for the mass spectra; to Professor Raymond A. Young, Department of Forestry, University of Wisconsin, Madison, for continuing support; and to the New Zealand Research Advisory Council for partial funding of this research.

Registry No. (*R**,*R**)-**1a**, 82247-15-2; (*R**,*S**)-**1a**, 86956-00-5; (*R**,*R**)-**1b**, 86956-01-6; (*R**,*S*)*-**1b**, 86956-02-7; (*R**,*R**)-**1c**, 82247-06-1; (*R**,*S**)-**1c**, 86956-03-8; **1c** 10-trimethylsilyloxy derivative, 86956-04-9; (*R**,*S**)-**1d**, 86968-53-8; (*R**,*R**)-**1d**, 86968-54-9; (*R**,*R**)-**3a**, 36483-10-0; (*R**,*S**)-**3a**, 7107-92-8; (*R**,*R**)-**3b**, 7595-29-1; (*R**,*S**)-**3b**, 7572-98-7; (*R**,*R**)-**5a**, 86956-05-0; (*R**,*S**)-**5a**, 86956-06-1; (*R**,*R**)-**5b**, 86956-07-2; (*R**,*S**)-**5b**, 86956-08-3; **6**, 28871-54-7; **7**, 28871-52-5; *trans*-**9**, 86956-09-4; *trans*-**10**, 86956-10-7; *cis*-**10**, 86956-11-8; lignin, 9005-53-2.

Reactions of Azines. 6. Thermal Rearrangements of 1,1-Disubstituted-2,3-diaza-4-methyl-1,3,5,6-heptatetraene to 4,9-Dihydropyrazolo[1,5-*b*]isoquinolines and Side Products

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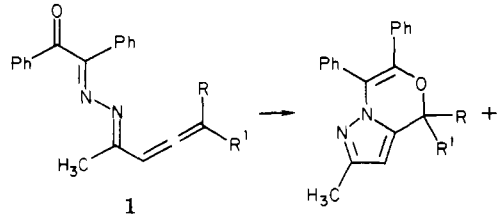
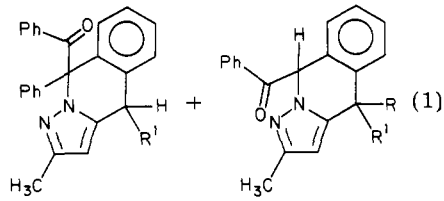
The preparation of 4,9-dihydropyrazolo[1,5-*b*]isoquinolines (**16** or/and **18**) was accomplished by allowing the corresponding ketenes to react with (2-((diphenylmethylene)hydrazono)propylidene)triphenylphosphorane (**10**) and (2-((methylphenylmethylene)hydrazono)propylidene)triphenylphosphorane (**11**). It was determined that the predicted stability of the carbocation of the intermediate azomethine imine **15**, or **17**, on the 1- and 5-positions on the pyrazole backbone allowed one to predict the major product **16** or **18** of the reaction. An X-ray analysis of the thermodynamically more stable product of the reaction of phenylketene with ylide **10** showed it to be in the trans geometry, **18d-1**, with the three central rings essentially planar (170.7° angle) about the C-4/C-9 axis.

The usefulness of di-α,β-unsaturated azines as synthons for a variety of N-substituted pyrazoles[1a-e] as well as tetrahydroindazoles,[1b] pyrazolopyrans,[1b] and cyclopentapyrazoles[1b] has been demonstrated. It has also been shown that keto allenyl azines, **1**, when R = H (R^1 = H, vinyl, Ph), give exclusively pyrazolo[5,1-*c*]-1,4-oxazines, **2**, whereas when the allenyl substituents are not hydrogen and one of the R's is phenyl, the major products are pyrazolooxazines, **2**, and 4,9-dihydropyrazolo[1,5-*b*]isoquinolines, **3**, and at times 4.[2]



1 **2**



3 **4**

In an attempt to develop a method for the preparation of 4,9-dihydropyrazolo[1,5-*b*]isoquinolines without the inclusion of the pyrazolo[5,1-*c*]-1,4-oxazine side products, we examined the reactions of allenyl-substituted azines without a carbonyl or π system (other than the aromatic moiety) at the other end of the azine from the allenyl group.

Results and Discussion

The hydrazones of benzophenone and acetophenone were allowed to react with propargyltriphenylphosphonium bromide (**7**) to give 2-((diphenylmethylene)hydrazono)-propyltriphenylphosphonium bromide (**8**) and 2-((methylphenylmethylene)hydrazono)propyltriphenylphosphonium bromide (**9**). The ^{31}P NMR spectrum

$$\underset{\textbf{5, R = Ph}\\ \textbf{6, R = CH}_3}{\text{PhRC=NNH}_2} + \underset{\textbf{7}}{\text{HC}\equiv\text{CCH}_2\text{P}^+\text{Ph}_3\text{Br}^-} \rightarrow$$

$$\underset{\textbf{8a, R = Ph}\\ \textbf{9a, R = CH}_3}{\text{PhRC=NNH(H}_3\text{C)C=CHP}^+\text{Ph}_3\text{Br}^-} +$$

$$\underset{\textbf{8b, R = Ph}\\ \textbf{9b, R = CH}_3}{\text{PhRC=NN=C(CH}_3\text{)CH}_2\text{P}^+\text{Ph}_3\text{Br}^-} \rightarrow$$

$$\underset{\textbf{10, R = Ph}\\ \textbf{11, R = CH}_3}{\text{PhRC=NN=C(CH}_3\text{)CH=PPh}_3} \quad (2)$$

clearly showed that the predominant form of both **8** and **9** is the N-substituted vinylphosphonium species **8a** and **9a**. The ratios found were **8a**/**8b** = 2/1 and **9a**/**9b** = 3/1. The isomers of **8a** showed ^{31}P NMR in the 15.8–16.7 ppm range and **9a** at 16.8–17.8 ppm, whereas the **8b** (azine methylphosphonium) isomers showed ^{31}P NMR at 22.1

† For X-ray structure.

(1) (a) Schweizer, E. E.; Hirwe, S. N *J. Org. Chem.* **1982**, *47*, 1652. (b) Albright, T. A.; Evans, S.; Kim, C. S.; Labaw, C. S.; Russiello, A. B.; Schweizer, E. E. *Ibid* **1977**, *42*, 3691. (c) Schweizer, E. E.; Kim, C. S.; Labaw, C. S.; Murray, W. P. *J. Chem. Soc., Chem. Commun.* **1973**, 7. (d) Stern, R. L.; Krause, J. G. *J. Heterocycl. Chem.* **1968**, *5*, 263. (e) Stern, R. L.; Krause, J. G. *J. Org. Chem.* **1968**, *33*, 213.

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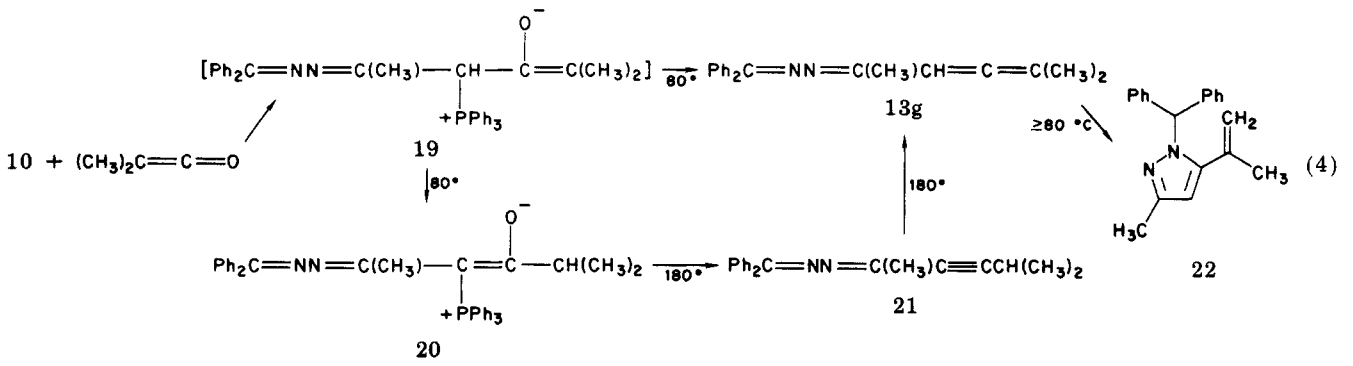
0022-3263/83/1948-3889$01.50/0

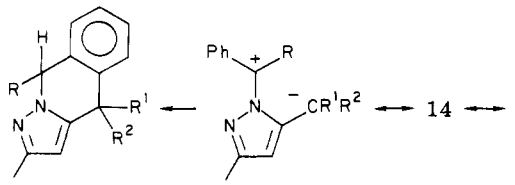


ppm and **9b** at 22.9–23.2 ppm. It has been shown previously that N-substituted vinylphosphonium salts absorb in the ^{31}P range 12.9–18.6 ppm, and imine methylphosphonium salts appear in the ^{31}P range 19.1–22.5 ppm.[3] The proton NMR data (see Experimental Section) also support the presence of the structures proposed.

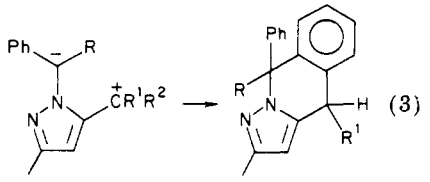
The phosphonium ylides **10** and **11** were obtained by allowing the corresponding salts **8** and **9** to react with potassium hydroxide in ethanol at −15 °C.

The phosphonium ylides **10** and **11** when allowed to react with ketenes gave predominantly 4,9-dihydropyrazolo[1,5-*b*]isoquinolines (**16** or/and **18**) (see Scheme I).

The "criss-cross" cycloaddition of the allenyl azines **13** would give the resonance-stabilized azomethine imine **15** ↔ **14** ↔ **17**. The preference for the formation of the



18 **17**



(3)

15 **16**

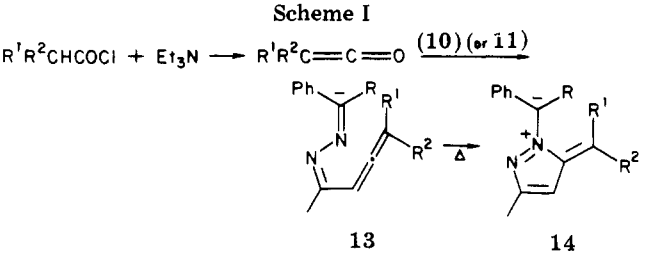
18b, R = R¹ = Ph; R² = CH_3
18c, R = Ph; R¹ = R² = H
18d, R = R¹ = Ph; R² = H
18e, R = Ph; R¹ = Et; R² = H
18f, R = Ph; R¹ = CH_2Ph; R² = H
18i, R = R¹ = CH_3; R² = Ph

16a, R = R¹ = Ph
16b, R = Ph; R¹ = CH_3
16h, R = CH_3; R¹ = Ph
16i, R = R¹ = CH_3

pyrazoloisoquinoline **16** or **18** seems to lie in favor of **16** where R¹ = Ph and R² = R, i.e., where the groups attached to the 1 and 5 positions on the pyrazole backbone are identical. For instance, where CR^1R^2 and CRPh are both CPh_2, only **16a** is formed; similarly where CR^1R^2 and CRPh are both $C(CH_3)Ph$, the ratio of **16i**/**18i** is 74/26.

Furthermore, if the groups CR^1R^2 and CRPh are not equal, the group that provides greater carbocation stabilization determines the predominance of species **16** or **18**. Thus the following results were observed: (a) Where CR^1R^2 = CPh_2 and CRPh = $C(CH_3)Ph$, only **16h** was found. (b) Where CR^1R^2 = $C(CH_3)Ph$ and CRPh = CPh_2, **16b**/**18b** = 40/60. (c) Where CR^1R^2 = CHH, CPhH, $C(CH_2CH_3)H$, or $C(CH_2Ph)H$ and CRPh is always CPh_2,

Scheme I



13 **14**

13a, R = R¹ = R² = Ph
13b, R = R¹ = Ph; R² = CH_3
13c, R = Ph, R¹ = R² = H
13d, R = R¹ = Ph; R² = H
13e, R = Ph; R¹ = Et; R² = H
13f, R = Ph; R¹ = CH_2Ph; R² = H
13g, R = Ph; R¹ = R² = CH_3
13h, R = CH_3; R¹ = R² = Ph
13i, R = R¹ = CH_3; R² = Ph
13j, R = CH_3; R¹ = R² = H

only **18c**, **18d**, **18e**, and **18f** were found, respectively.

Two isomers were isolated with structure **18d**. On heating, one of the structures was shown to convert slowly into the other (25% conversion in **12h**). The most stable isomer was shown by X-ray (Figure 1) to be the trans isomer, **18d-1**. It is assumed that the less stable isomer is the cis isomer **18d-2**. The X-ray data showed that the two halves of **18d-1**, sighting along an axis defined by the C-4 eclipsing the C-9 carbon atom, are inclined to each other at an angle of 170.7°. This is in sharp contrast to an angle of approximately 145° reported for 9,10-dihydroanthracene[4a] and the nonplanarity presumed for *trans*-9,10-disubstituted-9,10-dihydroanthracenes.[4b,c] The angle found along the C-4/C-9 axis in **18d-1** is closer to the planarity calculated for 1,4-cyclohexadiene[5a] and 9,10-dihydroanthracene.[5b]

No pyrazoloisoquinolines (**16** or **18**) were found in the two cases studied. In the reaction of dimethylketene with **10**, which would lead to the allene **13g**, 1-(diphenylmethyl)-3-methyl-5-(2-propenyl)pyrazole (**22**) and the betaine **20** were observed. On heating the betaine **20** at 180 °C, the acetylenic azine **21** and the pyrazole **22** were observed. Extended heating of **21** (or **20**) gave only **22**, presumably via **13g**. The formation of acetylenes from unsaturated betaines is a well-documented reaction.[6]

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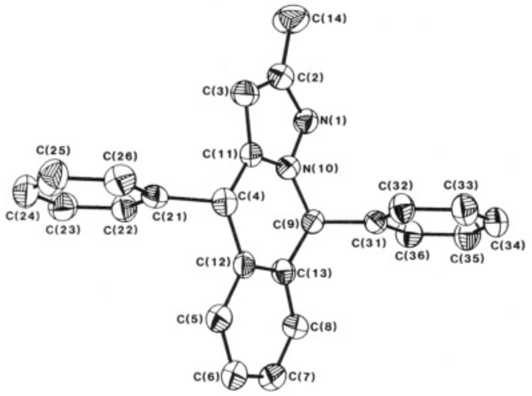
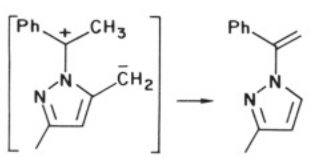


Figure 1. An ORTEP diagram of **18d-1** with 40% probability ellipsoids. The numbering scheme shown corresponds to that used in the text; a concordance accompanies the supplementary tables that relates the chemical and crystallographic numbering schemes. The angle between the best-fit planes obtained from C(4), C(12), C(13), C(9), and C(4), C(11), N(10), C(9) is 9.3°.

A similar product is observed for the reaction of ketene with **11**, via the azine **13j**, to give 1-(1-phenylethenyl)-3,5-dimethylpyrazole (**23**).

$Ph(CH_3)C{=}NN{=}C(CH_3){-}CH{=}C{=}CH_2 \longrightarrow$

13j



(5)

23

Several of the reaction series yielded products in addition to the expected isoquinolines. The phosphorane **10**, when allowed to react with benzylketene via allene **13f**, gave the corresponding pyrazoloisoquinoline **18f** and 2,3-diaza-4-methyl-1,1,8-triphenylocta-1,4-dien-6-yne (**24f**). A possible pathway is shown below in eq 6.

$$Ph_2C{=}NN{=}C(CH_3)CH{=}C{=}CHR^2 \rightarrow$$

13f

$$[Ph_2C{=}NN{=}C(CH_3)CH_2C{\equiv}CR^2] \rightarrow$$

$$Ph_2C{=}NNH(CH_3)C{=}CHC{\equiv}CR^2$$

24e, R^2 = Et
24f, R^2 = CH_2Ph

$$\mathbf{24e} \xrightarrow{n\text{-PrCOCl}} Ph_2C{=}NN(n\text{-PrCO})(CH_3)C{=}CHC{\equiv}CR^2$$

25e, R^2 = Et

(6)

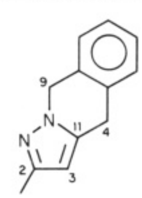
Similarly the reaction of ethylketene with phosphorane **10** gave the pyrazoloisoquinoline **18e** as well as 2,3-diaza-4-methyl-1,1-diphenylnona-1,4-dien-6-yne (**24e**) and the acylated product **25e**.

Thus it has been demonstrated that the 4,9-dihydropyrazolo[1,5-*b*]isoquinolines (**16** and/or **18**) may be produced in high yields, with relatively few side products, from the corresponding allenyl azines.

Experimental Section

General. Dry nitrogen was routinely used as the reaction atmosphere in all reactions. All glassware was baked at 110–120 °C for a minimum of 1 h before being used. Melting points were obtained with a Thomas-Hoover apparatus and are uncorrected. Eastman Chromagram (silica gel with a fluorescent indicator on polyethylene) precoated sheets (TLC) were employed in thin-layer chromatographic operations. Column chromatography was accomplished on 35 × 350 mm silica gel column.

The ^1H, ^{13}C, and ^{31}P NMR of approximately 10% solutions in $CDCl_3$ were obtained on a Bruker Spectrospin Instrument, Model WM 250. Chemical shifts are reported in parts per million (δ scale) employing tetramethylsilane (phosphoric acid for ^{31}P NMR) as an internal standard. In reporting NMR data, the following abbreviations have been employed: coupling constant in Hertz (J), singlet (s), broad singlet (brs), doublet (d), doublet of doublets (dd), doublet of quartets (dq), triplet (t), quartet (q), quintet (p), and multiplet (m). The numbering system for the phosphonium salts and ylides is $Ph(R)C^1\text{-}N\text{-}N\text{-}C^4(CH_3)\text{-}C^5\text{-}P$ and for the pyrazoloisoquinolines is as shown:



All compounds whose ^1H and ^{13}C NMR are not listed in this Experimental Section may be found in Table 6S and 7S, respectively (available as supplementary material). The ranges of the ^1H parameters for the 4,9-dihydropyrazolo[1,5-*b*]isoquinolines **16** and **18** were as follows: C(2)–CH_3, C(3)–H, C(4)–H, C(9)–H, aromatic, C(4)–CH_3, and C(9)–CH_3 at 2.2–2.3, 5.5–6.0, 4.0–5.5, 5.4–6.6, 6.7–7.5, 1.3–2.0, and 2.3–2.5 ppm, respectively. The ranges of the ^{13}C parameters for the 4,9-dihydropyrazolo[1,5-*b*]isoquinolines **16** and **18** were as follows: C(2)–CH_3, C(2), C(3), C(4), C(9), C(11), C(4)–CH_3, and C(9)–CH_3 at 13.6–14.1, 147.9–149.3, 101.3–103.9, 27.7–44.6, 56.4–73.2, 141.9–148.0, 19.5–30.7, and 28.4–29.7, respectively. The composition of inseparable reaction products was determined by an examination of the ^1H NMR of the crude products. Electron impact mass spectra were recorded using a Du Pont CEC 21-110 D instrument with a resolution of 3300. Elemental analyses were performed by Microanalysis Inc. of Wilmington, DE.

All solvents were used in anhydrous condition. Propargyltriphenylphosphonium bromide was prepared by the procedure of Eiter and Oediger.[7] α-Phenylpropionyl chloride was prepared from the acid employing thionyl chloride.[8] Diphenylacetyl chloride and β-phenylpropionyl chloride were purchased from Pfaltz and Bauer, Inc. Phenylacetyl chloride, isobutyryl chloride, and butyryl chloride were purchased from the Aldrich Chemical Co. All of these acyl chlorides were purified by distillation prior to use.

Preparation of 2-((Diphenylmethylene)hydrazono)propyltriphenylphosphonium Bromide (8). A slurry of 4.02 g (20.5 mmol) of benzophenone hydrazone[9] (**5**) and 7.6 g (20 mmol) of propargyltriphenylphosphonium bromide (**7**) in 20 mL of methylene chloride was heated under reflux with stirring for 6 h. The yellowish clear solution was added dropwise into 200 mL of boiling benzene and then stirred at ambient temperature for 1.5 h as a pale yellow precipitate appeared slowly. After the yellow solid was filtered and reprecipitated from methylene chloride/ethyl acetate, 10.5 g (91%) of a white analytically pure solid was obtained. TLC showed one spot (petroleum ether/ethanol 6/4), mp 222–223 °C; ^1H NMR (for **8a**) δ 2.43 (s, 3 H, $H_3CC{=}CH$), 4.00 (d, J_{PH} = 15.0, 1 H, $CH\text{-}P{\equiv}$), 6.68–7.66 (m, 25 H, Ar), 9.14 (br s, NH); (for **8b**) 2.39 (s, 3 H, $={CCH_3CH_2}$), 5.20 (d, J_{PH} = 13.3, 2 H, $CH_2P{\equiv}$), 6.68–7.66 (m, 25 H,Ar); ^{13}C NMR (for **8a**) δ 23.0 (d, J_{CCP} = 15.8, CH_3), 61.5 (d, J_{CP} = 110.3, $CH{-}P{\equiv}$), 119.3 (d, J_{CP} = 88.6, $P{-}C_{ipso}$); (for **8b**) 20.4 (d, J_{CCP} = 7.9, CH_3), 33.1 (d, J_{CCP} = 57.1, CH_2P), 122.8 (d, J_{CP} = 88.7, $P{-}C_{ipso}$); ^{31}P NMR (for **8a**) δ 15.79 + 16.73 (67%); For **8b** 22.06 (33%).

Anal. Calcd for $C_{34}H_{30}BrN_2P$: C, 70.58; H, 5.39. Found: C, 70.71; H, 5.24.

Preparation of 2-((Methylphenylmethylene)hydrazono)propyltriphenylphosphonium Bromide (9). Acetophenone hydrazone[10] (**6**), 18.4 g (0.137 mol), in 100 mL of

(7) Eiter, K.; Oediger, H. *Justus Liebigs Ann. Chem.* **1965** *682*, 62.
(8) Vogel, A. I. "Practical Organic Chemistry", Longmans, Green and Co.: New York, 1948; p 364.
(9) Smith, L. I.; Howard, K. L. "Organic Syntheses"; Wiley: New York, 1944; Collect. Vol. No. 24, p 53.
(10) Lock, G.; Stach, K. *Chem. Ber.* **1944** *77B* 293.

methylene chloride and 52 g of propargyltriphenylphosphonium bromide (7) (0.136 mol) were mixed. The reaction mixture became a golden yellow solution and some precipitates appeared after heating under reflux for 2 h with stirring. The heating was terminated and the precipitates were removed by filtration. The filtrate was added to 300 mL of ethyl acetate; 42 g (60%) of a pale yellow solid was obtained. After reprecipitation of the solid from methylene chloride/ethyl acetate an analytical sample was obtained: mp 261–265 °C; ^{1}H NMR (for **9a**) δ 2.33 (s, 3 H, H_3CCNH), 2.78 (s, 3 H, H_3CCPh), 3.72 (d, J_{PH} = 18.1, 1 H, CHP≡), 6.25–7.97 (m, 20 H, Ar), 11.1 (s, 1 H, NH); For **9b** 2.31 (s, 3 H, H_3CC=N), 2.74 (s, 3 H, H_3CCPh), 5.35 and 5.38 (d, J_{PH} = 23.2, 2 H, CH_2P≡), 6.25–7.97 (m, 20 H, Ar); ^{13}C NMR (for **9a**) δ 19.0 (C-1-CH_3), 23.4 (d, J_{CCP} = 15.5, C-4-CH_3), 58.2 (d, J_{CP} = 113.3, C-5), 119.8 (d, J_{CP} = 89.2, P-C_{ipso}), 137.6 (C-4), 162.5 (C-1); (for **9b**) 17.3 (C-1-CH_3), 19.48 (d, J_{CCP} = 8.9, C-4-CH_3), 34.0 (d, J_{CP} = 56.9, C-5), 119.8 (d, J_{CP} = 89.2, P-C_{ipso}), 137.5 (C-4), 157.1 (C-1); ^{31}P NMR (for **9a**) δ 16.8 + 17.8 (73%); (for **9b**) 22.9 + 23.2 (27%).

Anal. Calcd for $C_{29}H_{28}BrN_2P$: C, 67.58; H, 5.48. Found: C, 67.98; H, 5.80.

Preparation of (2-((Diphenylmethylene)hydrazono)-propylidene)triphenylphosphorane (10). Potassium hydroxide (1 g, 18 mmol) was dissolved in 20 mL of ethanol. This solution was cooled to about −15 °C (ice/methanol) and then 4.6 g (8 mmol) of **8** was added with vigorous stirring. A yellow–orange precipitate was formed, and the mixture was allowed to stir at ambient temperature for $^1/_2$ h. After the residue was filtered and reprecipitated from methylene chloride/heptane, 3.4 g (86%) of analytically pure fine yellow crystals were obtained. TLC showed one spot (petroleum ether/ethanol–6/4): mp 203–204 °C; ^{1}H NMR δ 1.96 (d, J_{PH} = 12.5, 1 H, Ph_3P=C*H*), 2.44 (d, J_{PH} = 1.7, 3 H, C-4-CH_3), 6.70–7.68 (m, 25 H, Ar); ^{13}C NMR δ 19.1 (d, J_{CCP} = 15.7, C-4-CH_3), 44.5 (d, J_{CP} = 112.2, C-5), 138.6 (C-4), 172.5 (C-1); ^{31}P NMR δ 13.88. Precise mass was calcd for $C_{34}H_{29}N_2P$; 496.207; found, 496.208.

Preparation of (2-((Methylphenylmethylene)-hydrazono)propylidene)triphenylphosphorane (11). Potassium hydroxide (2.8 g, 50 mmol) was dissolved in 60 mL of ethanol; 10.4 g of **9** (20 mmol) was allowed to react with the base solution as described in the preparation of **10**. Fine yellow crystals, mp 208–210 °C (6.0 g, 69%), were obtained.[11] ^{31}P NMR δ 13.03 (44%), 13.70 (56%); precise mass calcd for $C_{29}H_{27}N_2P$, 434.191; found, 434.191.

Reaction of Ylide 10 with Diphenylketene. Preparation of 2-Methyl-4,9,9-triphenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (16a). Method A. Diphenylketene was prepared in advance.[12] Triethylamine (1.3 g, 13 mmol) in 5 mL of ether was added dropwise with stirring, over a period of 0.5 h, to a cooled (ice bath) solution of diphenylacetyl chloride (2.8 g, 12 mmol) in 25 mL of ether. The reaction mixture was allowed to stand overnight in a refrigerator. The mixture was filtered, and the filtrate was concentrated to dryness on a rotary evaporator. The residue was dissolved in 10 mL of benzene and added dropwise with stirring over a 20-min period at room temperature to a mixture of ylide **10** (3.5 g, 7 mmol) and benzene (60 mL). The reaction mixture became clear and red, was stirred at room temperature for 0.5 h, and then was heated under reflux for 4 h. After vacuum evaporation of the solvent, the residue showed three distinct spots by TLC: product **16a**, triphenylphosphine oxide, and starting ylide **10**. Chromatography with methylene chloride gave, after evaporation of the solvent, 3.0 g of crude **16a**. Recrystallization from 10 mL of ethanol/benzene (2/1) gave 2.3 g (85%) of analytically pure white crystals, mp 195.5–197 °C; precise mass calcd for $C_{30}H_{24}N_2$, 412.194; found, 412.193.

Method B: Diphenylketene prepared in situ. A solution of diphenyl acetyl chloride (0.74 g, 3.2 mmol) in benzene (5 mL) was added dropwise with stirring at room temperature during 0.5 h to a slurry of ylide **10** (1.25 g, 2.5 mmol) and triethylamine (0.41 g, 4.0 mmol) in 30 mL of dry benzene. The reaction and separation were accomplished as described in method A and yielded 0.89 g (86%) of pure **16a**.

(11) The ^{1}H NMR and ^{13}C NMR are rather too complex to be interpreted because of the presence of three isomers (by ^{31}P NMR).

(12) Taylor, E. C.; McKillop, A.; Hawks, G. H. "Organic Synthesis"; Wiley: New York, 1972; Collect. Vol. No. *52*, p 36.

Reaction of Ylide 11 with Diphenylketene. Preparation of 2,9-Dimethyl-4,9-diphenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (16h). Method B was employed using diphenylacetyl chloride (0.74 g, 3.2 m mol) in benzene (5 mL) added to ylide **11** (1.1 g, 2.5 mmol) and triethylamine (0.41 g, 4. mmol) in benzene (30 mL). The pyrazoloisoquinoline (0.81 g, 93% yield), one spot by TLC) was isolated as a mixture of stereoisomers, in a ratio of approximately 3/1 by ^{1}H NMR. Precise mass, for a once-crystallized sample (from ethanol), calcd for $C_{25}H_{22}N_2$, 350.178; found, 350.177. Multiple recrystallizations from ethanol gave a pure samples of **16h**, the major stereoisomer, mp 128–129 °C. The ^{1}H and ^{13}C NMR spectra of **16h′**, the minor stereoisomer, were obtained by subtraction of the NMR of **16h** from the NMR spectra of the mixture of stereoisomers, precise mass (for **16h**) calcd for $C_{25}H_{22}N_2$, 350.178; found, 350.174.

Reaction of Ylide 10 with Phenylketene. Preparation of *trans*- and *cis*-2-Methyl-4,9-diphenyl-4,9-dihydropyrazolo-[1,5-*b*]isoquinoline (18d-1 and 18d-2). Method B was employed using phenylacetyl chloride (0.75 g, 4.9 mmol) in benzene (5 mL) and ylide **10** (1.25 g 2.5 mmol) and triethylamine (0.61 g, 6.0 mmol) in benzene (30 mL).

After removal of the solvent in vacuo, the crude reaction mixture was dissolved in 2 mL of CH_2Cl_2 and chromatographed with petroleum ether/ethyl acetate (7/3). Eluates were collected and checked by TLC. The second fraction was a yellow solid mixture (by ^{1}H NMR) of **18d-1** and **18d-2** (0.55 g, 65%). This mixture was recrystallized from 3 mL of ethanol/benzene (3/1, v/v) to give the pure isomer **18d-1** as white crystals, mp 196–198 °C. The X-ray data appear as supplementary material. Precise mass calcd for $C_{24}H_{20}N_2$, 336.163; found, 336.166.

Crystallographic Structural Determination of 18d-1. A colorless crystal of $C_{23}H_{20}N_2$, **18d-1**, measuring 0.20 × 0.23 × 0.30 mm was found to belong to the noncentrosymmetric orthorhombic space group, $Pna2_1$ [No. 33, C_{2v}^9]: a = 17.754 (5), b = 5.888 (1), c = 17.416 (5) Å, V = 1820.4 (5) Å^3, Z = 4, μ = 0.63 cm^{-1} (Mo Kα). The absence of a mirror plane or inversion center in the molecule and statistics based upon the distribution of E values suggested that the centrosymmetric alternative *Pnam* (nonstandard setting of *Pnma* [No. 62, D_{2h}^{16}]) was incorrect; the choice of the noncentrosymmetric space group was verified by the successful and reasonable structure ultimately obtained. A total of 2760 reflections was collected by a Nicolet R3 automated diffractometer; of this total, 2060 unique reflections at the $I \geq 2\sigma(I)$ level were used for solution and refinement. The structure was solved by direct methods; the initial E map provided the locations of all nonhydrogen atoms. A difference Fourier map obtained after the anisotropic refinement of these atoms revealed the locations of all hydrogen atoms except for those of the methyl group. In the final blocked-cascade least-squares refinement cycles the positions of the located hydrogen atoms were refined isotropically, and those of the methyl-group hydrogen atoms were included (but not refined) in idealized positions (d(C–H) = 0.96 Å). At convergence, R_F = 5.0%, R_{wF} = 5.2%, and GOF = 1.13. A final difference map revealed only a diffuse background with a highest peak of 0.42 e$^-$ Å^3. Included in the final refinement cycles was a substantial correction for secondary extinction; low angle reflections displayed a systematically greater value for F(calc) vs. F(obsd). Additional information is available as supplementary material. The structure factor tables are available from one of the authors (A.L.R.) by direct correspondence.

The mother liquor from the above mentioned recrystallization was evaporated to half its original volume, and after standing overnight gave a second crop of crystals of **18d-1**. The filtrate was treated with 2 mL of 95% ethanol and cooled to 0 °C. Pure white crystals of **18d-2** were obtained, mp 150–152 °C; precise mass calcd for $C_{24}H_{20}N_2$, 336.163; found, 336.163.

Transformation of (18d-2) into (18d-1). Compound **18d-2** (0.1 g) was dissolved in 5 mL of dry benzene and heated under reflux for 12 h. After removal of the solvent in vacuo, the ^{1}H NMR spectrum of the residue showed that both **18d-2** and **18d-1** were present in a ratio of 3/1.

A similar treatment with compound **18d-1** showed no change.

Reaction of Ylide 10 with Methylphenylketene. Preparation of 2,4-Dimethyl-4,9-diphenyl-4,9-dihydropyrazolo-[1,5-*b*]isoquinoline (18b) and 2,4-Dimethyl-9,9-diphenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (16b). Ylide **10** (1.9

g, 3.7 mmol) was allowed to react for 24 h, via method B, with triethylamine (0.76 g, 7.5 mmol) and α-phenylpropionyl chloride (1.02 g, 6.1 mmol) in 50 mL of benzene. The chromatographed product gave two mixed fractions with a total of 1.31 g and a combined ratio of **16b** to **18b** of 6/4. Pure white recrystalline **18b** was obtained by recrystallization of the second fraction from ethanol, mp 179–181 °C; precise mass calcd for $C_{25}H_{22}N_2$, 350.178; found, 350.175.

Analytically pure **16b** was obtained as light yellow crystals after two further chromatographic separations and crystallization of the original first fraction from heptane: mp 134–136 °C; precise mass calcd for $C_{25}H_{22}N_2$, 350.178; found, 350.177.

Reaction of Ylide 11 with Methylphenylketene. Preparation of 2,4,9-Trimethyl-4-phenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (18i) and 2,4,9-Trimethyl-9-phenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (16i). Ylide **11** (1.65 g, 3.8 mmol) was allowed to react for 28 h, employing method B, with triethylamine (0.76 g, 7.5 mmol) and α-phenylpropionyl chloride (1.02 g, 6.1 mmol) in 50 mL of benzene. Column chromatography gave 0.21 g (19%) of **18i** pure (by TLC), as a pale yellow oil; a mixture of **16i** and its stereoisomer, **16i'**, was also recovered pure, in a ratio of 1/3, as a yellow oil. Attempts to crystallize **18i** or **16i** (**16i'**) from a wide variety of solvents were unsuccessful. Precise mass calcd for $C_{20}H_{20}N_2$, 288.163; found, 288.164 (for 18i) and 288.163 (for **16i** and **16i'**).

Reaction of Ylide 10 with Benzylketene. (a) Ylide **10** (2.5 g, 5 mmol) was allowed to react, by method B, with triethylamine (0.76 g, 7.5 mmol) and β-phenylpropionyl chloride (1.05 g, 6.3 mmol) for 34 h. The reaction mixture was chromatographed with petroleum ether/ethyl acetate (7/3). When elution of fraction (1) was completed, methanol was mixed into the above eluting solvent in a ratio increasing gradually from 5% to 10%, to collect fraction 2. The following data were obtained for the two fractions collected.

(1) 2-Methyl-4-benzyl-9-phenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (18f). A light yellow solid (0.38 g, 22%) was obtained. Recrystallization from methanol gave an analytically pure sample, mp 174–176 °C; precise mass calcd for $C_{25}H_{22}H_2$, 350.178; found, 350.176.

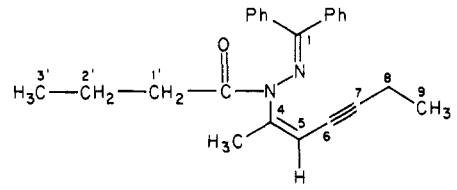
(2) 4-Methyl-1,1,8-triphenyl-2,3-diazaocta-1,4-dien-6-yne (24f). Compound **24f** (0.76 g, 43%), was obtained, after recrystallization from methanol, an analytically pure sample was obtained: mp 167.5–169 °C; ^{1}H NMR δ 2.04 (s, 3 H, CH_3), 3.89 (s, 2 H, CH_2Ph), 5.56 (s, 1 H, =CH), 7.15–7.27 (m, 15 H, Ar), 9.05 (brs, 1 H, NH); ^{13}C NMR δ 12.8 (C-4-CH_3), 39.3 (CH_2Ph), 106.2 (C-5), 140.4 (C-4), 145.7 (C-1); precise mass calcd for $C_{25}H_{22}N_2$, 350.178; found, 350.176.

(b) When the reaction was carried out as described above, but with only 4 h of refluxing time, a mixture was obtained consisting of **18f**, **24f**, and **4-methyl-1,1,8-triphenyl-2,3-diaza-1,3,5,6-octatetraene (13f)** in a ratio of approximately 4/3/3 (by ^{1}H NMR). The total yield was recrystallized from methylene chloride/heptane (1/10), affording an analytically pure sample as white crystals, mp 142–162 °C; precise mass of the mixture calcd for $C_{25}H_{22}N_2$, 350.178; found, 350.182; ^{1}H NMR of **13f** (by subtraction of **18f** and **24f**) δ 1.97 (s, 3 H, CH_3), 2.93 (dq, 2 H, CH_2Ph), 4.05 (dd, J = 11.1, 1 H, =CH), 5.32 (s, 1 H, HC=).

Attempted Thermal Reaction of 24f. Heating of 100 mg of **24f** in a pressure tube filled with dry nitrogen at 180 °C for 3 h gave unchanged **24f**.

Reaction of Ylide 10 with Ethylketene. Ylide **10** (1.9 g, 3.8 mmol) was allowed to react, by method B, with triethylamine (0.76 g, 7.5 mmol) and butyryl chloride (0.48 g, 4.5 mmol). After heating the mixture under reflux for 24 h the solvent was evaporated in vacuo and the residue chromatography. Eluting with petroleum ether/ethyl acetate (7/3) afforded the first two fraction (a, b). Then elution with petroleum ether/ethyl acetate/methanol (11/4/1) gave the third fraction (c).

(a) 3-Butyryl-4-methyl-1,1-diphenyl-2,3-diazanona-1,4-dien-6-yne (25e) was obtained as an oil, 0.41 g (30% yield). On crystallization from methanol it gave an analytically pure sample, mp 92–93 °C; ^{1}H NMR δ 1.00 (t, J = 7.4, 3 H, C-9-H_3),[13] 1.07 (t, J = 7.4, 3 H, C-3'-H_3) 1.73 (m, 2 H, C-2'-H_2), 2.37 (s, 3 H, C-4-CH_3), 2.59 (q, 2 H, C-8-H_2), 3.02 (t, J = 7.4, 2 H, C-1'-H_2), 5.30 (s, 1 H, C-5-H), 7.04–7.36 (m, 10 H, Ar); ^{13}C NMR δ 13.8 (C-4-CH_3), 14.3 (C-3'),[13] 14.5 (C-9), 18.0 (C-2'), 26.9 (C-8), 37.2 (C-1), 112.1 (C-5), 154.1 (C-1), 174.5 C=O); precise mass calcd for $C_{24}H_{26}N_2O$, 358.204; found, 358.201.



25e

(b) 2-Methyl-4-ethyl-9-phenyl-4,9-dihydropyrazolo[1,5-*b*]isoquinoline (18e) was recovered (0.30 g, 27% yield) as a white solid. An analytically pure sample was obtained by recrystallization from heptane, mp 117–118 °C; precise mass calcd for $C_{20}H_{20}N_2$, 288.163; found, 288.159.

(c) 4-Methyl-1,1-diphenyl-2,3-diazanona-1,4-dien-6-yne (24e) was recovered as a white solid (0.18 g, 16%); after recrystallization from heptane an analytical sample was obtained, mp 129–131 °C; ^{1}H NMR δ 1.05 (t, J = 7.9 3 H, C-9-H_3), 2.13 (s, 3 H, C-4-CH_3), 2.48 (q, 2 H, C-8-H_2), 5.64 (s, 1 H, C-5-H), 7.04–7.34 (m, 10 H, ArH), 9.71 (brs, 1 H, N*H*); ^{13}C NMR δ 12.8 (C-4-CH_3), 14.4 (C-9), 27.3 (C-8), 105.5 (C-5), 142.8 (C-4), 145.6 (C-1); precise mass calcd for $C_{20}H_{20}H_2$, 288.163; found, 288.161.

Butyrylation of 24e. Butyryl chloride (22 mg, 0.21 mmol) in 2 mL of dry acetonitrile was added dropwise over 15 min to a solution of **28e** (58 mg, 0.2 mmol) and triethylamine (21 mg, 0.21 mmol); stirring was continued at ambient temperature for 2 h. After evaporation of the solvent and chromatography of the residue (petroleum ether/ethyl acetate 8/2), compound **25e** was obtained (60 mg, 85%). The melting point and mixture melting point were identical with those of **25e** obtained in the previous experiment.

Reaction of Ylide 10 with Dimethylketene. Ylide **10** (1.9 g, 3.8 mmol), triethylamine (0.57 g, 5.6 mmol), and isobutyryl chloride (0.42 g, 4.0 mmol) were allowed to react by method B for 2 h. After removal of the solvent, the residue was chromatographed with petroleum ether/ethyl acetate (7/3) to afford fraction a and with petroleum ether/ethyl acetate/methanol (14/6/1) to afford fraction b.

(a) 1-(Diphenylmethyl)-3-methyl-5-isopropenylpyrazole (22) was isolated as a white solid (0.15 g, 14%). An analytically pure samples was obtained by recrystallization from methanol, mp 75–78 °C; ^{1}H NMR δ 2.03 (s, 3 H, $(H_3C)C{=}CH_2$), 2.22 (s, 3 H, C-3-CH_3), 5.01 (d, J = 1.7, $(H_3C)C{=}CH_2$-cis), 5.29 (d, J = 1.7, 1 H, $(H_3C)C{=}CH_2$-trans), 5.98 (s, 1 H, C-4-H), 6.72 (s, 1 H, C*H*$(Ph)_2$), 7.17–7.32 (m, 10 H, Ar); ^{13}C NMR δ 13.9 (C-3-CH_3), 24.3 ($(H_3C)C{=}CH_2$), 64.9 (N-C*H*$(Ph)_2$), 104.3 (C-4), 117.4 (=CH_2), 135.1 ($H_3CC{=}CH_2$), 146.2 (C-5), 148.1 (C-3); precise mass calcd for $C_{20}H_{20}N_2$, 288.163; found, 288.160.

(b) (4,7-Dimethyl-1,1-diphenyl-6-hydroxy-2,3-diazaocta-1,3,5-trien-5-yl)triphenylphosphonium hydroxide inner salt (*Z*,*E*) (20) was isolated (1.5 g, 72%) as a green-yellow solid. An analytically pure sample was obtained by recrystallization from methylene chloride/heptane (1/10), mp 160–162 °C. The pure *Z* or *E* isomers could not be isolated by TLC or column chromatography. ^{31}P NMR δ 9.58 (34%), 16.37 (66%). On the basis of previous work,[14] it is assumed that the former peak is for the *Z* isomer the latter for the E isomer. ^{1}H NMR (presumed *Z* isomer) δ 1.01 (d, J = 6.9, 6 H, $CH(CCH_3)_2$), 1.89 (s, 3 H, N=CCH_3), 2.72 (m, 1 H, C*H*$(CH_3)_2$), 6.94–7.68 (m, 25 H, Ar); ^{1}H NMR (presumed *E* isomer) δ 0.93 [d, J = 6.5, 6 H, $CH(CH_3)_2$), 2.25 (s, 3 H, N=CCH_3), 2.87 (m, 1 H, C*H*$(CH_3)_2$), 6.94–7.68 (m, 25 H, Ar); ^{13}C NMR (presumed *Z* isomer) δ 19.7 ($CH(CH_3)$), 28.5 (N=C—CH_3), 34.4 ($CH(CH_3)_2$), 139.1 (N=*C*—CH_3), 160.1 (*C*=Ph_2), 162.7 (d, J_{CP} = 9.8, =*C*—P Ph_3), 193.4 (=*C*—O^e); ^{13}C NMR (presumed *E* isomer) δ 19.6 ($CH(CH_3)_2$), 22.8 (N=CH_3), 34.8 ($CH(CH_3)_2$), 138.7 (N=*C*—CH_3), 159.2 (=*C*—Ph_2), 162.7 (d, J_{CP} = 9.8 =*C*-P^+Ph_3), 196.0 (=*C*—O^-); precise mass calcd for $C_{38}H_{35}N_2OP$, 566.249; found, 566.248.

(13) May be reversed with C-3'-H_3.

(14) Snyder, J. P.; Bestmann, H. J. *Tetrahedron Lett.* **1972**, 3317.

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.

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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

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