolerates the presence of acetals, ketals, ethers (including tetrahydropyranyl ethers and benzyl ethers), epoxides, lactones, free hydroxyl groups, esters, and sulfonate esters, as evidenced by the examples above. The chemoselectivity of the process is illustrated not only by the examples above (note especially example **8** with five different functional groups) but also by the observation that conversion of cyclohexyl bromide to allylcyclohexane is readily accomplished even in the presence of an equimolar amount of benzaldehyde, *without* formation of 1-phenyl-3-buten-1-ol. Thus the known,[7] facile, acid-catalyzed addition of allylstannanes to aldehydes does not appear to compete with free-radical allyl transfer under these very mild conditions.

Despite some limitations on the structures of allylstannanes that can be successfully utilized in the above reactions,[8] it should be noted that allyl and 2-substituted allylstannanes afford, by simple oxidative cleavage processes, perhaps the most useful class of compounds for further transformations in organic synthesis: aldehydes and ketones. Moreover, the reaction described above appears to be extraordinarily tolerant of both steric hindrance and complex functionality in the substrate. Finally, the process is an extremely useful complement to various oxidative cyclization processes such as halolactonization and selenolactonization,[9] particularly in view of the stereochemical control that can be achieved in such oxidative additions,[10] and also promises to be of utility for replacing C–O chirality with C–C chirality during "chiral pool" manipulations.[11]

The above results may be accommodated by a free-radical chain mechanism. Thus an initiation event[12] (via a variety of possible pathways) yields a carbon-centered radical from the organic substrate. Addition to the allylstannane, followed by β-scission of the trialkylstannyl radical, then affords the observed product. The trialkylstannyl radical so produced may then continue the chain.

A final comment concerns the stereochemistry associated with the process. Although such a free-radical process is expected to

(3) (a) We first encountered this process as a solution to a particularly demanding C–C bond forming event in the context of a total synthesis of (±)-perhydrohistrionicotoxin: Keck, G. E.; Yates, J. B. *J. Org. Chem.* **1982**, *47*, 3590. (b) Allyltri-*n*-butylstannane was prepared according to the procedure of Seyferth and Weiner (Seyferth, D.; Weiner, M. A. *J. Org. Chem.* **1961**, *26*, 4797).

(4) (a) Kosugi, M.; Kurino, K.; Takayama, K.; Migita, T. *J. Organomet. Chem.* **1973**, *56*, C11. (b) Grignon, J.; Pereyre, M. *Ibid.* **1973**, *61*, C33. (c) Grignon, J.; Servens, C.; Pereyre, M. *Ibid.* **1975**, *96*, 225.

(5) Methallyltri-*n*-butylstannane can also be utilized for the coupling reaction. For example, substrate **1** gave the expected product in 97% isolated yield using method A.

(6) Photochemical initiation (method B) was achieved by using a conventional 450-W Hanovia medium-pressure mercury lamp equipped with a Pyrex filter.

(7) (a) Konig, K.; Neumann, W. P. *Tetrahedron Lett. 1967*, 495. (b) Naruta, U.; Ushida, S.; Maruyama, K. *Chem. Lett.* **1979**, 919. (c) Hosomi, A.; Iguchi, H.; Endo, M.; Sakurai, H. *Ibid.* **1979**, 977.

(8) For an indication of these limitations, note: Matarasso-Tchiroukhine, E.; Cadiot, P. *J. Organomet. Chem.* **1976**, *121*, 169.

(9) For a recent review of organoselenium-induced cyclization processes, note: Nicolaou, K. C. *Tetrahedron* **1981**, *37*, 4097.

(10) For recent examples of stereocontrolled halolactonizations, note: (a) Chamberlin, A. R.; Dezube, M.; Dussault, P. *Tetrahedron Lett.* **1981**, 4611. (b) Corey, E. J.; Hase, T. *Ibid.* **1979**, 335. (c) Bartlett, P. A.; Myerson, J. *J. Am. Chem. Soc.* **1978**, *100*, 3950.

(11) For recent reviews on the synthesis of natural products from the "chiral pool" note: (a) Hanessian, S. *Acc. Chem. Res.* **1979**, *12*, 159. (b) Seebach, D.; Hungerbuhler, E. "Modern Synthetic Methods, 1980"; Scheffold, R., Ed.; Salle (Frankfurt) Sauerlander (Aarau), 1980; pp 91–171. (c) Fraser-Reid, B.; Anderson, R. C. *Fortschr. Chem. Org. Naturst.* **1980**, *39*, 1.

(12) As shown in Table I, either chemical or photochemical initiation could be utilized with halides or selenides as substrates. With thioacylimidazoles such as **14**, however, chemical initiators such as AIBN were found to lead to the formation of substantial amounts of side products resulting from addition to *carbon* at the thioacylimidazole, followed by scission of the imidazole moiety.

be devoid of any intrinsic stereochemistry, in some cases stereochemistry can be enforced by conventional methods. In this context, substrate **10**, with a conformationally locked six-membered ring, gave essentially complete equatorial incorporation of the allyl unit upon reaction with allyltri-*n*-butylstannane, and mannose derivative **12** was found to yield exclusively the product expected from approach of allyltri-*n*-butylstannane to the least hindered face of the intermediate radical. The lyxose derivative **14** likewise affords a single allylated product (as a mixture of anomers) whose stereochemistry has not yet been rigorously confirmed. More detailed investigations of factors controlling stereochemistry, as well as applications in natural product synthesis, are in progress and will be reported in due course.

Acknowledgment. Support of this research by the National Science Foundation and the National Institutes of Health (through Grant No. GM-28961) is gratefully acknowledged. Funds for the VG Micromass 7070 mass spectrometer used in this work were provided by the National Science Foundation and the University of Utah Institutional Funds Committee.

Enzymatic Cyclization of Geranyl Pyrophosphate to Bornyl Pyrophosphate. Role of the Pyrophosphate Moiety

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Within the last several years cell-free investigations of the biosynthesis of both monoterpenes and sesquiterpenes have led to a clearer understanding of the mechanisms by which the acyclic precursors geranyl and farnesyl pyrophosphate are converted to cyclic metabolites.[2] As a result, a coherent picture has begun to emerge for the critical cyclization processes[3] that lie at the heart of terpenoid biogenetic theory.[4] Of particular importance has been the recent demonstration that an enzyme system from *Salvia officinalis* (sage) catalyzes the conversion of geranyl pyrophosphate (**1**) to *d*-bornyl pyrophosphate (**2**).[5] The recognition that the enzymatic cyclization product is itself a pyrophosphate ester provides a unique opportunity to examine experimentally the role of the pyrophosphate moiety in the isomerization–cyclization process. We report below oxygen-18 labeling studies that establish a remarkably tight coupling of the pyrophosphate and terpenoid partners that exists within the enzyme active site and results in an essentially complete lack of positional isotope exchange[6] of the pyrophosphate ester oxygen atom during the conversion of geranyl to bornyl pyrophosphate.

Scheme I

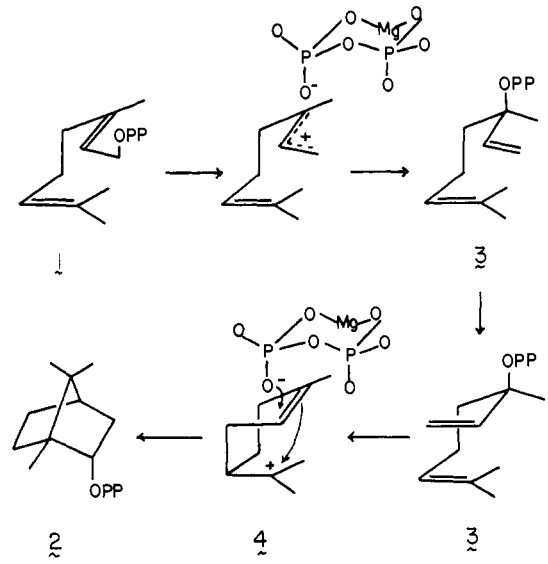

Table I. Conversion of [1-$^3H_2$,α-^{32}P]Geranyl Pyrophosphate and [1-$^3H_2$,β-^{32}]Geranyl Pyrophosphate to *d*- and *l*-Bornyl Pyrophosphate and Determination of the $^3H/^{32}P$ Ratio of the Derived Monophosphate[a]

	$^3H/^{32}P$	
geranyl pyrophosphate[b]	*d*-bornyl phosphate (sage)	*l*-bornyl phosphate (tansy)
[1-$^3H_2$,α-^{32}P]-, 9.4[c]	9.5	9.6
[1-$^3H_2$,β-^{32}P]-, 10.5[d]	522	482

[a] A minimum of 3.5×10^5 dpm of ^3H were recovered in each product, of which 25% was counted. Data are half-life corrected. [b] The location of the ^{32}P in each substrate was verified by enzymatic hydrolysis to the corresponding monophosphate with apyrase (Del Campo, G.; Puente, J.; Valenzuela, M. A.; Cori, O. *Biochem. J.* 1977, *167*, 525) and by hydrogenation (Jacobson, H. I.; Griffin, M. J.; Jensen, E. V. *J. Am. Chem. Soc.* 1957, *79*, 2068), and subsequent acid hydrolysis to 3,7-dimethyloctyl phosphate, followed by purification of these products by TLC. [c] Specific activity 150 Ci ^3H/mol. [d] Specific activity 300 Ci ^3H/mol.

A working model for the formation of *d*-bornyl pyrophosphate from geranyl pyrophosphate, consistent with available experimental data[2,5,7] and based on closely related chemical models,[8] is illustrated in Scheme I. According to this mechanism, geranyl pyrophosphate (**1**) is first isomerized to its tertiary allylic isomer, linalyl pyrophosphate (**3**).[9] Ionization of the cisoid conformer of **3** and electrophilic attack on the 6,7-double bond would generate a transient α-terpinyl cation (**4**). Subsequent electrophilic attack on the newly formed cyclohexene double bond and capture of the resultant carbocation by the pyrophosphate anion generate bornyl pyrophosphate with the observed stereochemistry. During the course of these reasonable, but as yet hypothetical, transformations the inorganic pyrophosphate moiety released by the ionization of the geranyl substrate may become more or less free of its cationic

(1) Fellow of the Alfred P. Sloan Foundation, 1978–1982; National Institutes of Health Research Career Development Award, 1978–1983.

(2) For recent comprehensive reviews of monoterpene and sesquiterpene biosynthesis, respectively, see: (a) Croteau, R. In "Biosynthesis of Isoprenoid Compounds"; Porter, J. W., Spurgeon, S. L., Ed.; Wiley: New York, 1981; pp 225–282. (b) Cane, D. E. *Ibid.*, pp 283–374.

(3) For a recent review see: Cane, D. E. *Tetrahedron* **1980**, *36*, 1109.

(4) (a) Ruzicka, L. *Pure Appl. Chem.* **1963**, *6*, 493; *Proc. Chem. Soc.* **1959**, *7*, 82. (b) Hendrickson, J. B. *Tetrahedron* **1959**, *7*, 82. (c) Parker, W.; Roberts, J. S.; Ramage, R. *Q. Rev. Chem. Soc.* **1967**, *21*, 331.

(5) Croteau, R.; Karp, F. *Arch. Biochem. Biophys.* **1979**, *198*, 512; **1977**, *184*, 77. Croteau, R.; Karp, F. *Biochem. Biophys. Res. Commun.* **1976**, *72*, 440.

(6) Rose, I. A. *Adv. Enzymol.* **1979**, *50*, 361.

(7) (a) Croteau, R.; Felton, M. *Arch. Biochem. Biophys.* **1981**, *207*, 460. Gambliel, H.; Croteau, R. *J. Biol. Chem.* **1982**, *257*, 2335. (b) Cane, D. E.; Swanson, S.; Murthy, P. P. N. *J. Am. Chem. Soc.* **1981**, *103*, 2136. (c) Suga, T.; Shishibori, T.; Morinaka, H. *J. Chem. Soc., Chem. Commun.* **1980**, 167. (d) Gotfredsen, S. E. *Diss. ETH Zurich No. 6243*, described in ref 2b and in ref 3, pp 1150–1151. (e) Arigoni, D. *Pure Appl. Chem.* **1975**, *41*, 219. (f) Anastasis, P.; Freer, I.; Gilmore, C.; Mackie, H.; Overton, K.; Swanson, S. *J. Chem. Soc., Chem. Commun.* **1982**, 268.

(8) (a) Gotfredsen, S.; Obrecht, J. P.; Arigoni, D. *Chimia* **1977**, *31*, 62. Weinstein, S.; Valkanas, G.; Wilcox, C. F. *J. Am. Chem. Soc.* **1972**, *94*, 2286. Stephan, K. *J. Prakt. Chem.* **1898**, *58*, 109. (b) Poulter, C. D.; King, C.-H. R. *J. Am. Chem. Soc.* **1982**, *104*, 1420, 1422.

(9) Linalyl pyrophosphate itself has been shown to serve as a substrate for bornyl pyrophosphate synthetase. Cf. ref 2a and 12.

0002-7863/82/1504-5831$01.25/0