The Thermal Rearrangement of 20. Compound **20** (1.30 g, 2.3 mmol) was sealed in a pressure tube filled with dry nitrogen and heated (a) for 3 h, and in a second experiment (b) for 1 h at 180 °C. The reaction mixtures were chromatographed and eluted with petroleum ether/ethyl acetate (7/3). Reaction gave 0.44 g (67%) of **22**; reaction b gave **22** (0.07 g, 11%), and also 0.43 g (65%) of *4,7-dimethyl-1,1-diphenyl-2,3-diazaocta-1,3-dien-5-yne* (**26**) as a yellow oil. The analytical sample of **21** was obtained by short path distillation (bath temperature 170 °C, 0.3 mmHg); it contained a trace of **22**, which could not be separated from **21**. The analytical data for **21** (by subtraction of **22**) are as follows, IR 2210 cm^{-1} (—C≡C-); ^1H NMR δ 1.16 (dd, J = 6.8, 6 H, CH-(CH_3)$_2$), 2.04 (s, 3 H, N=C—CH_3), 2.72 (m, 1 H, $CH(CH_3)_2$), 7.18–7.80 (m, 10 H, Ar); ^{13}C NMR δ 21.3 (N=C—CH_3), 22.5 (CH(CH_3)$_2$), 23.6 ($CH(CH_3)_2$), 75.6 (C≡C—CH), 107.7 (C≡C—CH), 143.1 (N=C—CH_3), 159.4 (=C—Ph_2); precise mass calcd for $C_{20}H_{20}N_2$, 288.163; found, 288.161.

Reaction of Ylide 10 with Ketene. (a) Preparation of 2-Methyl-9-phenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (18c). Ketene was prepared according to the procedure of Williams and Hurd[15] under a dry nitrogen atmosphere. The ketene stream was bubbled through the slurry of ylide **10** (1.25 g, 2.5 mmol) in 25 mL of benzene. After addition of ketene for 2 min with stirring, the reaction mixture became a clear red solution. The ketene stream was allowed to pass through the stirred solution for a further 2 min. The solution was stirred at ambient temperature for an additional 0.5 h, and under reflux for further 26 h. After removal of solvent in vacuo, the residue was chromatographed eluting with petroleum ether/ethyl acetate (7/3). The first fraction was collected, and the solvent was evaporated in vacuo, affording 0.48 g (74%) of **18c**, a light yellow solid. An analytical sample was obtained by recrystallization from heptane, mp 114–115.5 °C; precise mass calcd for $C_{18}H_{16}N_2$, 260.131; found, 260.131.

(b) Isolation of 1,1-Diphenyl-2,3-diaza-4-methyl-1,3,5,6-heptatetraene (13c). The ketene stream[15] was bubbled through the slurry of ylide **10** (1.25 g, 2.5 mmol) in 25 mL of benzene at 0 °C for 3 min and allowed to react at ambient temperature for 2 h. The solution was isolated as above, affording 0.55 g (85g) of **13c** as a yellow oil; IR 1932 cm^{-1} (C=C=C); ^1H NMR δ 2.09 (s, 3 H, C-4-CH_3), 5.09 (d, J = 6.7, 2 H, =CH_2), 6.00 (t, 1 H, CH=), 7.14–7.79 (m, 10 H, Ar); ^{13}C NMR δ 14.9 (CH_3), 79.3 (CH_2), 96.7 (CH), 158.2 and 159.8 (C-1 and C-4 or reversed), 213.3 (=C=); precise mass calcd for $C_{18}H_{16}N_2$, 260.131; found, 260.128.

Reaction of Ylide 11 with Ketene. Preparation of 1-(1-Phenylvinyl)-3,5-dimethylpyrazole (23). A slurry of ylide **11** (2.2 g, 5 mmol) in 60 mL of benzene was allowed to react with ketene and then treated as described in the preparation of **18c**. The reaction afforded 0.75 g (76%) of 23 as a yellow oil; on short-path distillation (bath temperature 105 °C, 0.05 mmHg) a colorless analytical sample of **23** was obtained: ^1H NMR δ 2.02 (s, 3 H, 5-CH_3), 2.27 (s, 3 H, 3-CH_3), 5.36 (s, 1 H, =CH_2), 5.69 (s, 1 H, =CH_2), 5.92 (s, 1 H, 4-H); ^{13}C NMR δ 11.6 (C-5-CH_3), 12.1 (C-3-CH_3), 106.1 (C-4), 111.6 (C=CH_2), 136.6 (C=CH_2), 145.2 (C-5), 148.7 (C-3); precise mass calcd for $C_{13}H_{14}N_2$, 198.116; found, 198.115.

Acknowledgment. This work was supported in part by a generous grant (GM27620) from the National Institute of General Medical Science. We also thank Dr. Roger Crecely of the University of Delaware for obtaining and discussing with us the ^1H, ^{31}P, and ^{13}C NMR spectra reported in this work. Purchase of the Brucker WM250 was supported in part by a grant (GM27616) from the National Institutes of Health. The acquisition of the Nicolet R3-X-ray crystallographic system was supported in part by a grant (CHE-82-05 589) from the National Science Foundation.

Registry No. **5**, 5350-57-2; **6**, 13466-30-3; **7**, 2091-46-5; **8a**, 87101-38-0; **8b**, 87101-39-1; **9a**, 87101-40-4; **9b**, 87101-41-5; **10**, 87101-42-6; **11**, 87101-43-7; **13c**, 87101-45-9; **16a**, 87101-46-0; **16b**, 87101-47-1; *cis*-**16h**, 87101-48-2; *trans*-**16h**, 87101-49-3; *cis*-**16i**, 87101-50-6; *trans*-**16i**, 87101-51-7; **18b**, 87101-52-8; **18c**, 87114-17-8; *cis*-**18d**, 87101-53-9; *trans*-**18d**, 87101-54-0; **18e**, 87101-55-1; **18f**, 87101-56-2; **18i**, 87101-57-3; (*E*)-**20**, 87101-58-4; (*Z*)-**20**, 87101-59-5; **21**, 87101-60-8; **22**, 87101-61-9; **23**, 87101-62-0; **24e**, 87101-63-1; **24f**, 87101-64-2; **25e**, 87101-65-3; diphenylketene, 525-06-4; methylphenylketene, 3156-07-8; ketene, 463-51-4; phenylketene, 3496-32-0; ethylketene, 20334-52-5; benzylketene, 87101-44-8.

Supplementary Material Available: Supplementary Material Available: Tables of the experimental data for the crystallographic structural determination (10 pages). Table 1S, atomic coordinates; Table 2S, bond distances; Table 3S, bond angles; Table 4S, anisotropic temperature factors; Table 5S, hydrogen atom coordinates; and Table 6S, calculated vs. observed structure factors. Ordering information is given on any current masthead page.

(15) Williams, J. W.; Hurd, C. D. *J. Org. Chem.* **1940**, *5*, 122.

Palladium-Catalyzed Cyclizations of Bromodialkenyl Ethers and Amines

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A variety of vinylic bromoalkenyl alkenyl ethers were reacted with piperidine and a palladium acetate–tri-*o*-tolylphosphine catalyst. Intramolecular vinylic substitution occurred in many cases. Five-membered rings formed most easily, followed by six and then seven. Larger rings were much more difficult to produce. Substitution at the reacting double bond sometimes altered the ring closure preference since the less substituted double bond carbons are more reactive. Bromoalkenyl 2,4-hexadienyl ethers, bromoalkenyl 4-hydroxy-2-butenyl ethers, and bromodialkenylamines behaved similarly to the above ethers, showing a preference for formation of five-membered ring products over six and a very low tendency to form medium-sized rings. The reactions are of preparative value for forming various substituted five-, six-, and seven-membered ring oxygen and nitrogen heterocycles.

We have shown in previous work that various bromodienes can be cyclized with palladium catalysts and piperidine to produce cycloalkene derivatives.[1] The reaction proved to be most useful for the formation of five-membered rings. A typical example is the cyclization of 2-bromo-1,6-heptadiene. The reaction is believed to proceed by way of a π-allylic palladium intermediate which is attacked by the piperidine.

Related palladium-catalyzed cyclizations of haloaromatic amides have been reported, also. For example, *N*-acryoyl-*o*-bromoanilines cyclize to oxindole derivatives.[2-4] We

(1) Narula, C. K.; Mak, K. T.; Heck, R. F. *J. Org. Chem.* **1983**, *48*, 2792.

(2) Terpko, M. O.; Heck R. F. *J. Am. Chem. Soc.* **1979**, 101, 5281.
(3) Mori M.; Ban, Y. *Tetrahedron Lett.* **1979**, 1133.

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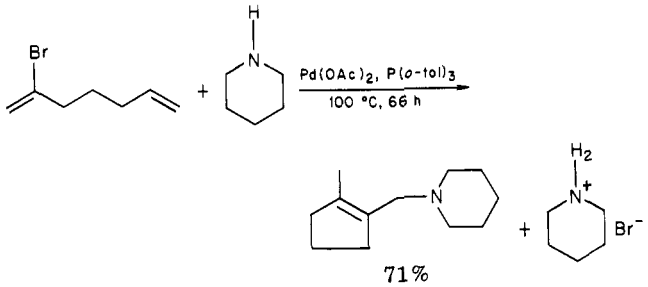
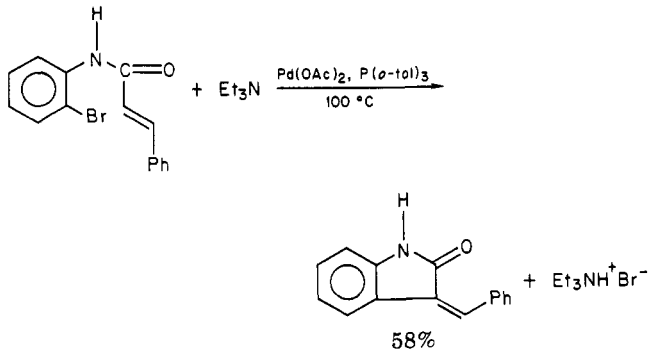
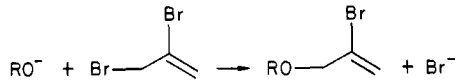




now report an extension of our previous work to the cyclization of bromodialkenyl ethers and bromodialkenylamines, which form oxygen and nitrogen heterocycles, respectively.

Results and Discussion

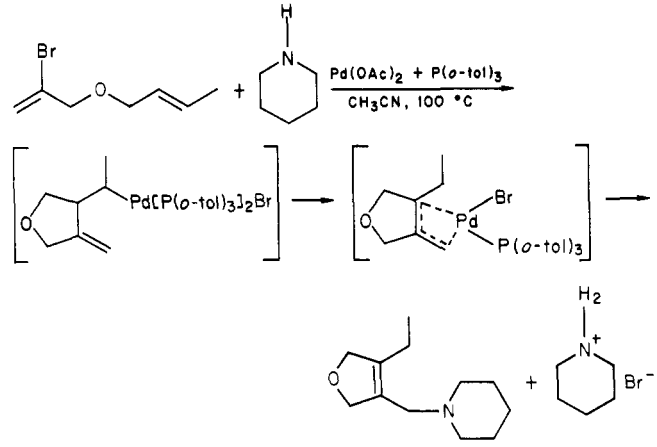
Bromodialkenyl Ethers. Ten 2-bromoallyl alkenyl and hydroxy alkenyl ethers, three 2-bromoalkenyl 2,4-hexadienyl ethers, 3-bromo-3-butenyl acrylate, *o*-bromophenyl 3-butenyl ether, and allyl *o*-bromobenzyl ether were prepared for this study. All were prepared by Williamson type syntheses from alkoxides or phenoxides and alkenyl halides. The 2-bromoallyl ethers were obtained from the appropriate alkoxide and 2,3-dibromopropene. The 2-



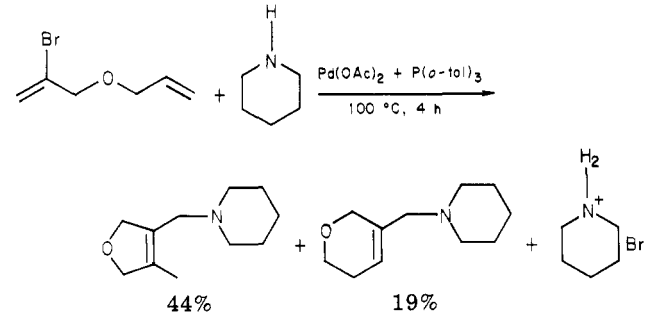
bromoallyl ethers apparently underwent competing side reactions under the conditions of their formation, and consequently yields of these ethers were low, in the range of 15–50% of theory. These ethers also failed to give molecular ions in the mass spectrometer. The physical properties of the bromodialkenyl ethers prepared are given in Table III (supplementary material).

Cyclizations of Bromodialkenyl Ethers. The reactions may be considered in four groups: (1) the 2-bromoallyl alkenyl ethers; (2) the bromoalkenyl 2,4-dienyl ethers; (3) the bromoalkenyl 4-hydroxy-2-butenyl ethers; (4) 2-bromophenyl 3-butenyl ether and 2-bromobenzyl allyl ether (two bromoaryl ethers). Each group reacts slightly differently. The data are summarized in Table I. The properties of the cyclic products produced are given in Table IV (supplementary material).

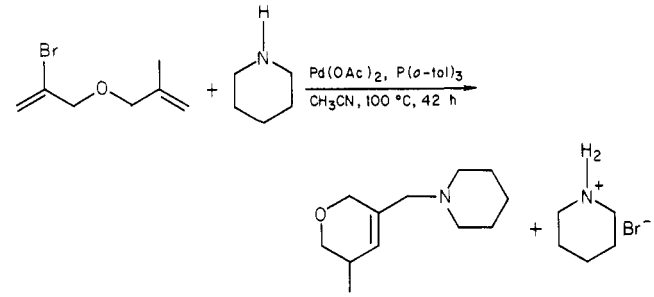
2-Bromoallyl Alkenyl Ethers. The cyclization reaction produces π-allyl–palladium complexes as intermediates in this case by a palladium hydride elimination and reverse readdition mechanism.[1] Five-membered rings are preferred over six when both olefinic carbons of the alkenyl group are similarly substituted. Thus, 2-bromoallyl 2-butenyl ether cyclizes exclusively to the five-membered ring product in 60% yield. Allyl 2-bromoallyl ether, on



the other hand, gave a 2:1 mixture of five- and six-membered ring products. This ether contrasts with the cor-



responding bromodiene, 2-bromo-1,6-heptadiene, which cyclized only to the cyclopentene derivative.[1] In intermolecular reactions, 2-bromopropene adds exclusively to the terminal double bond carbon of alkenes such as 1-hexene.[5] Substitution on the second carbon of the allyl ether moiety shifts the ring closure totally to the dihydropyran derivative. Thus, 2-bromoallyl 2-methallyl ether reacts as follows:

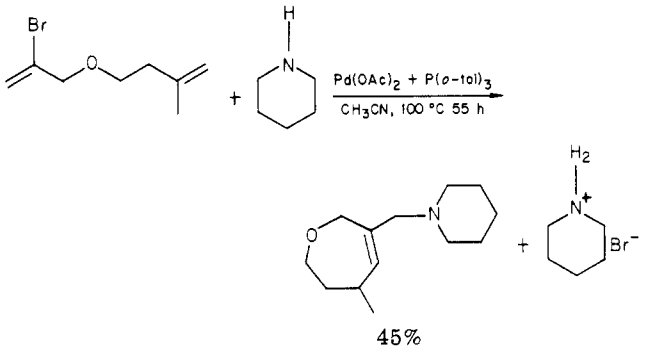


The seven-membered-ring compound was the only volatile product found when the related 2-bromoallyl 3-methyl-3-butenyl ether was cyclized. Under the same conditions as were employed to prepare the five- and six-membered-ring products, the seven-membered-ring compound was formed in 45% yield (GLC).

Attempts to prepare eight- or nine- and twelve- or thirteen-membered rings were not very successful. While some twelve- and/or thirteen-membered ring piperidine adducts were apparently formed from 2-bromoallyl 9-decenyl ether, the yield was less than 15% and mixtures of two or more products were obtained. Decomposition

(4) Mori M.; Shiba, K.; Ban, Y. *Tetrahedron Lett.* **1977**, 1807.

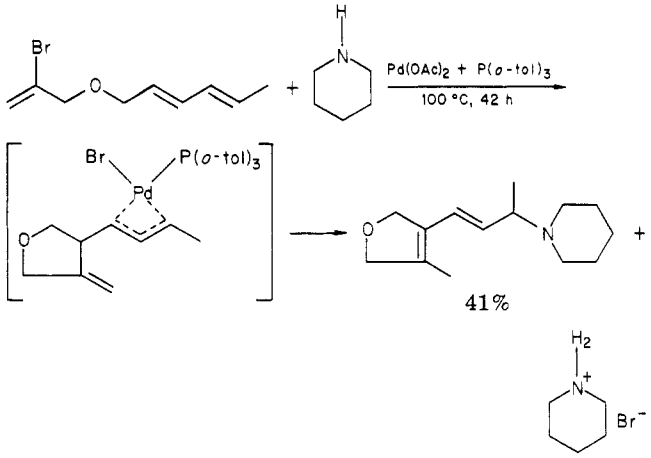
(5) Patel, B. A.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 3898.



products of the bromoallyl ether were the major products. No cyclic products could be isolated from the 2-bromoallyl 5-hexenyl ether–piperidine reaction in the absence of solvent or with DMF as solvent.

2-Bromoallyl 2-cyclohexenylmethyl ether and allyl 2-bromo-2-butenyl ether failed to give cyclic products under similar conditions, even though five- or six-membered rings could have been formed. 3-Bromo-3-butenyl acrylate gave only a polymeric product on attempted cyclization. Analyses of the polymer indicated that only 2.5% bromine was present, suggesting that it could have been mainly a polymer of the dienyllactone product.

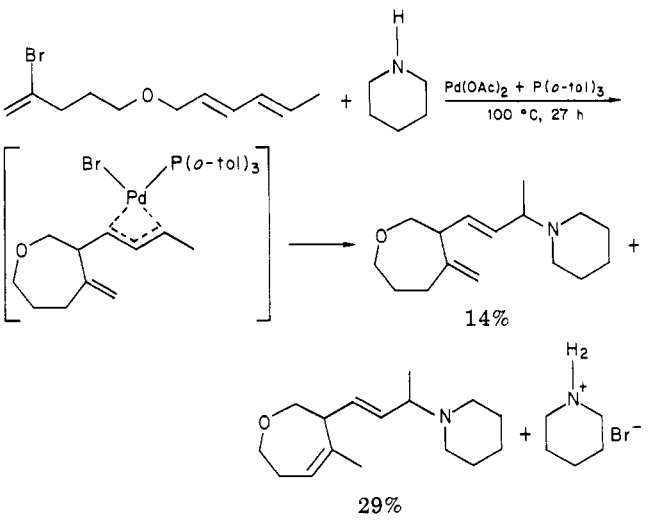
Bromoalkenyl 2,4-Dienyl Ethers. The 2-bromoalkenyl 2,4-hexadienyl ethers behaved similarly to the 2-bromoalkenyl alkenyl ethers with piperidine. 2-Bromoallyl 2,4-hexadienyl ether and piperidine with the usual $Pd(OAc)_2$–$P(o\text{-tol})_3$ catalyst at 100 °C gave a 42% yield of the five-membered-ring piperidine derivative. The reaction is undoubtedly proceeding by way of a π-allylic palladium intermediate. The exocyclic double bond which



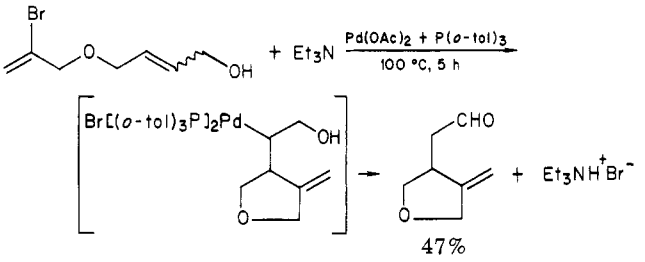
must have been formed initially has totally been converted into the conjugated endocyclic isomer. Likewise, 4-bromo-4-pentenyl 2,4-hexadienyl ether with piperidine and the palladium catalyst cyclized at 100 °C to a mixture of two isomeric seven-membered-ring piperidine derivatives in 43% yield. It is curious that the rearranged alkene product is not the conjugated isomer as it was in the preceding example. Perhaps there is a chelating effect of the diene on the palladium hydride in the intermediate which favors formation of the nonconjugated isomer in this example.

Again, an attempt to produce a larger ring, an eight-membered ring, by cyclizing 5-bromo-2-hexenyl 2,4-hexadienyl ether with piperidine led only to the formation of decomposition products and no cyclic compounds.

Bromoalkenyl 4-Hydroxy-2-butenyl Ethers. Previous work showed that the double bond of allylic alcohols was unusually reactive to organopalladium compounds,[6a]

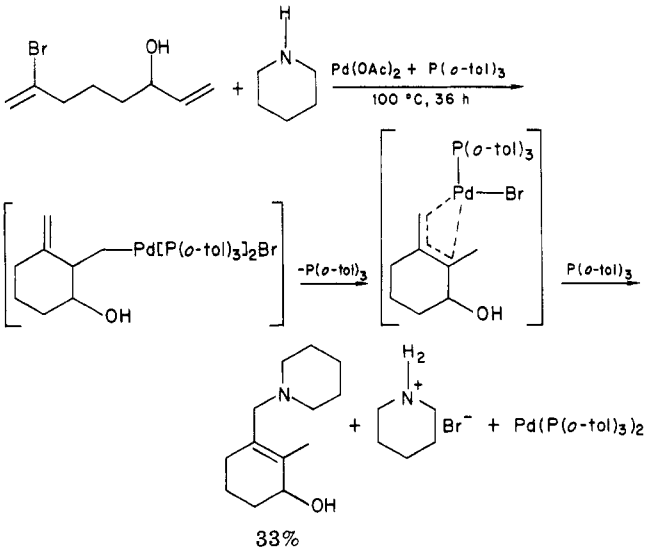


so we attempted to carry out intramolecular versions of this reaction to form cyclic products. Cyclization occurred easily in the five-membered-ring example, 2-bromoallyl 4-hydroxy-2-butenyl ether (*E* and *Z* mixture) with triethylamine as the base. The product, cyclic aldehyde, was obtained in 47% yield. Once again an attempt to form



an eight-membered-ring failed. 5-Bromo-2-hexenyl 4-hydroxy-2-butenyl ether (*E,Z* mixture) under the usual reaction conditions did not produce a significant amount of cyclic product.

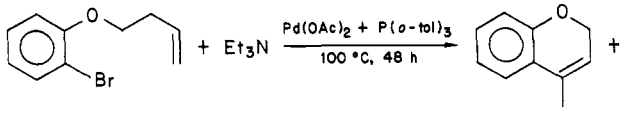
Cyclization of an allylic alcohol with an all carbon chain also was achieved. 7-Bromo-1,7-octadien-3-ol with piperidine and the usual catalyst produced 2-methyl-3-(piperidinomethyl)-2-cyclohexenol as the only volatile product in 33% yield. A π-allylic intermediate is probably formed here also.



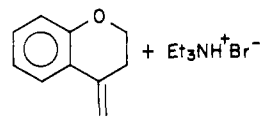
(6) (a) Melpolder, J. B.; Heck, R. F. *J. Org. Chem.* **1976**, *41*, 265. (b) We are indebted to a referee for suggesting this alternative explanation.

It is not immediately clear why amino alcohol is obtained in this reaction as the sole product, while the ether example above gave unsaturated aldehyde. Perhaps the intermediate π-allylic species in the present example has the palladium coordinated to the hydroxyl substituent and they, therefore, are cis to each other, in which case the favored cis elimination of palladium hydride from the carbon bearing the hydroxyl group is not possible. Another possibility is that elimination to form the carbonyl compound must occur from the σ tertiary allylic palladium intermediate and this is so unfavorable that it doesn't form,[6b] although a 1,4-elimination might be expected if the other σ allylic isomer were favored.

2-Bromoaryl Ethers. The aromatic ether, 3-butenyl *o*-bromophenyl ether, cyclized with triethylamine and the usual catalyst to form a mixture of two isomeric 1-benzopyran derivatives in 75% yield.

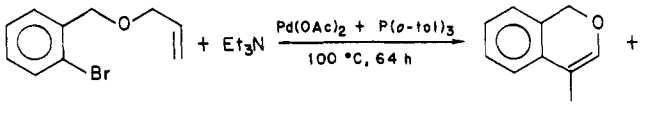


47%

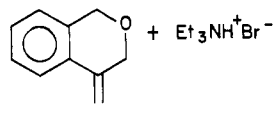


28%

Cyclization of the related isomeric ether, allyl *o*-bromobenzyl ether, also proceeded in good yield, 69%, to form two isomeric 2-benzopyrans.



48%

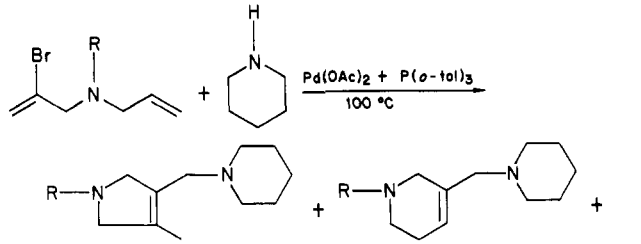


21%

Bromodialkenylamines. Allyl(2-bromoallyl)amine and its *N*-methyl and *N*-acetyl derivatives, *N*-methyl-*N*-(2-bromoallyl)-3-butenylamine, and *N*-(3-bromo-3-butenyl)-3-butenylamine were studied. The *N*-methylamines were prepared by methylation of the secondary amines with methyl iodide, while the secondary amines came from the reactions of either allylamine or 3-butenylamine with 2,3-dibromo-1-propene or 1,3-dibromo-2-butene. Acetylation of allyl(2-bromoallyl)amine with acetic anhydride gave the *N*-acetyl derivative. The properties and spectra of these compounds are given in Table V (supplementary material).

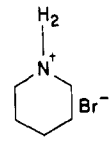
Cyclization of Bromodialkenylamines. The secondary amine, allyl(2-bromoallyl)amine, with piperidine and the $Pd(OAc)_2$-$P(o\text{-tol})_3$ catalyst gave only 19% of cyclized products; the piperidine adduct of the pyrroline was the major product, while the *N*-methyl derivative gave 33% of the five- and 11% of the six-membered-ring piperidine adducts. The best yields were obtained with the *N*-acetyl derivative where a 1:1 mixture of the five- and six-membered-ring products were produced in a total yield of 76%.

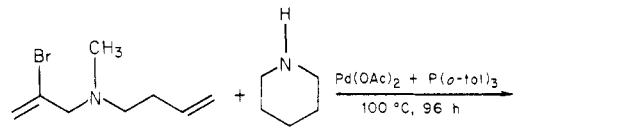
The *N*-methyl-*N*-(2-bromoallyl)-3-butenylamine cyclized to six-membered-ring products, a mixture of two isomeric piperidine adducts and two dienes in 63% total yield.

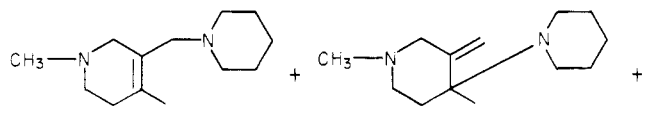


15% (R = H)
33% (R = CH_3)
38% (R = CH_3CO)

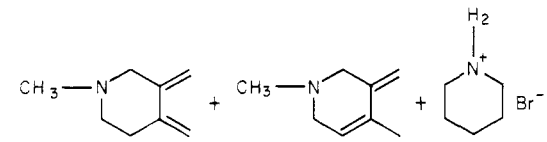
4% (R = H)
11% (R = CH_3)
38% (R = CH_3CO)







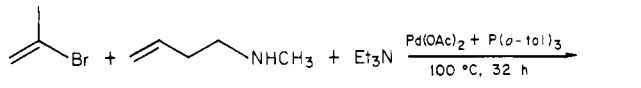
57% 4%

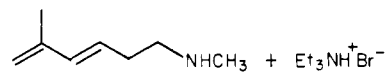


1% 1%

Attempted cyclization of (3-bromo-3-butenyl)-3-butenylamine, which could have given seven- or eight-membered-ring products, failed. Only nonvolatile products were formed. The properties of the cyclic products formed are given in Table V (supplementary material).

An attempt to form a heterocycle by an intramolecular attack of a secondary amine moiety upon a π-allylic palladium group situated so that five- or eight-membered rings could be formed failed and only elimination occurred to form the dienylamine. 3-Butenylmethylamine was reacted with 2-bromopropene and triethylamine with a $Pd(OAc)_2$-$P(o\text{-tol})_3$ catalyst and the only volatile product was (5-methyl-3,5-hexadienyl)methylamine, formed in 32% yield. Apparently, intramolecular amine-promoted elimination is favored over substitution.



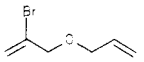
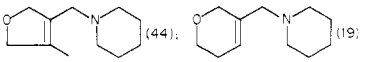
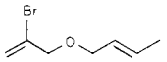
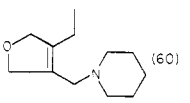
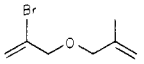
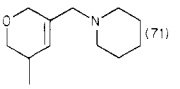
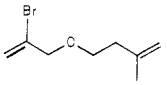
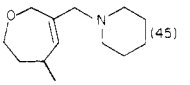
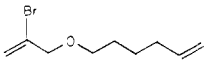
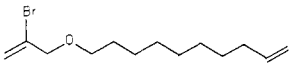
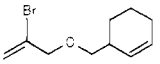
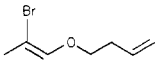
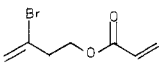
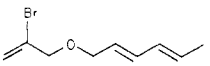
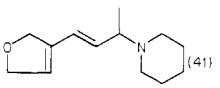
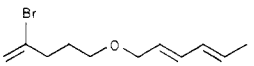
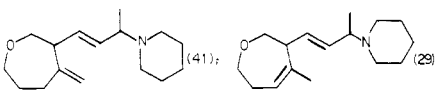
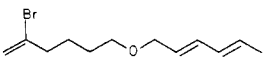
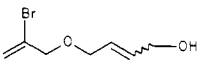
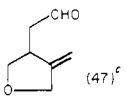
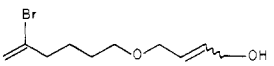
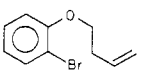
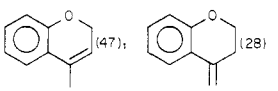
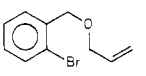
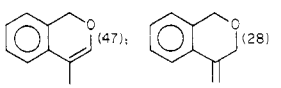


32%

Conclusions

From the examples studied, the order of preference for ring closure for the alkenyl 2-bromoalkenyl ethers is that a five-membered ring is better than a six, and six is better than a seven, which in turn is much better than the larger rings. The order may be altered if the double bond carbons are not similarly substituted. Unsubstituted double bond carbons are more reactive than monosubstituted carbons,

Table I. Palladium-Catalyzed Cyclizations of Bromodialkenyl Ethers with Amine

ether	conditions	amine	products (% yield)
	100 °C, 4 h	piperidine	 (44); (19)
	CH_3CN solvent, 100 °C, 64 h	piperidine	 (60)
	CH_3CN solvent, 100 °C, 42 h	piperidine	 (71)
	CH_3CN solvent, 100 °C, 55 h	piperidine	 (45)
	100 °C, 70 h[a]	piperidine	very little, if any, cyclic product
	CH_3CN solvent, 100 °C, 43 h[b]	piperidine	mixture of at least two cyclic products (15)
	125 °C, 48 h[b]	piperidine	very little, if any, cyclic product
	100 °C, 3.5 h[b]	piperidine	very little, if any, cyclic product
	100 °C, 18 h[b]	Et_3N	polymer
	100 °C, 42 h	piperidine	 (41)
	100 °C, 27 h[b]	piperidine	 (41); (29)
	100 °C, 47 h[b]	piperidine	very little, if any, cyclic product
	100 °C, 5 h[b]	Et_3N	 (47)[c]
	100 °C, 21 h[b]	Et_3N	very little, if any, cyclic product
	100 °C, 48 h	Et_3N	 (47); (28)
	100 °C, 64 h	Et_3N	 (47); (28)

[a] Catalyst: 5 mol % $Pd(OAc)_2$ and 10 mol % P(o-tol)$_3$. [b] Catalyst: 2 mol % $Pd(OAc)_2$ and 4 mol % P(o-tol)$_3$. [c] Yield by GLC, isolated yield 32%.

and disubstituted double bond carbons do not react. The bromoalkenyl 2,4-dienyl ethers and the bromoalkenyl 4-hydroxy-2-butenyl ethers appeared to react similarly, although few examples were studied.

The cyclizations of the alkenyl(2-bromoallyl)amines showed a preference for five-membered-ring closure over six when the amine nitrogen was unsubstituted or *N*-methylated, while one *N*-acetyl derivative gave equal amounts of the five- and six-membered rings. In another example, the six-membered ring was shown to be much preferred over the seven. An example in which a seven- or eight-membered ring could have been formed gave only polymeric products.

The ether cyclization reactions have synthetic value for the preparation of some substituted five-, six-, and seven-membered ring products, while the amines cyclize to five- and six-membered ring products with (in one case) an N-acylated derivative cyclizing in the highest yield.

Experimental Section

Bromodialkenyl Ethers. All of the alkenyl 2-bromo-2-propenyl ethers, the bromoalkenyl dienyl ethers, and the bromoalkenyl 4-hydroxy-2-butenyl ethers were prepared by the same method. To a stirred suspension of 0.25 mol of sodium hydride (added as a 50% dispersion in mineral oil) in 100 mL of dry THF at room temperature under nitrogen was added 0.25 mol of the unsaturated alcohol or dienol in 15 mL of THF and the mixture was stirred at room temperature. The solution became warm and gas was evolved. After the initial reaction subsided, the solution was heated under a reflux condenser until the alcohol had all reacted as determined by GLC. The cooled reaction mixture was then treated with 0.22-0.25 mol of the appropriate dibromoalkene dissolved in 15 mL of THF. The reaction mixture was stirred at room temperature overnight and then heated at reflux temperature until the dibromide had reacted as determined by GLC.

The reaction mixture was cooled, treated with aqueous sodium chloride, and extracted with several portions of ether. The extracts were dried over sodium sulfate, the solvent was removed under reduced pressure, and the products were distilled in vacuo. The yields and physical properties of the ethers are given in Table II (supplementary material).

All of the alcohols used in these reactions were commercially available. 2,3-Dibromo-1-propene was obtained from the Aldrich Chemical Co., while the other dibromoalkenes were prepared by the methods described below.

1,3-Dibromo-2-butene. To a stirred mixture of 56 g (0.80 mol) of 2-butyn-1-ol (Farchan Labs) and 0.45 g of iron powder (to decompose peroxides) was added 194 g (2.4 mol) of 48% hydrobromic acid. The mixture was stirred at room temperature overnight and then at 70 °C for 3 h. The reaction mixture was cooled and extracted with methylene chloride. The extracts were washed with 5% aqueous sodium bicarbonate and saturated aqueous sodium chloride and dried over $CaSO_4$. The solvent was removed under reduced pressure and the residue distilled. The product, 58.7 g, bp 60–67 °C (13 mm), was crude 3-bromo-2-buten-1-ol.

In a 250-mL three-necked flask was placed 35 g (0.13 mol) of phosphorus tribromide and 7.9 g (0.10 mol) of pyridine. The mixture was stirred at 0 °C and the 58.7 g (0.39 mol) of 3-bromo-2-buten-1-ol was added slowly and the temperature kept below 5 °C. After stirring for 1 h at 0–5 °C, stirring was continued overnight at room temperature. The product then was distilled from the reaction mixture, bp 63–67 °C (13 mm). The crude distillate was washed with aqueous sodium bicarbonate, dried over sodium sulfate, and redistilled, bp 63–66 °C (13 mm). A yield of 41 g (24%) was obtained. The reported boiling point is 73 °C (23 mm).[7] The product is mainly the *Z* isomer as determined by GLC and NMR; NMR ($CDCl_3$, 60 MHz) δ 2.35 (s, 3 H), 4.00 (d, J = 7 Hz, 2 H), 5.9 (t, J = 7 Hz, 1 H).

2,5-Dibromo-1-pentene. In a 250-mL three-necked flask was placed 23 g (0.096 mol) of pent-4-yn-1-yl *p*-toluenesulfonate,[8] 20 g (0.23 mol) of lithium bromide, and 120 mL of acetone. The mixture was heated at reflux temperature for 17 h. After cooling, the solvent was removed under reduced pressure and ice water was added to the residue. The product was extracted with ether, the extracts were dried and concentrated, and the product was distilled, bp 134–136 °C. There was obtained 11.2 g (79%) of the bromide. The reported boiling point is 80–82 °C (110 mm).[9]

The above 5-bromo-1-pentyne, 14.5 g (0.098 mol), was placed in a 250-mL three-necked flask equipped with a mechanical stirrer, gas inlet tube, and a condenser. The flask was cooled in a dry ice–acetone bath and 8 g of gaseous hydrogen bromide was passed into the stirred solution over a period of 1.3 h. The reaction mixture was then allowed to warm up to room temperature. The product was washed with aqueous sodium bicarbonate, dried, and then distilled. There was obtained a 52% yield of the bromide: bp 57–59 °C (5 mm); NMR ($CDCl_3$, 60 MHz) δ 2.25 (m, 2 H), 2.70 (t, J = 6, 2 H), 3.50 (t, 2 H), 5.65 (s, 1 H), 5.83 (s, 1 H).

2,6-Dibromo-1-hexene. To 70.5 g (0.26 mol) of phosphorus tribromide was added 8 g (0.10 mol) of pyridine with stirring over a 10-min period. The contents of the flask were cooled to 0 to −5 °C with an ice–salt mixture, and a solution of 39 g (0.4 mol) of 5-hexyn-1-ol (Farchan Labs) and 2.2 g (0.03 mol) of pyridine was added dropwise with stirring at a rate such that the temperature did not rise above 0 °C. After stirring for an additional hour the mixture was allowed to warm to room temperature and it was left overnight. Distillation of the mixture, bp 70–104 °C (12 mm), gave the crude dibromide. This product was washed with water and aqueous sodium bicarbonate and dried over Na_2SO_4. Redistillation gave 38% recovered 5-hexyn-1-ol and 44% 2,6-dibromo-1-hexene: bp 99–102 °C (12 mm) [lit.[10] bp 97–99 °C (12 mm)]; NMR ($CDCl_3$, 60 MHz) δ 1.80 (t, t, 4 H), 2.50 (t, 2 H), 3.45 (t, 2 H), 5.50 (s, 1 H), 5.60 (s, 1 H).

3-Bromo-3-butenyl Acrylate. To a stirred mixture of 56 g (0.8 mol) of 3-butyn-1-ol (Farchan Labs) and 0.45 g (8 mmol) of iron powder (to decompose peroxides) was added 97 g (1.2 mol) of 48% hydrobromic acid. The reaction mixture was stirred for 2 days at 45 °C. The organic phase was then extracted with methylene chloride and the extracts were washed with aqueous sodium bicarbonate and saturated aqueous sodium chloride, dried ($CaSO_4$), and concentrated under reduced pressure. The residue was distilled to give a 28% yield of 3-bromo-3-buten-1-ol: bp 70–75 °C (11 mm) [lit.[11] bp 64–65 °C (8.6 mm)]; NMR ($CDCl_3$, 60 MHz) δ 2.67 (t, J = 6, 2 H), 2.83 (s, 1 H), 3.81 (t, J = 6, 2 H), 5.55 (s, 1 H), 5.73 (s, 1 H).

To 30.2 g (0.20 mol) of the alcohol cooled in an ice bath was added dropwise with stirring, 18.1 g (0.2 mol) of acryloyl chloride. After stirring at room temperature for 1 h, the solution was poured onto ice and the product was extracted with methylene chloride. After the extracts were washed with aqueous sodium bicarbonate and dried ($CaSO_4$), the solvent was removed under reduced pressure and the ester was distilled, bp 45 °C (0.3 mm). The yield was only 8.1 g or 20%. The NMR spectrum and molecular weight (HRMS) of the product are given in Table II (supplementary material).

3-Butenyl *o*-Bromophenyl Ether. A mixture of 17.3 g (0.10 mol) of *o*-bromophenol, 16 g (0.118 mol) of 4-bromo-1-butene, 13.8 g (0.10 mol) of anhydrous potassium carbonate, and 100 mL of dry acetone in a 250-mL round-bottomed flask was heated at reflux temperature for 46.5 h. The acetone was removed by distillation and 100 mL of water was added to the residue. The product was extracted with ether. The ether extract was washed with 10% aqueous sodium hydroxide and dried. The solvent was evaporated and the product was distilled, bp 73 °C (0.1 mm). The yield was 13.7 g (60% of theory) of the ether. The physical properties and NMR spectrum of the product are given in Table II (supplementary material).

Allyl *o*-Bromobenzyl Ether. To 69.7 g (1.20 mol) of allyl alcohol was gradually added 6.9 g (0.3 mol) of sodium metal in small pieces. After the metal had dissolved, the solution was cooled in ice water while 75 g (0.3 mol) of *o*-bromobenzyl bromide was added. The mixture was heated to reflux temperature for 2 h. Then water was added to dissolve the sodium bromide formed and the product was extracted with methylene chloride. The extracts were dried (Na_2SO_4), and the solvent was removed under reduced pressure. Distillation of the residue gave 53 g (78%) of the pure ether, bp 76 °C (0.07 mm).

General Procedure for the Cyclization of Bromodialkenyl Ethers and Amines. Mixtures of 0.5–1.0 mmol of palladium acetate, 1–2 mmol of tri-*o*-tolylphosphine, 50 mmol of the bromodialkenyl ether or amine, and 250 mmol of piperidine (or triethylamine) in capped 250-mL Pyrex bottles were heated with shaking until they were homogeneous and then at 100 °C in a steam bath or an oil bath at 125 °C until GLC analysis of a small sample of the mixture showed the absence of the bromodialkenyl ether or amine. When the reactions were complete, the bottles were cooled to room temperatures, and ether was added followed by 6 N hydrochloric acid. Enough acid was added to make the aqueous solution strongly acidic. The aqueous phase was separated and extracted again with ether. The ether phase generally contained unreacted bromodialkenyl ethers and their decomposition products and in the case of the 2-bromoallyl 4-hydroxy-2-butenyl ether, the product aldehyde. This was isolated by washing the ether phase with water, aqueous sodium bicarbonate, and water again, drying, and then removing the ether under reduced pressure and distilling the product. The acidic aqueous phases were then made basic with 6 N sodium hydroxide and the amines formed were extracted with two portions of ether. The combined extracts were dried (Na_2SO_4), and concentrated, and the products were either distilled or separated by preparative GLC.

7-Bromo-1,7-octadien-3-ol. To an ice-cooled solution of 21 g (0.11 mol) of 2-bromo-1,7-octadiene[1] in 250 mL of dry chloroform was added a solution of 21.25 g (0.124 mol) of *m*-chloroperbenzoic acid (previously washed with a phthalate buffer at pH 7.4 and dried) in 100 mL of dry chloroform. The solution was stirred for 48 h at room temperature and then a 10% aqueous solution of sodium sulfite was added to destroy excess peracid. The organic layer was separated and washed with aqueous sodium bicarbonate, water, and saturated aqueous sodium chloride. After drying

(7) Carothers, W. H.; Collins, D. M.; Kirby, J. E. *J. Am. Chem. Soc.* **1933**, *55*, 786.
(8) Eglinton, G.; Whiting, M. C. *J. Chem. Soc.* **1950**, 3650.
(9) Olomucki, M. *Ann. Chim. (Paris)* **1964**, *5*, 845.
(10) Colonge, J.; Lasfarques, P. *Bull. Soc. Chim. Fr.* **1962**, 177.
(11) Semmelhack, M. F.; Brickner, S. J. *J. Org. Chem.* **1981**, *46*, 1723.

($MgSO_4$) the solvent was removed under reduced pressure and the epoxide was distilled, bp 95 °C (3 mm). The yield was 14.39 g or 68% of theory.

To an ice-cooled solution of 29.61 g (0.21 mol) of 2,2,6,6-tetramethylpiperidine in 100 mL of dry (sodium–benzophenone) benzene was added 140 mL of 1.5 M *n*-butyllithium (0.21 mol) in hexane dropwise under nitrogen. After stirring for 10 min, 210 mL of 1 M diethylaluminum chloride in hexane (pyrophoric) (0.21 mol) was added dropwise. The mixture was stirred for 30 min at 0 °C and 14.39 g (0.070 mol) of the above epoxide in 150 mL of dry benzene was added dropwise. The mixture was stirred at 0 °C for 3 h and then at room temperature overnight. About 300 mL of 1 M hydrochloric acid was now added with stirring. The organic phase was separated, washed with water, and dried ($MgSO_4$). The solvent was removed under reduced pressure and the product distilled, bp 70 °C (0.1 mm). The yield of the dienol was 70% of theory. NMR ($CDCl_3$, 250 MHz) δ 1.48–1.70 (m, 4 H), 1.98 (s, 1 H), 2.45 (m, 2 H), 4.10 (m, 1 H), 5.09–5.27 (m, 2 H), 5.40 (t, J = 1, 1 H), 5.58 (t, J = 1, 1 H), 5.83 (m, 1 H).

Cyclization of 7-Bromo-1,7-octadien-3-ol. A mixture of 0.0456 g (0.2 mmol) of $Pd(OAc)_2$, 0.1216 g (0.4 mmol) of tri-*o*-tolylphosphine, 4.10 g (20 mmol) of 7-bromo-1,7-octadien-3-ol, and 5.11 g (60 mmol) of piperidine in a capped, nitrogen-filled Pyrex bottle was warmed until it was homogeneous and then heated at 100 °C for 36 h. The cooled reaction mixture was diluted with 50 mL of 6 N sodium hydroxide and 50 mL of ether. After shaking, the aqueous layer was extracted twice more with ether. The combined ether extracts were washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. Distillation of the residue gave a single product, 2-methyl-3-piperidinomethyl-2-cyclohexenol, 1.35 g (33%), bp 102–105 °C (0.06 mm). The molecular weight by high-resolution mass spectroscopy was 209.178; calcd 209.178; NMR ($CDCl_3$, 250 MHz) δ 1.40–1.76 (m, 11 H), 1.80 (s, 3 H), 2.01 (m, 2 H), 2,86 (m, 4 H), 3.96 (br s, 1 H).

Allyl(2-bromoallyl)amine. A solution of 5.7 g (0.10 mol) of allylamine (Aldrich) and 10 g (0.10 mol) of triethylamine was added dropwise to an ice-cooled, stirred solution of 20 g (0.10 mol) of 2,3-dibromopropene in 25 mL of ether. The reaction mixture was stirred at room temperature overnight. The precipitated triethylamine hydrobromide was then removed by filtration and washed with ether, and the filtrate was concentrated and distilled. There was obtained 10.4 g (60%) of the secondary amine, bp 83–85 °C (30 mm). Other data appear in Table IV (supplementary material).

***N*-Acetyl-*N*-allyl(2-bromoallyl)amine.** A mixture of 12.47 g (70 mmol) of the above amine, 10 g of triethylamine, and 8.63 g (86 mmol) of acetic anhydride was stirred at room temperature for 2 days. Ether and water were added and the ether phase was separated, washed with aqueous sodium bicarbonate, and distilled. There was obtained an 80% yield of the acetyl derivative, bp 105–108 °C (1.5 mm). Other data appear in Table IV (supplementary material).

***N*-Methyl-*N*-allyl(2-bromoallyl)amine.** A solution of allyl(2-bromoallyl)amine in ether was reacted with 50% excess methyl iodide and stirred overnight at room temperature. The viscous oil which separated from the solution was isolated by decanting the ether. It was washed with ether and then treated with excess 50% aqueous potassium hydroxide. The liberated amine was extracted with ether. The extracts were dried ($MgSO_4$) and distilled. A 70% yield of the tertiary amine, bp 81–82 °C (30 mm), was obtained. Additional data on the product are given in Table IV (supplementary material).

***N*-Methyl-*N*-(2-bromoallyl)-3-butenylamine.** A mixture of 10.15 g (143. mmol) of 3-butenylamine[12] and 14.4 g (143. mmol) of triethylamine was added dropwise to an ice-cooled, stirred solution of 28.6 g (130 mmol) of 2,3-dibromopropene in 30 mL of ether. The reaction mixture was stirred magnetically overnight. The next day the triethylamine hydrobromide was removed by filtration and washed with ether, and the combined ether solutions were concentrated and distilled. There was obtained 14.96 g (52%) of the secondary amine, bp 78–80 °C (45 mm).

The *N*-methyl derivative was prepared as described above for the preparation of *N*-methyl-*N*-allyl(2-bromoallyl)amine. there was obtained 11.25 g of a mixture of the *N*-methylamine, and 20% unreacted secondary amine, bp 78–82 °C (45 mm). The mixture obtained was dissolved in 50 mL of ether, treated with 8.30 g (60 mmol) of benzoyl chloride, and then shaken with 20 mL of 50% aqueous potassium hydroxide. After shaking for about 15 min, the ether layer was separated, dried ($MgSO_4$), and distilled to give 5.38 g (20%) of the pure tertiary amine, bp 80–82 °C (45 mm). Other properties are given in Table IV (supplementary material).

***N*-(3-Bromo-3-butenyl)-3-butenylamine.** A solution of 3.65 g (51 mmol) of 3-butenylamine, 5.2 g (52 mmol) of triethylamine, 11.0 g (47 mmol) of 1,3-dibromo-2-butene, and 50 mL of benzene was heated under reflux for 4 days. The reaction mixture was cooled, the triethylamine hydrobromide was removed by filtration, and the filtrate was concentrated and distilled. There was obtained 1.97 g (20%) of the secondary amine, bp 109–111 °C (25 mm). Properties of the product are given in Table IV (supplementary material).

***N*-Methyl-5-methyl-3,5-hexadienylamine.** A mixture of 2.44 g (20 mmol) of *N*-methyl-3-butenylamine (prepared by the reduction of *N*-methyl-3-butenamide with aluminum hydride), 3.13 g (30 mmol) of 2-bromopropene, 9.10 g (90 mmol) of triethylamine, 0.0684 g (0.3 mmol) $Pd(OAc)_2$, and 0.1824 g (0.6 mmol) of tri-*o*-tolylphosphine in a capped, nitrogen-flushed Pyrex bottle was placed in a steam bath for 32 h. Then after cooling, 10 mL of 6 N sodium hydroxide and 50 mL of ether were added. The ether layer was separated, and the aqueous phase was extracted twice more with 20-mL portions of ether. The combined extracts were dried ($MgSO_4$), the solvents were removed under reduced pressure, and the product was distilled. There was obtained 1.24 g (32%) of the dienylamine, bp 60–62 °C (3 mm). Other properties of the product are listed in Table IV (supplementary material).

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Supplementary Material Available: Tables II, III, IV, and V containing yields, boiling points, analyses or molecular weights (HRMS), and NMR spectral data for the new compounds prepared in this investigation (8 pages). Ordering information is given on any current masthead page.

(12) Yoon, N. M.; Brown, H. C. *J. Am. Chem. Soc.* **1968**, *90*, 2927.