benzene, 0.91 g (9.0 mmol) of triethylamine 1.86 g (10.0 mmol) of (*E*)-1,3-bis(trimethylsilyl)-1-propene, and a trace of trimethylvinylsilane. The mixture was heated with stirring at 50 °C for 15 h, and 35.9 mg (0.16 mmol) of palladium acetate, 0.34 g (2.0 mmol) of silver nitrate, and a trace of trimethylvinylsilane were thereafter added to the reaction mixture, which was then heated for an additional 3 h at 50 °C. (The addition of fresh reagents reduced the time necessary for completion.) The crude product was worked up and purified by flash chromatography as above, yielding 1.10 g (52%) of the title compound as a colorless oil: ^{1}H NMR (CCl_4) δ −0.18 (s, 9 H), 0.16 (s, 9 H), 2.15 (s, 2 H), 5.41 (s, 1 H), 7.20 (m, 5 H); mass spectrum, *m/e* 262 (M^+). Anal. Calcd for $C_{15}H_{26}Si_2$: C, 68.62; H, 9.98; Si, 21.40. Found: C, 68.67; H, 9.95; Si, 21.36.

Minor amounts of (*E*)-1,3-bis(trimethylsilyl)-2-phenyl-1-propene **13** (<2%) and a small amount of an unidentified isomer were present in the purified material. Enrichment of **13**, by preparative gas chromatography resulted in the isolation of a mixture of **4** and **13** in a ratio of 4:1. These isomers were separable by analytical GC–MS, and both isomers gave identical mass spectra. The signals from the vinylic and allylic protons in **13** appeared at δ 5.23 (s, 1 H) and 1.97 (s, 2 H), respectively. Compound **4** was obtained as a single compound by purification by HPLC.

Acknowledgment. We gratefully acknowledge the support of A.H. through grants from the Swedish Natural Science Research Council and of Mr. T. Klingstedt for stimulating discussions.

Chemoselectivity in Palladium-Catalyzed Reactions of 2-Bromoallyl Esters

Godson C. Nwokogu[1]

Department of Chemistry, University of Maine, Orono, Maine 04469

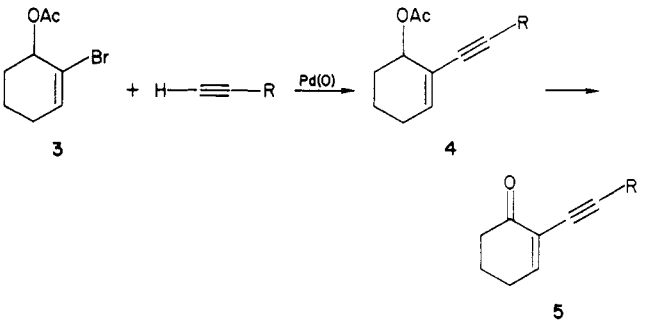
Received January 9, 1985

The chemoselectivity of palladium-catalyzed reactions of 2-bromoallyl esters has been established. With compatible carbon nucleophiles, 2-bromoallyl esters gave products of coupling to the vinyl bromide moiety instead of nucleophilic allylic substitution. Products from reactions with nitrogen nucleophiles and in the absence of added nucleophiles are also consistent with the absence or minor importance of the (π-allyl)palladium complex formation as a competing pathway. These results illustrate an unusual influence of the 2-bromo substituent on the usual ease of fission of the allylic C–O bond.

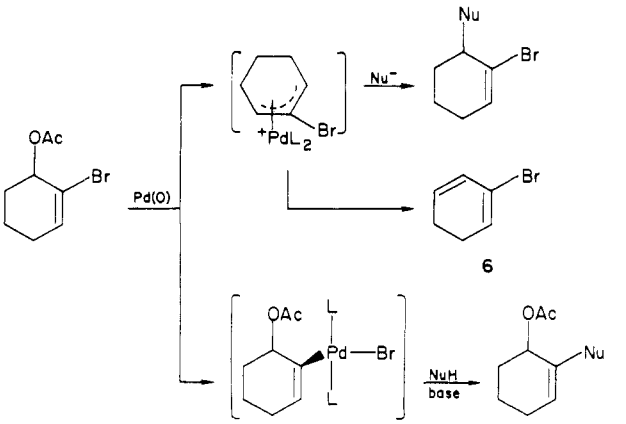
Two types of palladium-catalyzed reactions that find frequent use in organic syntheses are the coupling reactions of vinyl or aryl halides[2-8] and the nucleophilic substitution of allyl esters.[9] The mechanisms of these two types of palladium-catalyzed reactions have received good attention,[3,9] but selectivity between them in the same molecule has so far attracted only cursory examination. Recently, examples of selectivity between different ester groups situated allylic to the same double bond were reported and rates of nucleophilic allylic substitution of different ester groups in different molecules were also compared.[10,11] But in general, the influence of substituents on the vinyl carbons on the reactivity of the allylic C–O bond has not been addressed.

Our interest in the chemoselectivity of palladium-catalyzed reactions of 2-bromoallyl esters arose from difficulties in attempts[12] to ethynylate, with the help of various palladium catalysts, the ethylene glycol ketal of 2-bromo-

Scheme I



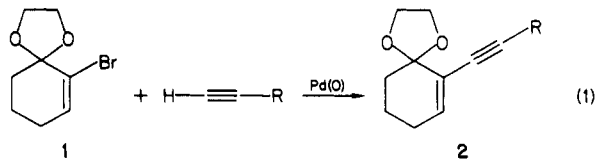
Scheme II



(1) Present address: Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061.
(2) Cassar, L. *J. Organomet. Chem.* **1975**, *93*, 253. Sekiya, A.; Ishikawa, N. *Ibid.* **1976**, *118*, 349. Dieck, H. A.; Heck, F. R. *Ibid.* **1975**, *93*, 259.
(3) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. Fitton, J.; Rick, E. A. *J. Organomet. Chem.* **1971**, *28*, 287.
(4) Takahashi, S.; Kuroyama, Y.; Sonogashira, K.; Hagihara, N. *Synthesis* **1980**, 627.
(5) Minato, A.; Suzuki, K.; Tamao, K.; Kumada, M. *Tetrahedron Lett.* **1984**, *25*, 83.
(6) Dang, H. P.; Linstrumelle, G. *Tetrahedron Lett.* **1978**, 191.
(7) Ratovelomanana, V.; Linstrumelle, G. *Tetrahedron Lett.* **1981**, *22*, 315.
(8) Rossi, R.; Carpita, A.; Quirici, M. G.; Gaudenzi, M. L. *Tetrahedron* **1982**, *38*, 631.
(9) Trost, B. M. *Acc. Chem. Res.* **1980**, *13*, 635, and references therein.
(10) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y. *Tetrahedron Lett.* **1982**, *23*, 4809.
(11) Tanigawa, Y.; Nishimura, K.; Kawasaki, A.; Murahashi, S.-I. *Tetrahedron Lett.* **1982**, *23*, 5549.

0022-3263/85/1950-3900$01.50/0

cyclohexenone (1) (eq 1). It was therefore anticipated that



1 2 (1)

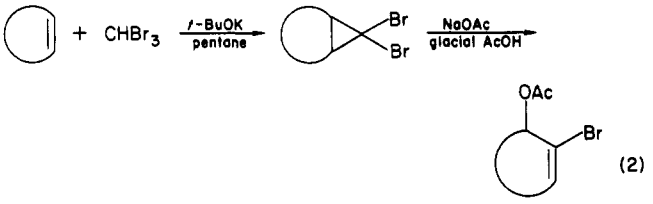
if 2-bromo-2-cyclohexenyl acetate (3) could be ethynylated, instead, by the same procedure, then the product 4 could be converted to the enynone 5 if necessary (Scheme I).

The success of this route to 5, however, would depend on the chemoselectivity of the palladium-catalyzed reaction of 3. This is because allylic substitution, vinyl coupling, and elimination are all mechanistically possible under the reaction conditions (Scheme II).

Preliminary findings from our investigation of this selectivity in 2-bromoallyl acetates have been communicated.[13] The study has now been completed and extended to 2-bromoallyl carbonates and phosphates, the other most often used allyl esters. We present, here, details of our results.

Results and Discussion

All 2-bromoallyl acetates were prepared according to eq 2.[14] The carbonates and phosphates were prepared from



(2)

the corresponding 2-bromoallyl alcohols[15,16] by standard methods.[10,11,17] The chloro and iodo analogues were not used in this investigation because they are not as accessible as the bromides from alkenes[14,18,19] and are therefore not expected to offer any preparative advantage over the bromides.

The 2-bromoallyl esters exhibited similar but unusual mass spectral fragmentation patterns in which the parent ion was either of very low intensity or absent. A similar observation with 2-bromoallyl ethers has been reported by Heck et al.[20] The base peak in the mass spectrum (MS) of each 2-bromoallyl ester corresponds to loss of bromine atom, instead of one molecule of the corresponding acid as would be expected in the absence of the 2-bromo substituent. These fragmentation patterns were the initial indication of unusual properties for the allylic C–O and vinylic C–Br bonds in these substrates.

Except with the secondary and tertiary cyclic amines—pyrrolidine, piperidine, and their *N*-methyl analogues—the reactions of 2-bromoallyl esters were either too slow or did not occur at all in the other solvents regularly used for palladium-catalyzed vinyl coupling[2-8] and allylic substitutions.[9] For example, the vinyl coupling product 7 (eq 3) could be detected only in trace quantity by gas chromatography–mass spectral (GC–MS) analysis of the crude product after 18 h of reaction time. The bromo acetate 3 was recovered unreacted in 77% yield. The recovery of 3 is, in itself, unusual when contrasted with the usual products from the reaction of simple allyl esters with primary and secondary amines in the presence of palladium catalysts.[9,11,21,22]

Table I. Palladium-Catalyzed Reaction of 2-Bromoallyl Acetates with Pyrrolidine

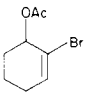
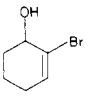
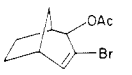
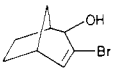
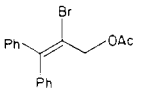
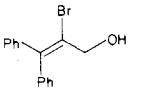
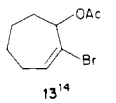
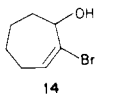
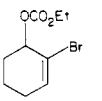
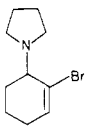
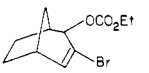
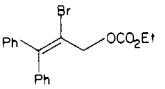
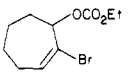
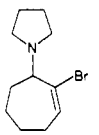
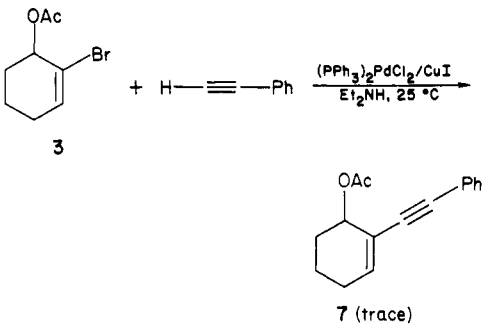
entry	substrate	product	yield (%)
1	 3[14]	 8[15]	87
2	 9	 10[16]	74
3	 11[14]	 12	100
4	 13[14]	 14	89

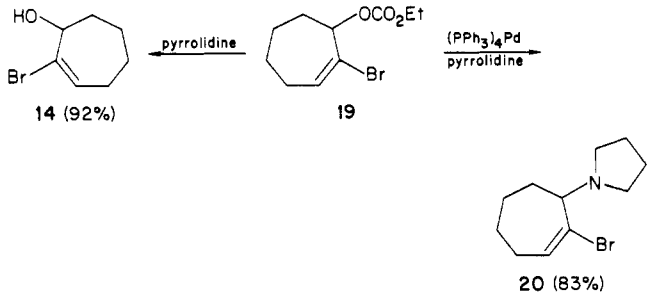
Table II. Palladium-Catalyzed Reaction of 2-Bromoallyl Carbonates with Pyrrolidine

entry	substrate	alcohol (%)	amine (%)
1	 15	8(60)	 16 (20)
2	 17	**10**(78)	0
3	 18	**12**(77)	0
4	 19	0	 20 (83)

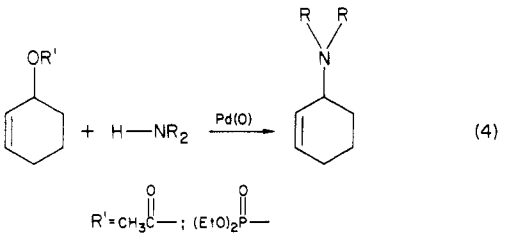


(12) Unpublished results from work with Professor David J. Hart.
(13) Nwokogu, G. C. *Tetrahedron Lett.* **1984**, *25*, 3263.
(14) Sandler, S. R. *J. Org. Chem.* **1967**, *32*, 3876.
(15) Sonnenberg, J.; Winstein, S. *J. Org. Chem.* **1962**, *27*, 748.
(16) Maskill, H.; Wilson, A. A. *J. Chem. Soc., Perkin Trans. 2* **1982**, 39.
(17) Kitagawa, Y.; Hashimoto, S.; Iemura, S.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1976**, *98*, 5030.
(18) Bergman, E. *J. Org. Chem.* **1963**, *28*, 2210.
(19) Skell, S. P., Garner, A. Y. *J. Am. Chem. Soc.* **1956**, *78*, 3409.
(20) Shi, L., Narula, C. K.; Mak, K. T.; Kao, L.; Xu, Y.; Heck, R. F. *J. Org. Chem.* **1983**, *48*, 3894.
(21) Atkins, K. E.; Walker, W. E.; Manyik, R. M. *Tetrahedron Lett.* **1970**, 3821.

Scheme III

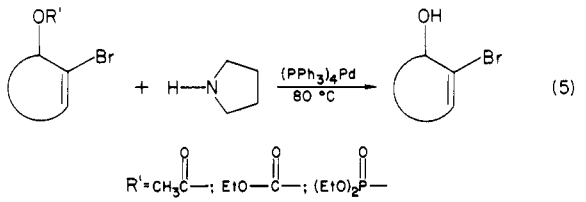


Reaction of 2-Bromoallyl Esters with Nitrogen Nucleophiles. The usual reaction of simple allyl esters with primary and secondary amines in the presence of palladium catalysts is amination (eq 4).[9,11,21,22] But when



(4)

we treated 2-bromoallyl esters with pyrrolidine in the presence of palladium catalysts, aminolysis of the ester group occurred in most cases (eq 5). For example, all

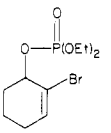
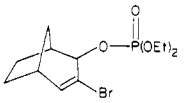
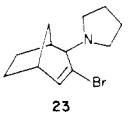
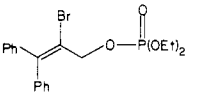
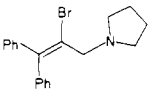
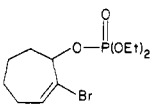


(5)

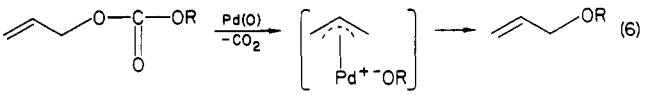
2-bromoallyl acetates gave the corresponding 2-bromoallyl alcohols (Table I) under this reaction condition. With the 2-bromoallyl carbonates, some substrates suffered aminolysis, some underwent amination, and some gave product mixtures resulting from both aminolysis and amination (Table II). For example, while the bromo carbonate **15** gave a mixture of the bromo alcohol **8** and 1-(2-bromo-2-cyclohexenyl)pyrrolidine (**16**), substrates **17** and **18** gave the corresponding alcohols **10** and **12** only. The bromo carbonate **19** gave the product of amination **20** only and the corresponding alcohol **14** was not observed in the GC–MS analysis of the crude product. Treatment of **19** with pyrrolidine in the absence of palladium catalyst, however, gave the alcohol **14** solely, thus implicating the importance of the catalyst in the formation of **20** (Scheme III).

The obtention of amination products in the reaction of some 2-bromoallyl carbonates with pyrrolidine in the presence of palladium–phosphine complexes (Table II, entries 1 and 4) seems to implicate the participation of (π-allyl)palladium intermediates to the extent that such products were formed. But the absence of 2-bromoallyl ethers as products in these and other reactions of 2-bromoallyl carbonates is strong evidence against the formation of such an intermediate. Previous reports[10,23-25] of palladium-catalyzed reactions of simple allyl carbonates

Table III. Palladium-Catalyzed Reaction of 2-Bromoallyl Phosphates with Pyrrolidine

entry	phosphate	amine	yield (%) with Pd	yield (%) without Pd
1	 21	**16**	59	46
2	 22	 23	70	1
3	 24	 25	65	91
4	 26	**20**	41	

in the absence of added nucleophiles have identified allyl ethers as the major products of such reactions. The alkoxide ion generated by decomposition of the carbonate is supposed to attack the (π-allyl)palladium complex to give the ether products (eq 6). GC–MS analysis of the crude



(6)

products from reactions with the bromo carbonates **15** and **19** showed no traces of 2-bromoallyl ethers. In order to rule out that this result might have been due to the more abundant nitrogen nucleophile—pyrrolidine—winning out over the less abundant alkoxide species in the competition for any (π-allyl)palladium species formed, similar reactions with 2-bromoallyl carbonates **15** and **19** were run in *N*-methylpyrrolidine. These reactions will be discussed shortly, but it should be noted here that no bromoallyl ether products were detected either.

2-Bromoallyl phosphates gave products of amination only, when heated at 80 °C in pyrrolidine with Pd catalysts (Table III). Phosphates **21** and **24** suffered amination even in the absence of catalyst, with **24** reacting at room temperature while **21** needed refluxing. The bromo phosphate **22** gave only traces of the amination product **23** after heating at 80 °C for 5 h without a catalyst. Its substantial conversion to the pyrrolidine derivative at the same reaction time when the catalyst was present indicates that the catalyst facilitates this process.

The structure of the product and the observed influence of the catalyst in these reactions of 2-bromoallyl phosphates may be taken to point to the intermediacy of a (π-allyl)palladium complex. But the formation of these pyrrolidine-substituted products in the absence of catalysts suggest that the catalyst may not necessarily be involved by the formation of a (π-allyl)palladium complex. Allyl phosphates are known to undergo noncatalyzed nucleophilic substitution with strong nucleophiles like Grignard[26] and alkylaluminum[16] reagents. We did not, however, find

(22) Tsuji, J. In "Organic Synthesis with Palladium Compounds"; Springer: New York, 1980.
(23) Giube, F.; Saint M'Leux, Y. *Tetrahedron Lett.* **1981**, *22*, 3591.
(24) Bacvall, J.-E.; Nordberg, R. E.; Vagberg, J. *Tetrahedron Lett.* **1983**, *24*, 411.
(25) Tsuji, J.; Minami, I.; Shimizu, I. *Tetrahedron Lett.* **1984**, *25*, 2791.
(26) Haley, R. C.; Miller, J. A.; Wood, H. C. S. *J. Chem. Soc. C* **1969**, 264.

Scheme IV

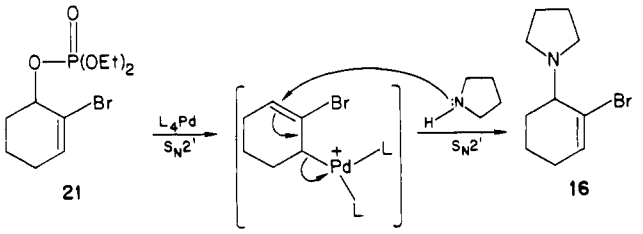
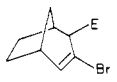
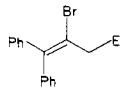


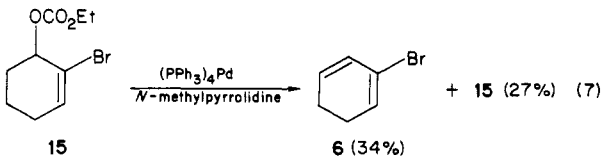
Table IV. Recovery of 2-Bromoallyl Esters after Reflux in *N*-Methylpyrrolidine with Palladium Catalysts

		E		
entry	substrate	acetate	ethyl carbonate	diethyl phosphate
1		67	27[a]	0[b]
2		97	81	82
3			93	0[c]
4		93	87	75

[a] 34% of **6** also obtained. [b] 100% of **6** obtained. [c] Unidentified water-soluble oil obtained.

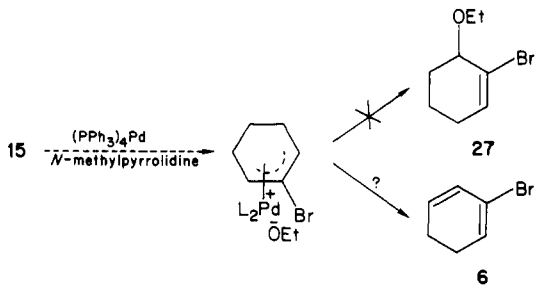
any previous examples of such uncatalyzed substitutions with amines. The sluggish reaction of the bromo phosphate **22** in the absence of the catalyst is consistent with previous reports on the solvolytic rate of exo-4-substituted 3-halobicyclo[3.2.1]oct-2-enes.[16,27,28] The amination reaction of the phosphates (and probably of the carbonates **15** and **19**) and the rate enhancement of this reaction by the catalyst may be explained with a sequence of S_N2' or S_N2 or a combination of both processes. This is illustrated in Scheme IV for sequential S_N2' steps. Fiaud and Malleron[29] have proposed this scheme in more detail to rationalize the deviations in the Pd-catalyzed alkylation of optically pure vs. racemic allyl acetates from results predicted on the basis of the singular intermediacy of the (π-allyl)palladium complex.

Reaction of 2-Bromoallyl Esters in the Absence of Nucleophiles. All 2-bromoallyl acetates were recovered in high yields after refluxing for 6–8 h in *N*-methylpyrrolidine with various palladium catalysts. The carbonates were also recovered unchanged except in the case of the bromo carbonate **15** (Table IV, E = ethyl carbonate, entry 1) which gave the elimination product 2-bromo-1,3-cyclohexadiene (**6**)[30] (eq 7). The phosphates **22** and

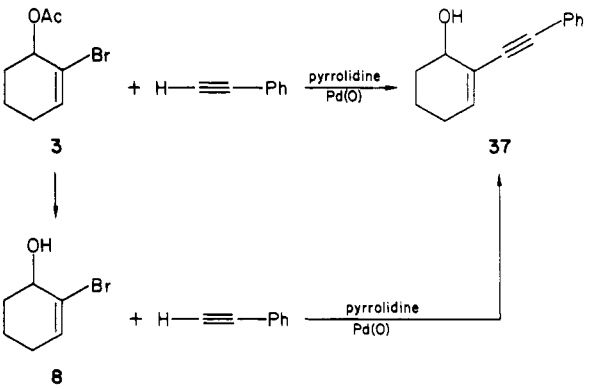


(7)

Scheme V

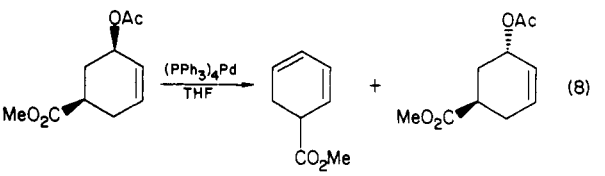


Scheme VI



26 were recovered in good yield when subjected to this reaction condition. The bromo phosphate **21** gave the bromo diene **6** quantitatively while **24** gave unidentified water-soluble oil.

The recovery of the acetates, most of the carbonates, and some of the phosphates under the above reaction conditions is contrary to what would be expected if these substrates formed (π-allyl)palladium complexes. Such complexes, when formed in the absence of added nucleophiles, should lead to dienes in the cases of the acetates and phosphates and allyl ethers for the carbonates. Trost et al.[31] have shown that this elimination occurs even in the absence of base for simple allyl acetates (eq 8). And in



(8)

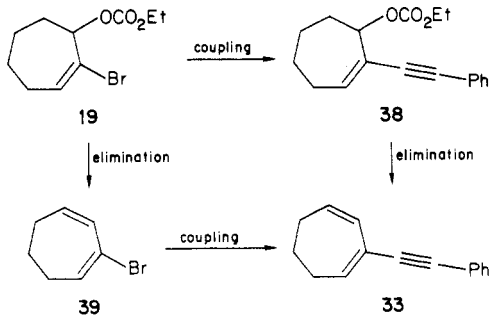
the case of the ethyl 2-bromo carbonate **15** which formed the elimination product **6** in 34% yield, the absence of the allyl ether product **27** (Scheme V) even in trace amounts (GC–MS analysis of the crude product showed no such product) casts doubt as to the formation of a (π-allyl)-palladium intermediate in the reaction. It would be expected that capture of any formed allyl cation by the ethoxide ion should compete, to some detectable extent, with elimination under the reaction condition.

Reactions of 2-Bromoallyl Esters with Carbon Nucleophiles. The carbon nucleophiles used to probe chemoselectivity in 2-bromoallyl esters are terminal alkynes and Grignard reagents.

The reaction of these bromo esters with terminal alkynes in either pyrrolidine or piperidine and presence of various palladium catalysts[13] gave enynols. For example, when the

(27) Moore, W. R.; Moser, W. R.; LaPrade, J. E. *J. Org. Chem.* **1963**, *28*, 2200.
(28) The synthetic sequence to the 3-bromobicyclo[3.2.1]oct-3-en-2-yl esters **3**, **17**, and **22** should lead to 4-exo stereochemistry. See also: ref 16 and 27.
(29) Fiaud, J. C.; Malleron, J. L. *Tetrahedron Lett.* **1981**, *22*, 1399.
(30) Bottini, A. T.; Schear, W. *J. Org. Chem.* **1965**, *30*, 3205. Grob, C. A.; Pfaendler, H. R. *Helv. Chim. Acta* **1970**, *53*, 2130.
(31) Trost, B. M.; Verhoeven, T. R.; Fortunak, J. M. *Tetrahedron Lett.* **1979**, 2301.

Scheme VII

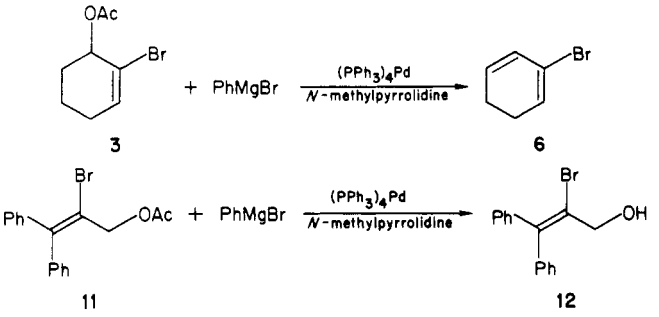


bromo acetate **3** was treated with phenylacetylene in pyrrolidine at 80 °C in the presence of 2 mol % of palladium acetate and 8 mol % of triphenylphosphine, the enynol **37** was obtained in 67% yield (Scheme VI). Based on results of this work discussed earlier, the formation of **37** is most probably preceded by the aminolysis of **3** to give the bromo alcohol **8**, which then undergoes coupling under the reaction condition to give **37**. In fact, **8**, prepared either from 2,3-dibromocyclohexene[15] or by aminolysis of **3** was converted to **37** in 92% in pyrrolidine (75% in piperidine) by using palladium acetate–triphenylphosphine catalyst system.

By using *N*-methylpyrrolidine as solvent, instead of pyrrolidine, the aminolysis of the ester group was avoided, and it was possible to examine selectivity between the vinyl halide and allylic ester moieties. The products in Table V show that coupling to the vinyl bromide is preferred over the formation of (π-allyl)palladium complex. Low total recoveries in some of the entries may be due to secondary reactions of the products because the total recoveries were appreciably higher when the same substrates were subjected to the same reaction conditions in the absence of nucleophiles (see Table IV).

In Table V, entries 6, 8, 11, 12, and 15, dienynes instead of the enyne ester corresponding to the bromoallyl esters were isolated as products. Such products could have arisen from either the secondary reaction of the initially formed enyne ester or from the bromo diene formed by elimination (Scheme VII). We have the following evidence that coupling precedes elimination: (a) The bromo acetates, including **13**, did not eliminate to give bromo dienes when treated under the same reaction condition in the absence of the alkynes; the carbonate **19** and phosphate **26**, which yielded the dienyne **33**, did not eliminate to the bromo diene **39** in the absence of the alkynes. Dienyne **33** was not, therefore, formed from **39** under the reaction condition. (b) Apart from the fact that the acetate **13** did not eliminate acetic acid to give the bromo diene **39**, the quantity of **33** in the product of reaction of the 2-bromoallyl acetate **13** with phenylacetylene depended on the reaction time. After 2 h of reaction, **33** was isolated in 60% while **32** was obtained in 40% yield. After 45 min of reaction, however, **33** was obtained in 16% and **32** in 81% yield. With the carbonate **19** and the phosphate **26**, only the dienyne product **33** was isolated, no matter how long the reaction was allowed to run, but again, it has to be remembered that these substrates did not undergo any reaction in the absence of alkynes in *N*-methylpyrrolidine. The dienyne **34** was the only product isolated from the coupling reaction of the carbonate **15** and phosphate **21**. We were unable, in this case, to establish the order for the coupling and elimination processes leading to the formation of **34**. This is due to the fact that these substrates, in the absence of nucleophiles, eliminated to some extent, to give the bromo diene **6** (see Table IV).

Reactions with phenylmagnesium bromide gave elimination products with the acetates **3** and **13** but led to the bromo alcohol **12** with the acetate **11**. It would be expected that due to the observed inertness of the allyl ester moiety in 2-bromoallyl esters toward the formation of (π-allyl)-palladium complexes, basic and nucleophilic reagents like Grignards would rather lead to elimination products or



nucleophilic attack on the ester carbonyl carbon.

The present study establishes the chemoselectivity of Pd-catalyzed reactions of 2-haloallyl esters and represents a first detailed examination of the influence of substituents on the vinyl carbons on the reactivity of the allyl ester moiety. The easy availability of 2-bromoallyl esters from alkenes and the chemoselectivity in the reaction of these substrates hold promise for broadening the application of such suitably modified allyl esters in syntheses.

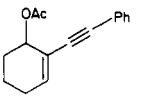
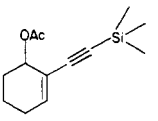
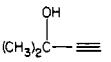
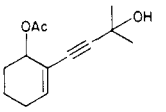
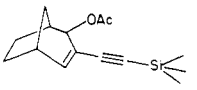
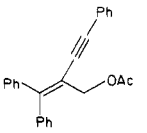
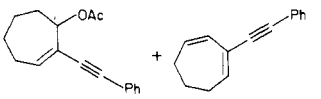
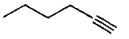
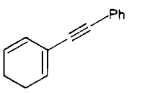
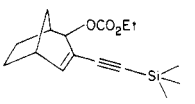
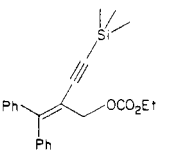
Experimental Section

General Procedures. ^{1}H NMR spectra were recorded at 60 MHz on a Hitachi Perkin-Elmer R-24B spectrometer with carbon tetrachloride (CCl_4) as solvent. Chemical shifts are given in δ units (ppm) relative to tetramethylsilane (Me_4Si) except in the cases of the products containing the trimethylsilyl group. Coupling constants (J) are given in hertz. Melting points were determined on a Thomas Hoover Unimelt apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Perkin-Elmer 457 grating infrared spectrophotometer. Low resolution mass spectra were obtained at 70 eV using a Hewlett-Packard 5985 B GC–MS system with a HP 18835 C capillary inlet system. Thin layer chromatography (TLC) was performed with silica gel plates from Eastman Kodak. Column chromatographic separations were carried out with silica gel, 70–230 mesh from Brinkman. Analytical samples were prepared on a Varian Aerograph Model 920 by using either 3% OV-17 on Gaschrom Q (column A) or 10% SE-30 on Chromosorb WHP (column B). Chemical analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN. Unless otherwise stated, chemicals were purchased from commercial suppliers and used without further purification. Pyrrolidine and *N*-methylpyrrolidine were distilled from potassium hydroxide. Anhydrous tetrahydrofuran (THF) and diethyl ether were dried by distillation from sodium benzophenone ketyl. All reactions with palladium catalysts were run under a continuous stream of nitrogen.

3-Bromobicyclo[3.2.1]oct-3-en-2-ol, 2-*exo*-Acetate (9). Norbonylene (20.00 g, 0.21 mol) and 33.10 g (0.29 mol) of potassium *tert*-butoxide were placed in 250 mL of pentane and cooled on an ice-salt bath. The reaction flask was equipped with a reflux condenser and a continuous stream of N_2 was maintained. To the stirred suspension was added bromoform (64.10 g, 0.25 mol) by dropping funnel over 30 min. After complete addition of bromoform, the mixture was stirred for 2 h and then allowed to warm to 25 °C in another 2 h.[27]

The suspension was filtered; the filtrate was washed consecutively with water and brine and dried ($MgSO_4$). The solvent was removed on a rotary evaporator without heating. The residual liquid was added to 44.80 g (0.55 mol) of anhydrous, fused sodium acetate in 100 mL of glacial acetic acid, and the mixture was refluxed at 160 °C for 3 h. After cooling to 25 °C, the resulting cake was broken up and triturated with hexane. The hexane extract was concentrated, and the residual liquid was treated with

Table V. Palladium-Catalyzed Reaction of 2-Bromoallyl Esters with Terminal Alkynes

entry	substrate	alkyne	product (%)	% recovd substrate
1	**3**	Ph—≡	 **7** (42)	27
2	**3**	$(CH_3)_3Si$—≡	 **28** (47)	15
3	**3**		 **29** (26)	27 22
4	**9**	$(CH_3)_3Si$—≡	 **30** (66)	48
5	**11**	Ph—≡	 **31** (32)[13]	0
6	**11**	Ph—≡	 **32** (81) + **33** (16)	
7	**11**		0	93
8	**15**	Ph—≡	 **34** (53)	0
9	**17**	$(CH_3)_3Si$—≡	 **35** (36)	36
10	**18**	$(CH_3)_3Si$—≡	 **36** (59)	0
11	**19**	Ph—≡	**33**(80)	0
12	**21**	Ph—≡	**34**(60)	0
13	**22**	$(CH_3)_3Si$—≡	0	0[a]
14	**24**	$(CH_3)_3Si$—≡	0	0[a]
15	**26**	Ph—≡	**33**(49)	0

[a] Unidentified water-soluble oily mass was obtained.

solid K_2CO_3 until the smell of acetic acid disappeared. The broth was extracted with hexane, and the extract was concentrated to obtain 27.00 g (52%) of **9** as a pale yellow liquid with a strong lingering sweet smell. Further purification was effected by bulb to bulb distillation at 3 torr, 160–80 °C: ^1H NMR (CCl_4) δ 6.40 (d, J = 6 Hz, 1 H), 4.90 (br s, 1 H), 2.80–2.30 (m, 2 H), 2.10 (s, 3 H), 2.00–1.20 (m, 6 H); MS, m/e (relative intensity) 165 (M^+ – Br, 40), 123 (100), 105 (30), 95 (50), 77 (35), 43 (50). Anal. Calcd for $C_{10}H_{13}BrO_2$: C, 49.00; H, 5.35. Found: C, 48.99; H, 5.21.

Ethyl 2-Bromo-2-cyclohexenyl Carbonate (15). 2-Bromo-2-cyclohexenol (**8**) (7.92 g, 44.51 mmol) prepared from 2,3-dibromocyclohexene according to Maskill et al.[16] was dissolved in 50 mL of anhydrous ether containing 9 mL of pyridine. The stirred mixture in a flask equipped with a reflux condenser and under a stream of N_2 was cooled on an ice bath while 10 mL of ethyl chloroformate was added dropwise. The resulting suspension was stirred for 12 h during which time it warmed up to room temperature.

The suspension was filtered and the solid was washed with another 50 mL of ether. The ether portions were washed with 50 mL of 4% HCl and then consecutively with water and brine and then dried ($MgSO_4$). The solvent was removed on a rotary evaporator, and the liquid residue was subjected to column chromatography with a 1:1 mixture of hexane and methylene chloride (CH_2Cl_2) to obtain 8.71 g (78%) of **15**. An analytical sample of **15** was prepared by GLC on column B at 180 °C: ^1H

NMR (CCl_4) δ 6.30 (t, J = 4 Hz, 1 H), 5.10 (m, 1 H), 4.20 (q, J = 6 Hz, 2 H), 2.30–1.60 (m, 6 H), 1.30 (t, J = 6 Hz, 3 H); MS, m/e (relative intensity) 169 (M^+ – Br, 40), 159 (5), 139 (15), 97 (100); IR (neat, cm^{-1}) 3000, 2890, 1750, 1370, 1250, 1150. Anal. Calcd for $C_9H_{13}BrO_3$: C, 43.39; H, 5.26. Found: C, 43.54; H, 5.30.

The following 2-bromoallyl carbonates were prepared from the corresponding alcohols by the same procedure as above.

3-Bromobicyclo[3.2.1]oct-3-en-2-yl Ethyl Carbonate (17). This compound was prepared from the alcohol **10**[16] obtained from the corresponding dibromide.[26] Yield, 86%. An analytical sample was prepared by GLC with column B at 210 °C: ^1H NMR (CCl_4) δ 6.25 (d, J = 6 Hz, 1 H), 4.70 (d, J = 3 Hz, 1 H), 4.15 (q, J = 6 Hz, 2 H), 2.55 (br s, 2 H), 1.95–1.45 (m, 6 H), 1.35 (t, J = 6 Hz, 3 H); MS m/e (relative intensity) 195 (M^+ – Br, 45), 123 (90), 95 (100), 77 (70); IR (neat, cm^{-1}) 3000, 2890, 1750, 1255. Anal. Calcd for $C_{11}H_{15}BrO_3$: C, 48.02; H, 5.50. Found: C, 48.41; H, 5.54.

2-Bromo-3,3-diphenyl-2-propenyl Ethyl Carbonate (18). The compound was prepared from the alcohol **12** obtained by base hydrolysis of the bromo acetate **11**; yield 83%. An analytical sample was prepared by column chromatography with a 9:1 mixture of hexane and ether: ^1H NMR (CCl_4) δ 7.10 (br s, 10 H), 4.80 (s, 2 H), 4.00 (q, J = 6 Hz, 2 H), 1.15 (t, J = 6 Hz, 3 H); MS, m/e (relative intensity) 281 (M^+ – Br, 15), 209 (50), 191 (100), 178 (55), 131 (50), 103 (60). Anal. Calcd for $C_{18}H_{17}BrO_3$: C, 59.85; H, 4.74. Found: C, 59.87; H, 4.63.

Ethyl 2-Bromo-2-cycloheptenyl Carbonate (19). To a suspension of 10 g (0.10 mol) of $CaCO_3$ in a solution of 4.00 g (0.10 mol) of NaOH in 50 mL of water was added 25.46 g (0.11 mol) of 2-bromo-2-cycloheptenyl acetate (**13**), and the suspension was refluxed for 3 h. The suspension was filtered, and the solid was washed with ether. All the filtrates were collected, washed successively with water and brine, and dried ($MgSO_4$). On removal of the solvent on the rotary evaporator, 15.51 g (74%) of the alcohol 2-bromo-2-cycloheptenol (**14**) was obtained: ^1H NMR (CCl_4) δ 6.10 (t, J = 7 Hz, 1 H), 4.70 (s, 1 H), 4.30 (br t, J = 3 Hz, 1 H), 2.30–1.30 (M, 8 H); IR (neat, cm^{-1}) 3400, 2940, 1720, 1240; MS, m/e (relative intensity) 192 (M^+ + 2, 5), 190 (M^+, 5), 174 (35), 172 (35), 150 (20), 148 (20), 111 (100), 93 (90). The alcohol was used to prepare the carbonate **19** according to the procedure described for **15**; yield 90%. An analytical sample of **19** was prepared by GLC with column B at 160 °C: ^1H NMR (CCl_4) δ 6.30 (t, J = 6 Hz, 1 H), 5.25 (br s, 1 H), 4.15 (q, J = 6 Hz, 2 H), 2.35–1.50 (m, 8 H), 1.30 (t, J = 6 Hz, 3 H); IR (neat, cm^{-1}) 3020, 2990, 1800, 1300; MS, m/e (relative intensity) 183 (M^+ – Br, 40), 111 (45), 93 (90), 91 (100), 77 (80), 45 (79). Anal. Calcd for $C_{10}H_{15}BrO_3$: C, 45.65; H, 5.75. Found: C, 45.64; H, 5.84.

2-Bromo-3,3-diphenyl-2-propenyl Diethyl Phosphate (24). To a solution of 7.50 g (26.07 mmol) of the alcohol **12** (prepared by base hydrolysis of the acetate **11**) in 40 mL of anhydrous ether at –78 °C and under a stream of N_2 was added in 10 min 16.3 mL of 1.6 M solution of n-butyllithium in hexane. The suspension was stirred for 30 min, and then a supernatant prepared from 6.30 mL of diethyl chlorophosphate and 10 mL of triethylamine in 20 mL of anhydrous ether at 0 °C was added by dropping funnel. The reaction mixture hardened at –78 °C but thawed and became stirrable again as it warmed and remained at room temperature during 24 h.

The suspension was filtered, the solid was washed with 50 mL of ether, and all the ether portions were collected. The solution was washed with 50 mL of 10% HCl and then with water and brine and dried ($MgSO_4$). Ether was removed by rotary evaporation and the residual viscous liquid was subjected to column chromatography by using a 3:1 mixture of hexane and ethyl acetate. The second material eluted amounted for 7.14 g (65%) of **24**. An analytical sample was prepared by repeating the column chromatography under the same conditions as the first: ^1H NMR (CCl_4) δ 7.10 (s, 10 H), 4.65 (d, J = 6 Hz, 2 H), 4.00 (m, 4 H), 1.20 (t, J = 6 Hz, 6 H); MS, m/e (relative intensity) 345 (M^+ – Br, 20), 191 (100), 165 (30), 81 (10); IR (neat, cm^{-1}) 3000, 1275, 1030. Anal. Calcd for $C_{19}H_{22}BrO_4P$: C, 53.66; H, 5.21. Found: C, 54.04; C, 5.40.

The other bromo phosphates were prepared from the corresponding alcohols by the same procedure.

2-Bromo-2-cyclohexenyl Diethyl Phosphate (21). The phosphate was prepared in 85% yield from the bromo alcohol **8**. An analytical sample was obtained by bulb to bulb distillation at 0.25 torr at 132 °C after column chromatography with a 3:1 mixture of hexane and ethyl acetate: ^1H NMR (CCl_4) δ 6.20 (br t, 1 H), 4.75 (br, 1 H), 4.05 (m, 4 H), 2.35–1.55 (m, 6 H), 1.35 (t, J = 6 Hz, 6 H). MS, m/e (relative intensity) 233 (M^+ – Br, 50), 205 (30), 177 (40), 127 (30), 99 (100), 81 (20), 79 (20); IR (neat, cm^{-1}) 3000, 1270, 1020. Anal. Calcd for $C_{10}H_{18}BrO_4P$: C, 38.36; H, 5.79. Found: C, 38.67; H, 6.03.

3-Bromobicyclo[3.2.1]oct-3-en-2-yl Diethyl Phosphate (22). This compound was prepared in 59% yield from the bromo alcohol **10**. An analytical sample was prepared by column chromatography with a 3:1 mixture of hexane and ethyl acetate: ^1H NMR (CCl_4) δ 6.35 (d, J = 6 Hz, 1 H), 4.50–3.70 (m, 5 H), 2.65 (br, 2 H), 2.05–1.10 (m, 6 H), 1.30 (t, J = 6 Hz, 6 H); MS, m/e (relative intensity) 259 (M^+ – Br, 100), 175 (70), 105 (60), 81 (40). Anal. Calcd for $C_{12}H_{20}BrO_4P$: C, 42.50; H, 5.94. Found: C, 42.74; H, 5.87.

2-Bromo-2-cycloheptenyl Diethyl Phosphate (26). This was prepared in 89% yield from the bromo alcohol **14**. An analytical sample was prepared by repeated column chromatography with a 3:1 mixture of hexane and ethyl acetate: ^1H NMR (CCl_4) δ 6.30 (br t, 1 H), 4.30–3.70 (m, 4 H), 3.30 (br t, 1 H), 2.40–1.50 (m, 8 H), 1.30 (t, J = 6 Hz, 6 H); MS, m/e (relative intensity) 148 (18), 124 (40), 101 (100), 83 (20). IR (neat, cm^{-1}) 3000, 1270, 1020. Anal. Calcd for $C_{11}H_{20}BrO_4P$: C, 40.38; H, 6.16. Found: C, 40.48; H, 6.02.

Reaction of 2-Bromo-2-cyclohexenyl Acetate (3) with Pyrrolidine. Preparation of 2-Bromo-2-cyclohexenol (8). To 10 mL of pyrrolidine was added 0.14 g (0.20 mmol) of bis(triphenylphosphine)palladium chloride ($(PPh_3)_2PdCl_2$) and the mixture was heated to 80 °C under a reflux condenser. The bromo acetate **3** (2.27 g, 10.34 mmol) was added and heating was continued for 2 h. The solvent was removed on a rotary evaporator, and the residual liquid was distilled (bulb to bulb, 6 mmHg, 200 °C) to obtain 2.60 g (86%) of a 1:1 mixture of the alcohol **8** and *N*-acetylpyrrolidine as verified from an ^1H NMR spectrum of the product. *N*-Acetylpyrrolidine could be removed by washing with dilute aqueous HCl with appreciable loss of material. The alcohol **8** crystallized after keeping it in the refrigerator for some days: mp 38–40 °C (lit.[15] mp 38.2–40.2 °C); ^1H NMR (CCl_4) δ 5.95 (t, J = 4 Hz, 1 H), 4.25 (br s, 1 H), 4.00 (br s, 1 H), 2.25–1.55 (m, 6 H); MS, m/e (relative intensity) 178 (M^+ + 2, 10), 176 (M^+, 10), 150 (20), 148 (20), 97 (100), 79 (30). With catalyst system Pd-$(OAc)_2$/PPh_3 the yield of **8** was also 86%.

The following bromo alcohols were obtained by the same procedure from the given 2-bromoallyl esters.

2-Bromo-3,3-diphenyl-2-propenol (12) from the Bromo Carbonate 18. This product was isolated as a 1:1 mixture with ethyl pyrrolidylcarbamate. The carbamate could be washed out with dilute HCl without loss of material: mp (hexane) 81–3 °C; ^1H NMR (CCl_4) δ 7.10 (s, 10 H), 4.60 (s, 1 H), 4.20 (s, 2 H); MS, m/e (relative intensity) 290 (M^+ + 2, 10), 288 (M^+, 10), 209 (100), 191 (60), 178 (80), 131 (65), 103 (60), 77 (55). Anal. Calcd for $C_{15}H_{13}BrO$: C, 62.30; H, 4.53. Found: C, 61.71; H, 4.55.

3-Bromo-4-*exo*-hydroxybicyclo[3.2.1]oct-2-ene (10) from the bromo acetate 9 or bromo carbonate 17: mp (hexane) 73–5 °C (lit.[16] mp 73–4 °C); ^1H NMR (CCl_4) δ 6.20 (d, J = 6 Hz, 1 H), 3.65 (d, J = 3 Hz, 1 H), 2.80 (s, 1 H), 2.70–2.30 (m, 2 H), 2.15–1.40 (m, 6 H); IR (neat, cm^{-1}) 3400, 3000, 1630, 1040; MS, m/e (relative intensity) 204 (M^+ + 2, 5), 202 (M^+, 5), 123 (80), 95 (100).

2-Bromo-2-cycloheptenol (14) from the Bromo Acetate 13. This product was isolated as a 1:1 mixture with *N*-acetylpyrrolidine which could be washed off with appreciable loss of material using dilute HCl. The physical characteristics of the product are identical with those for **14** obtained from hydrolysis of the bromo acetate **13** (see procedure for **19**).

1-(2-Bromo-2-cycloheptenyl)pyrrolidine (20). To 10 mL of pyrrolidine in a flask with a reflux condenser was added 0.24 g (0.21 mmol) of tetrakis(triphenylphosphine)palladium ($(PPh_3)_4Pd$), and the solution was heated to 80 °C. Then 2.68 g (10.13 mmol) of the bromo carbonate **19** were added and heating was continued for 5 h.

The reaction solvent was removed by rotary evaporation, and the residual oil was extracted with hexane. The extract was washed with water and brine and then dried ($MgSO_4$). Concentration of the hexane solution gave 2.08 g (84%) of **20**. An analytical sample was prepared by GLC with column B at 180

°C: ^{1}H NMR (CCl_4) δ 6.20 (br t, 1 H), 3.00 (br s, 1 H), 2.50 (m, 4 H), 2.15–1.45 (m, 12 H); MS, *m/e* (relative intensity) 245 (M^+ + 2, 20), 243 (M^+, 20), 216 (25), 214 (25), 164 (100), 136 (30), 134 (30), 70 (40). Anal. Calcd for $C_{11}H_{18}BrN$: C, 54.11; H, 7.43. Found: C, 54.25; H, 7.37.

The following pyrrolidine derivatives were prepared by the same procedure from the given 2-bromoallyl esters.

1-(3-Bromobicyclo[3.2.1]oct-3-en-2-yl)pyrrolidine (23). This derivative was prepared from the bromo phosphate **22**: ^{1}H NMR (CCl_4) δ 6.30 (d, *J* = 7 Hz, 1 H), 3.15–2.70 (m, 5 H), 2.50 (br, 2 H), 2.15–1.45 (m, 10 H); MS, *m/e* (relative intensity) 257 (M^+ + 2, 5), 255 nM$^+$, 5) 216 (50), 214 (50), 176 (30), 134 (60), 105 (55), 77 (55), 70 (100); high resolution mass spectrum calcd for $C_{12}H_{18}BrN$ 257.06021 (255.06225), found 257.06104 (255.06326).

1-(2-Bromo-2-cyclohexenyl)pyrrolidine (16). The compound was obtained as a minor product from the bromo carbonate **15** and as the major product from the bromo phosphate **21**. An analytical sample was prepared by GLC using column B at 160 °C: ^{1}H NMR (CCl_4) δ 6.10 (t, *J* = 3 Hz, 1 H), 3.30 (br s, 1 H), 2.65 (m, 4 H), 2.25–1.50 (m, 10 H); MS, *m/e* (relative intensity) 231 (M^+ + 2, 10), 229 (M^+, 10), 203 (12), 201 (12), 150 (15), 122 (100), 110 (30), 70 (25). Anal. Clacd for $C_{10}H_{16}BrN$: C, 52.19; H, 7.01. Found: C, 52.14; H, 6.67.

1-(2-Bromo-3,3-diphenyl-2-propenyl)pyrrolidine (25). This compound was prepared from the bromo phosphate **24** with and without palladium catalyst: ^{1}H NMR (CCl_4) δ 7.10 (s, 10 H), 3.50 (s, 2 H), 2.50 (m, 4 H), 1.70 (m, 4 H); MS, *m/e* (relative intensity) 343 (M^+ + 2, 1), 341 (M^+, 1), 262 (55), 191 (100), 165 (10), 84 (60); high resolution mass spectrum calcd for $C_{19}H_{20}BrN$ 343.07586 (341.07790), found 343.07661 (341.07630).

Treatment of Bromo Acetate 3 with *N*-Methylpyrrolidine in the Absence of Nucleophile. To 10 mL of *N*-methylpyrrolidine in a flask fitted with a reflux condenser were added 2.53 g (11.51 mmol) of **3**, 0.16 g (0.23 mmol) of $(PPh_3)_2PdCl_2$, and 0.02 g (0.12 mmol) of CuI. The mixture was heated to 80 °C and stirred for 5 h. Removal of the solvent, followed by bulb to bulb distillation of the residual liquid at 3 torr and 206 °C, gave 2.30 g (91%) of **3**.

The other bromo acetates in Table IV (E = acetate) were treated in a similar way with similar results.

Reaction of Allyl Bromo Carbonate 15 in *N*-Methylpyrrolidine and Absence of Added Nucleophile. Preparation of 2-Bromo-1,3-cyclohexadiene (6). Into a flask fitted with a reflux condenser were added 10 mL of *N*-methylpyrrolidine, 3.74 g (14.96 mmol) of the bromo carbonate **15**, and 0.25 g (0.22 mmol) of $(PPh_3)_4Pd$. The mixture was heated at 80 °C for 9 h. The solvent was removed without heating, on the rotary evaporator, to reduce loss of volatile products. The residual liquid was chromatographed first with hexane to obtain 0.80 g (34%) of **6**:[30] ^{1}H NMR (CCl_4) δ 5.95 (m, 1 H), 5.80 (m, 2 H), 2.20 (m, 4 H); MS, *m/e* (relative intensity) 160 (M^+ + 2, 50), 158 (M^+, 50), 79 (100), 77 (100). Continued elution of the column with a 1:1 mixture of CH_2Cl_2 and ether gave 1.03 g (27%) of **15**.

Reaction of the Diethyl Phosphate 21 in the Absence of Nucleophile with *N*-Methylpyrrolidine. Preparation of 6. A flask fitted with a reflux condenser was charged with 10 mL of *N*-methylpyrrolidine, 2.94 g (9.36 mmol) of bromo phosphate **21**, and 0.21 g (0.18 mmol) of $(PPh_3)_4Pd$, and the mixture was heated at 80 °C for 4 h. TLC at this stage showed total disappearance of **21**. The solvent was removed on a rotary evaporator without heating. The residue was taken up in ether, washed consecutively with 4% aqueous HCl, water, and brine, and dried ($MgSO_4$). Careful removal of the solvent on the evaporator gave 1.48 g (100%) of **6** identical in all respects with samples obtained by other methods.

2-[(Trimethylsilyl)ethynyl]-2-cyclohexen-1-ol, 1-Acetate (28). A mixture of 2.52 g (11.45 mmol) of the bromo acetate **3**, 0.26 g (0.22 mmol) of $(PPh_3)_4Pd$, 5 mL of *N*-methylpyrrolidine, and 1.50 g (15.00 mmol) of (trimethylsilyl)acetylene was sealed in a thick walled tube. The tube was placed in the oven at 80 °C for 3 h. The resulting suspension of crystals of amine salt was extracted with ether. After concentration, the residual oil was chromatographed first with hexane, followed by a 1:1 mixture of hexane and CH_2Cl_2, to obtain 1.65 g of a 3:1 mixture (by NMR analysis) of **28** and **3**, respectively. Calculated yields of these components based on the ratio and total quantity of material are 47% and 15%, respectively. An analytical sample of **28** was obtained from this mixture by GLC on column B at 210 °C: ^{1}H NMR (CCl_4) δ 6.05 (br t, *J* = 3 Hz, 1 H), 5.10 (br s, 1 H), 2.20–1.40 (m, 6 H), 1.85 (s, 3 H), 0.00 (s, 9 H); IR (neat, cm^{-1}) 3000, 2160, 1750, 1240, 900; MS, *m/e* (relative intensity) 236 (M^+, 10), 221 (20), 193 (50), 176 (80), 161 (70), 117 (60), 75 (80), 43 (100). Anal. Calcd for $C_{13}H_{20}O_2Si$: C, 66.05; H, 8.53. Found: C, 65.92; H, 8.69.

The following (trimethylsilyl)ethynyl products were prepared by the above procedure from the given 2-bromoallyl esters.

3-[(Trimethylsilyl)ethynyl]bicyclo[3.2.1]oct-3-en-2-ol, 2-Acetate (30). This compound was prepared from the bromo acetate **9**. An analytical sample was prepared by GLC with column B at 210 °C: ^{1}H NMR (CCl_4) δ 6.20 (d, *J* = 6 Hz, 1 H), 4.70 (br d, 1 H), 2.35 (m, 2 H), 2.00–1.10 (m, 6 H), 1.85 (2, 3 H), 0.00 (s, 9 H); IR (neat, cm^{-1}) 2960, 2880, 2160, 1735, 1240, 1020, 850; MS, *m/e* (relative intensity) 262 (M^+, 10), 233 (60), 159 (40), 117 (100), 73 (70), 75 (70), 43 (55). Anal. Calcd for $C_{15}H_{22}SiO_2$: C, 68.65; H, 8.45. Found: C, 68.72; H, 8.59.

Ethyl 3-[(trimethylsilyl)ethynyl]bicyclo[3.2.1]oct-3-en-2-yl carbonate (35) was prepared from the bromo carbonate **17**: ^{1}H NMR (CCl_4) δ 6.30 (d, *J* = 6 Hz, 1 H), 4.60 (br d, 1 H), 4.00 (q, *J* = 6 Hz, 2 H), 2.45 (m, 2 H), 1.90–1.30 (m, 6 H), 1.15 (t, *J* = 6 Hz, 3 H), 0.00 (s, 9 H); IR (neat, cm^{-1}) 3000, 2880, 2160, 1740, 1260, 1010, 850; MS, *m/e* (relative intensity) 292 (M^+, 30), 219 (75), 159 (80), 147 (60), 119 (55), 103 (60), 73 (100); high resolution mass spectrum calcd for $C_{16}H_{24}SiO_3$ 292.14947, found 292.15070.

2-(Diphenylmethylene)-4-(trimethylsilyl)-3-butynyl ethyl carbonate (36) was prepared from the bromo carbonate **18**: ^{1}H NMR (CCl_4) δ 7.05 (br s, 10 H), 4.50 (br s, 2 H), 4.00 (q, *J* = 7 Hz, 2 H), 1.15 (t, *J* = 7 Hz, 3 H), 0.00 (s, 9 H); IR CCl_4 (cm^{-1}) 3000, 2140, 1750, 1250, 1010; MS, *m/e* (relative intensity) 378 (M^+, 50), 305 (20), 273 (25), 215 (60), 73 (100); high resolution mass spectrum calcd for $C_{23}H_{26}SiO_3$ 378.16512, found 378.16664.

2-(Phenylethynyl)-2-cyclohepten-1-ol, 1-Acetate (32) and 2-(Phenylethynyl)-1,3-cycloheptadiene (33). Into a flask with a reflux condenser were introduced 10 mL of *N*-methylpyrrolidine and 2.94 g (10.65 mmol) of freshly distilled (bulb to bulb, 170 °C, 2 torr) bromo acetate **13**. After the addition of 0.24 g (0.20 mmol) of $(PPh_3)_4Pd$ and 1.26 g (12.37 mmol) of phenylacetylene, the mixture was heated at 80 °C for 45 min. A copious deposit of crystals of amine salt was observed along the sides of the reaction flask at this time, and TLC with hexane showed a new substance that is more mobile than the starting material. The reaction mixture was extracted with hexane, and the solvent mixture was removed on the rotary evaporator.

The liquid residue was taken up in 10 mL of hexane and this extract was washed down a column with more hexane to obtain 0.34 g (16%) of **33**: ^{1}H NMR (CCl_4) δ 7.25 (m, 5 H), 6.25 (br t, *J* = 6 Hz, 1 H), 5.85 (m, 2 H), 2.55–1.55 (m, 6 H); MS, *m/e* (relative intensity) 194 (M^+, 90), 178 (100), 165 (80), 115 (70). Compound **33** was very unstable. The hexane solution deposited, in a short time, a white spongy substance which could not dissolve any more in hexane. On complete removal of the solvent, **33** resinified after a short time to a yellowish gum. A high resolution mass spectrum of **33** was obtained through **32** which decomposes easily to **33** but is stable under ordinary condition of storage.

Subsequent elution of the column with a 1:1 mixture of hexane and ether resulted in the collection of 2.20 g (81%) of **32** as a viscuous, sweet smelling liquid. Attempted purification, by GLC, for analysis always led to a mixture of **32** and **33**: ^{1}H NMR (CCl_4) δ 7.30 (m, 5 H), 6.35 (br t, *J* = 6 Hz, 1 H), 5.45 (br s, 1 H), 2.50–1.50 (m, 8 H), 2.00 (s, 3 H); IR (CCl_4, cm^{-1}) 3000, 2200, 1750, 1240; MS, *m/e* (relative intensity) 194 ($M^+ - CH_3CO_2H$, 100), 179 (60), 178 (50), 166 (40), 115 (70), 43 (50); high resolution mass spectrum calcd for $C_{17}H_{18}O_2 - C_2H_4O_2 = C_{15}H_{14}$ 194.10955, found 194.10906.

Dienyne **33** was the sole product of similar reactions with the bromo carbonate **19** and the bromo phosphate **26**.

2-(Phenylethynyl)-2-cyclohexen-1-ol, 1-Acetate (7). This coupling product was prepared from the bromo acetate **3** according to the procedure described above for **33**. An analytical sample of **7** was prepared by GLC with column A at 200 °C: ^{1}H NMR (CCl_4) δ 7.20 (m, 5 H), 6.20 (m, 1 H), 5.33 (br s, 1 H), 2.00 (s, 3 H), 2.33–1.50 (m, 6 H); IR (neat, cm^{-1}) 3060, 2940, 2200, 1730, 1600, 1240; MS, *m/e* (relative intensity) 240 (M^+, 5), 180 (100), 165 (40). Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.76; H, 6.69.

2-(Phenylethynyl)-1,3-cyclohexadiene (34) was the sole product from reactions of the bromo carbonate **15** and the bromo phosphate **21** with phenylacetylene. This compound was as unstable as **33**. It therefore did not have enough stability during storage to allow for consistent analysis: ^{1}H NMR (CCl_4) δ 7.25 (m, 5 H), 6.25–5.75 (m, 3 H), 2.15 (br s, 4 H); MS, *m/e* (relative intensity) 180 (M^+, 100), 178 (95), 165 (70), 126 (10).

2-(3-Hydroxy-3-methyl-1-butynyl)-2-cyclohexen-1-ol, 1-Acetate (29). A solution of 2.36 g (10.72 mmol) of **3**, 1.10 g (13.08 mmol) of 3-methyl-1-butyn-3-ol, 0.15 g (0.22 mmol) of $(PPh_3)_2PdCl_2$, and 0.02 g (0.15 mmol) of CuI in 10 mL of *N*-methylpyrrolidine was heated at 80 °C for 4 h. The solvent was removed on a rotary evaporator, and the residual viscous liquid was extracted with hexane. After concentration, the sequence of extraction with hexane and concentration was repeated until a homogeneous solution was obtained when the residual liquid was taken up in hexane. The product, which was a mixture of **3** and **29**, weighed 1.79 g. This mixture was subjected to column chromatography, first with a 1:1 mixture of hexane and CH_2Cl_{25} to recover 0.64 g (27%) of **3**. Further elution with a 1:3 mixture of hexane and ether gave 0.61 g (26%) of **29**. This substance progressively turned into material insoluble in hexane: ^{1}H NMR (CCl_4) δ 6.10 (br t, J = 3 Hz, 1 H), 5.30 (br s, 1 H), 3.25 (br s, 1 H), 2.30–1.10 (m, 6 H), 2.10 (s, 3 H), 1.50 (s, 6 H); IR (neat, cm^{-1}) 3440, 3000, 2220, 1720, 1250; MS, *m/e* (relative intensity) 222 (M^+, 2), 162 (40), 147 (80), 129 (20), 91 (35), 73 (30), 43 (100); high resolution mass spectrum calcd for $C_{13}H_{18}O_3$ 222.12560, found 222.12753.

2-(Phenylethynyl)-2-cyclohexenol (37). To 4.99 g (22.68 mmol) of the bromo acetate **3** in 20 mL of pyrrolidine were added 0.21 g (0.92 mmol) of palladium acetate and 0.47 g (1.81 mmol) of triphenylphosphine. The stirred mixture was heated to 80 °C, and 4.65 g (45.65 mmol) of phenylacetylene was added. The reaction mixture was kept at 80 °C for 6 h.

The solvent was removed on a rotary evaporator, and the dense reddish liquid residue was extracted with 3 × 100 mL of hexane. The extract was washed with water and brine and dried ($MgSO_4$). After concentration, the product was chromatographed with a 1:1 mixture of hexane and CH_2Cl_2. The first fraction eluted was a mixture of unknown substances. Continued elution with the same solvent mixture, followed by 100% CH_2Cl_2, gave 3.02 g (67%) of **37** as a viscous oil: ^{1}H NMR (CCl_4) δ 7.30 (m, 5 H), 6.20 (t, J = 4 Hz, 1 H), 4.20 (br, 1 H), 2.80 (br s, 1 H), 2.30–1.50 (m, 6 H); IR (neat, cm^{-1}) 3400, 3060, 2940, 2200, 1600, 1050; MS, *m/e* (relative intensity) 198 (M^+, 80), 180 (75), 170 (100), 141 (80), 115 (70); high resolution mass spectrum calcd for $C_{14}H_{14}O$ 198.10447, found 198.10664.

This compound was also prepared by the same procedure from the bromo alcohol **8**.

Reaction of Bromo Acetate 11 with Phenylmagnesium Bromide. To a solution of 1.56 g (4.71 mmol) of **11** and 0.11 g (0.10 mmol) of $(PPh_3)_4Pd$ in 10 mL of *N*-methylpyrrolidine at 80 °C was added by syringe phenylmagnesium bromide prepared from 2.07 g (13.13 mmol) of phenyl bromide and excess magnesium in THF. Heating under reflux was continued for 5 h. After concentrating the reaction mixture, the residue was extracted with ether, and the ether extract was washed consecutively with water and brine and dried ($MgSO_4$). The residue, after removal of ether was chromatographed, first eluting with hexane. Subsequent use of a 3:1 mixture of hexane and ethyl acetate gave 1.48 g (82%) of 2-bromo-3,3-diphenyl-2-propenol (**12**) with physical characteristics identical with **12** obtained by other methods.

Reaction of the Bromo Acetate 3 with PhMgBr. To a solution of 2.15 g (9.78 mmol) of **3** and 0.22 g (0.20 mmol) of $(PPh_3)_4Pd$ in 10 mL of *N*-methylpyrrolidine at 80 °C was added PhMgBr prepared from 1.70 g (10.76 mmol) of PhBr and excess Mg in THF. After the addition (15 min), the mixture was heated for 1 h and then diluted with 50 mL of hexane and filtered. The filtrate was evaporated carefully, and the pale yellow oil was chromatographed with hexane to obtain 1.00 g (65%) of 2-bromo-1,3-cyclohexadiene (**6**) identical with samples obtained by other methods.

Acknowledgment. The author is grateful to John Toth and Sue Brackett for obtaining the low resolution mass spectral and GC–MS analyses. High resolution mass spectra were determined by Thomas Dorsey at the Massachussetts Institute of Technology Mass Spectrometry Facility, directed by Professor K. Biemann and supported by National Institutes of Health research grant No. RR00317 from the Biotechnology Resources Branch, Division of Research Resources.

Notes

Solid-Phase Synthesis, Separation, and Stereochemical Aspects of P-Chiral Methane- and 4,4′-Dimethoxytriphenylmethanephosphonate Analogues of Oligodeoxyribonucleotides

Wojciech J. Stec,*[1] Gerald Zon, William Egan, R. Andrew Byrd, Lawrence R. Phillips, and Kathleen A. Gallo

Division of Biochemistry and Biophysics, Food and Drug Administration, 8800 Rockville Pike, Bethesda, Maryland 20205

Received September 5, 1985

Oligonucleotides that are modified at the internucleotide phosphate moiety(ies) have attracted considerable attention. In addition to phosphorothioate analogues of oligodeoxyribonucleotides, which have a stereogenic phosphorus center and are therefore valuable probes for stereochemical investigations of the mechanism of action of phosphorolytic enzymes,[2] other analogues of interest include *O*-alkyl phosphotriester **1** and alkanephosphonate **2** congeners of oligodeoxyribonucleotides. Miller and Ts'o, and their associates,[3] have demonstrated that oligonucleotide phosphotriesters and methanephosphonates form base-paired complexes with complementary nucleic acids and that these complexes have greater stability toward dissociation than those containing the corresponding diesters, presumably due to less electrostatic repulsion between

(1) FDA International Visiting Scientist, 1983–84. Permanent address: Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, Department of Bioorganic Chemistry, 90-362 Lodz, Poland.

(2) Eckstein, F. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 423. Potter, B. V. L.; Eckstein, F. *J. Biol. Chem.* **1984**, *259*, 14243. See also: Gerlt, J. A.; Coderre, J. A.; Mehdi, S. *Adv. Enzymol. Relat. Subj. Biochem.* **1983**, *55*, 291.

(3) (a) Miller, P. S.; Agris, C. H.; Blake, K. R.; Murakami, A.; Spritz, S. A.; Reddy, P. M.; Ts'o, P. O. P. In "Nucleic Acids: The Vectors of Life"; Pullman, B., Jortner, J., Eds.; D. Reidel Publishing Co.: Boston 1983; pp 521–535, and references cited therein. (b) Miller, P. S.; Fang, K. N.; Kondo, N. S.; Ts'o, P. O. P. *J. Am. Chem. Soc.* **1971**, *93*, 6657.