ane–benzene–AcOEt (5:5:1)] to give 3 (53 mg, 77%).

Oxidation of (p-Methoxyphenyl)methyl Methyl Ether (2) with CAN in MeOH. To a solution of 2 (154 mg, 1.01 mmol) in MeOH (5 mL) was added a solution of CAN (1.23 g, 2.2 mmol) in MeOH (10 mL). After being stirred at room temperature for 5 min, the concentrated mixture was extracted with benzene. Workup of the extracts gave 3 (133 mg, 97%), whose spectral data were identical in all respects with those of the authentic sample.

Registry No. 1, 104-93-8; 2, 1515-81-7; 3, 123-11-5; 4, 80866-06-4; 9a, 4685-47-6; 9b, 6738-23-4; 9c, 1515-95-3; 9d, 1730-48-9; 9e, 98-51-1; 10a, 52289-54-0; 10b, 32723-67-4; 10c, 100-06-1; 10d, 1078-19-9; 10e, 939-97-9; 11d, 16821-24-2; 11e, 3395-87-7; diammonium hexanitratocerate, 16774-21-3.

Cyclization of Conjugated Azines. Synthesis and Thermal Rearrangements of 1,8-Diaryl-4,5-diaza-3-methyl- and -3-phenyl-1,3,5,7-octatetraenes (α,β-Unsaturated Azines) to 1-(1-Methyl-3-phenyl- and -1,3-diphenyl-1-propenyl)-5-arylpyrazoles

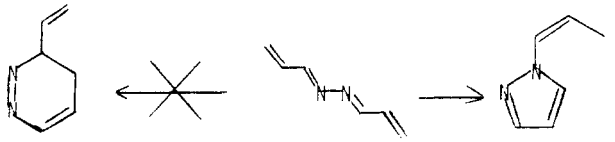
Edward E. Schweizer* and S. N. Hirwe

Department of Chemistry, University of Delaware, Newark, Delaware 19711

Received September 15, 1981

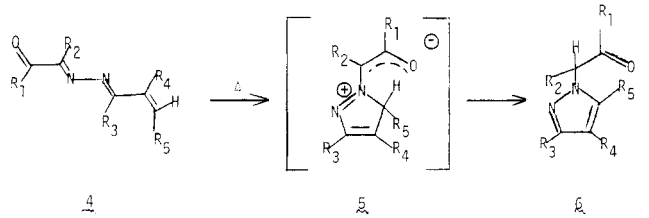
Methyl- (**20**) and phenyl-substituted (**29**) α,β-unsaturated azines were prepared and subjected to thermolyses. In all cases the thermolyses reaction produced two pyrazoles (**23**, **24** and **32**, **33**, respectively), except where the azine had a terminal methylene grouping. The ratios of the pyrazoles were determined from the ^{1}H NMR. The steric and electronic effects of the azine substituents on the ratios of the pyrazoles formed are discussed. The ^{13}C NMR of the isolated azines and pyrazoles are reported.

Symmetrical azines 1 derived from α,β-unsaturated carbonyl species and hydrazine yield *N*-propenylpyrazoles[1,2] **2** rather than the dihydropyridazines **3** which



one would have anticipated if the cyclization reaction were to proceed in the manner expected[3] for an all carbon 1,3,5-unsaturated system. This type of reaction is quite common to azine chemistry and is termed a "criss-cross" cycloaddition reaction.[4]

It has been shown in our laboratories that a variety of simple N-substituted pyrazoles as well as tetrahydroindazoles, pyrazolopyrans, and cyclopentapyrazoles may be prepared from α,β-unsaturated α-oxoazines **4**[5] by thermolysis.



We have also shown[6] that α-oxo-α-allenylazines **7** readily form pyrazolo[1,5-*b*]isoquinolines **8** and pyrazolo[5,1-*c*]-1,4-oxazines **9** apart from monocyclic N-substituted pyrazoles (Scheme I).

We propose that unsaturated azines with cumulated double bonds in conjugation with the azine moiety will prove to be versatile synthons for a large variety of fused pyrazolo-substituted species as shown in Scheme II.

In order to explore further the scope of the reaction of allenylazine species related to **7**, we wished to prepare these compounds without the carbonyl moiety. We chose to start this work by examining the reactions of simple unsymmetrical unsaturated azines, related to **4**, with no carbonyl groups.

It has been shown[5] that the azine **4** may be prepared readily from the monohydrazone of a diketone, **11** and (2-propynyl)triphenylphosphonium bromide (**12**). How-

$$\underset{\mathbf{11}}{R^1C(O)C(R^2)=NNH_2} + \underset{\mathbf{12}}{HC\equiv CCH_2P^+(Ph)_3Br^-} \rightarrow \rightarrow \mathbf{4}$$

ever, our attempts to make the hyrazone of cinnamaldehyde, **15**, directly always resulted in the formation of

$$\underset{\mathbf{13}}{PhCH=CHCHO} + \underset{\mathbf{14}}{H_2NNH_2} \rightarrow [\underset{\mathbf{15}}{PhCH=CHCH=NNH_2}] \rightarrow \underset{\mathbf{16}}{(PhCH=CHCH=N-)_2}$$

the symmetrical cinnamaldehyde azine **16**, thus thwarting our ability to prepare **17** from **15** and the salt **12**. We found, however, that **17** may be obtained readily (89% yield) by allowing (2-propynyl)triphenylphosphonium bromide (**12**) to react initially with an equivalent amount

(1) Stern, R. L.; Krause, J. G. *J. Org. Chem.* **1968**, *33*, 212.
(2) Stern, R. L.; Krause, J. G. *J. Heterocycl. Chem.* **1968**, *5*, 263.
(3) Huisgen, R.; Dahmen, A.; Huber, H. *J. Am. Chem. Soc.* **1967**, *89*, 7130.
(4) Wagner-Jauregg, T. *Synthesis* **1976**, 349 and references cited therein.
(5) Albright, T. A.; Evans, S.; Kim, C. S.; Labaw, C. S.; Russiello, A. B.; Schweizer, E. E. *J. Org. Chem.* **1977**, *42*, 3691-3697.
(6) Schweizer, E. E.; Evans, S. *J. Org. Chem.* **1978**, *43*, 4328-4334.
(7) Y is normally more electronegative than X or is able to stabilize a negative charge. For example: X = N, Y = O; X = C, Y = CE_2, NR, O (E = aromatic, O=CR, PR_3^+); Z = CR_2, NR, O. This is not meant to be an exhaustive list. Apart from the examples mentioned above[2,3,6] where X = Y = Z = C, X = Z = C, and Y = O, we have also prepared X = C, Y = O, and Z = N.[8]
(8) Schweizer, E. E.; Lee, K. J., unpublished results.

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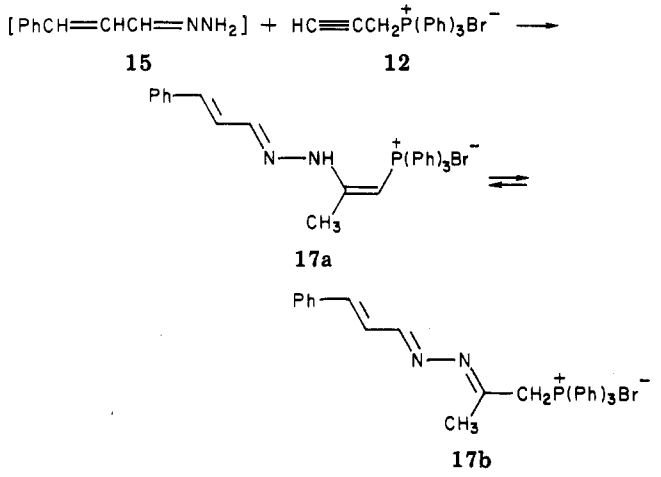
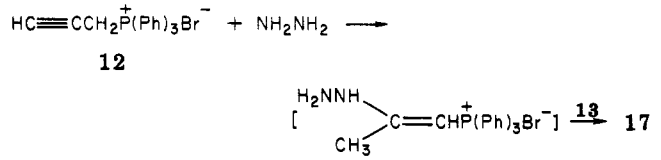


of hydrazine followed by the addition of cinnamaldehyde (13). The salt 17 was found, by proton NMR, to be in the



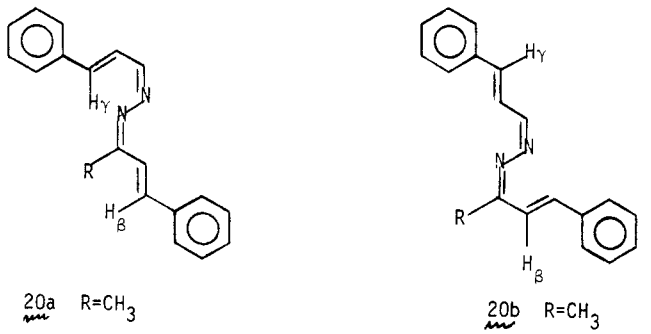
enamine form, 17a, rather than the azine form, 17b. This is in contrast to the adduct of benzil monohydrazone and salt 12 which was previously shown[6] to be in the azine form.

The ylide 18 was obtained readily (Scheme III) from salt 17 with alcoholic sodium ethoxide (−10 to −20 °C). The corresponding azines, 20, were obtained in 59–81% yield either by allowing the isolated ylide 18 to react with the corresponding aldehyde in refluxing acetonitrile for 2 h or by adding the corresponding aldehyde to an ethanolic solution of the ylide 18 and refluxing for 2 h.

The pure isolated azine 20 was heated (neat) at 200 °C for 1 h and gave two pyrazoles in 98–99% yield (see Table I).

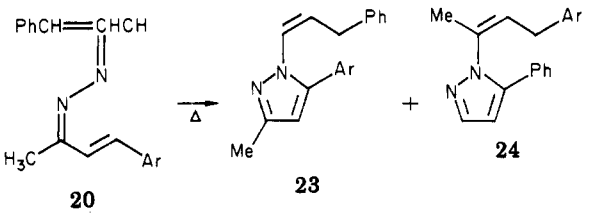
There are two influences which could affect the ratio of the unstable azomethine intermediates 21/22 and therefore the formation of the final pyrazoles 23/24. One influence is that of the steric effect that the methyl group may have on the orientation of the α,β-double bond to the azine (in 20), thus aiding, or not, the attack of the nitrogen unshared electron pair at the β-carbon atom. The second effect is the stabilizing (or destabilizing) effect that the methyl group and the substituent groups on Ar may have on the azomethine imines 21/22.

The two conformations which would be most likely to exist in the all-trans azine species just prior to the cyclization of 20 to 21 or 22 would be 20a or 20b. Space-filling



Fischer–Hirschfelder models show that the steric interaction between the CH_3 group and Hγ and Hβ is quite severe in 20a. In 20b the Hγ–CH_3 interaction is eliminated, and the Hβ–CH_3 interaction is much less than that observed in 20a. Thus from conformational considerations one would predict that 20b would be present to a greater extent than 20a and that this would enhance the formation of intermediate 21 over 22.

Table I. Pyrolysis of Azines 20 to Pyrazoles 23/24



	Ar[a]	temp,[b] °C	crude ratio of 23/24
23a/24a	p-$H_3COC_6H_4$	200	71/29
23b/24b	p-$H_3CC_6H_4$	200	73/27
23c/24c	C_6H_5	200	73/27
23c/24c	C_6H_5	150	75/25
23d/24d	p-ClC_6H_4	200	61/39
23e/24e	p-NCC_6H_4	200	41/59
23f/24f	o-$H_3CC_6H_4$	200	75/25
23g/24g	α-naphthyl	200	75/25
23h/24h	β-naphthyl	200	64/36
23i/24i	p-$O_2NC_6H_4$	200[c]	dec
23j/24j	o-$O_2NC_6H_4$	200[c]	dec
23k/24k	H[d]	200	100/0

[a] The individual pyrazoles were isolated by GC, and satisfactory exact mass and proton NMR data were obtained. [b] One H. [c] No rearrangement at 150 °C. [d] Bp 85–90 °C (0.03 mm), by micro boiling point technique.

From electronic considerations one would expect that the CH_3 group should destablize the delocalized carbanion in 22 over that in 21. Therefore, from both conformational and electronic considerations of the methyl effects one would have predicted an excess of 23 over 22, which is found to be the case (see Table I). The conversion of the pyrazole ratio 23/24 to less than 1 is only observed where a highly electrophilic p-cyano moiety is introduced on to the phenyl group, Ar, thus adding significant stability to the side-chain-delocalized anion in 22 over that in 21.

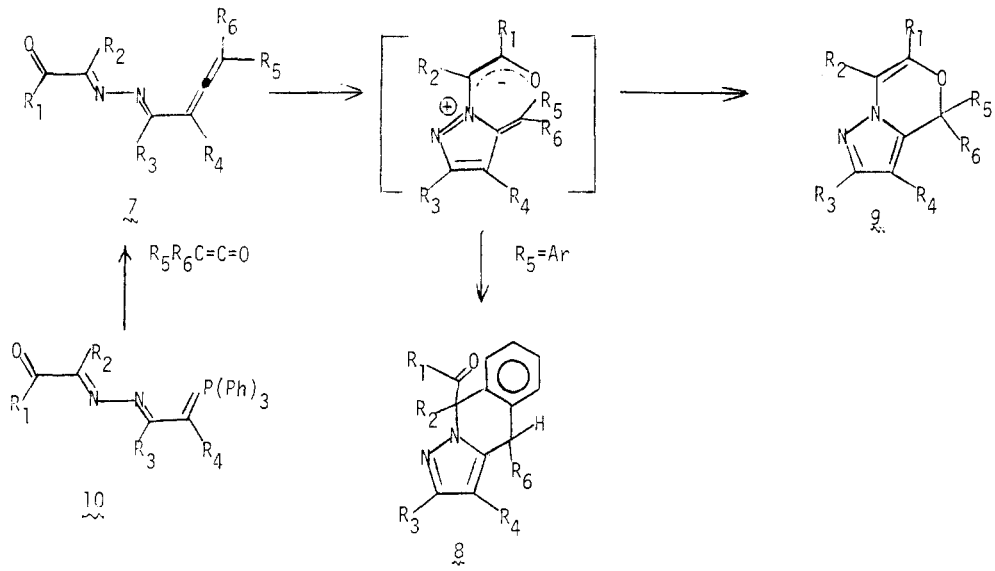
The ratios of products were determined on the crude pyrolysis mixture by ^1H NMR and gas chromatography and were found to be within ±3% of each other.

The nitro-substituted azines were recovered essentially unchanged at a pyrolysis temperature of 150 °C and decomposed at 200 °C; therefore, the pyrazole ratios were not obtained from these azines.

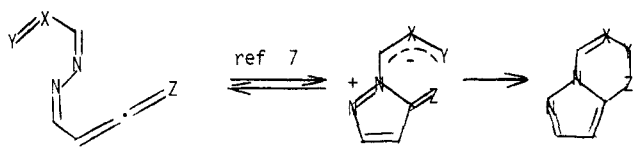
In view of the significant stabilizing effect of the p-cyano group which reverses the normal 23/24 ratio, we concluded that the preparation and the examination of the rearrangement products of azine 29 should be undertaken. The precursor to the azine 29, ylide 28, was prepared from (phenylethynyl)triphenylphosphonium bromide (25) in a manner similar to that used for the preparation of ylide 18 (see Scheme IV).

Attempts to condense ylide 28 with benzaldehyde in refluxing acetonitrile, over a 2-h period, in the manner used to obtain azine 20 from ylide 18 failed. This indicates that the phenyl-substituted ylide 28 is more stable than the methyl-substituted ylide 18. Ylide 28 condensed readily with benzaldehyde in refluxing absolute ethanol (2 h) to form azine 29. Although TLC showed one spot and mass spectral analyses gave an exact mass consonant with the azine 29, the NMR showed it to be contaminated significantly with rearranged products. Therefore, we opted to

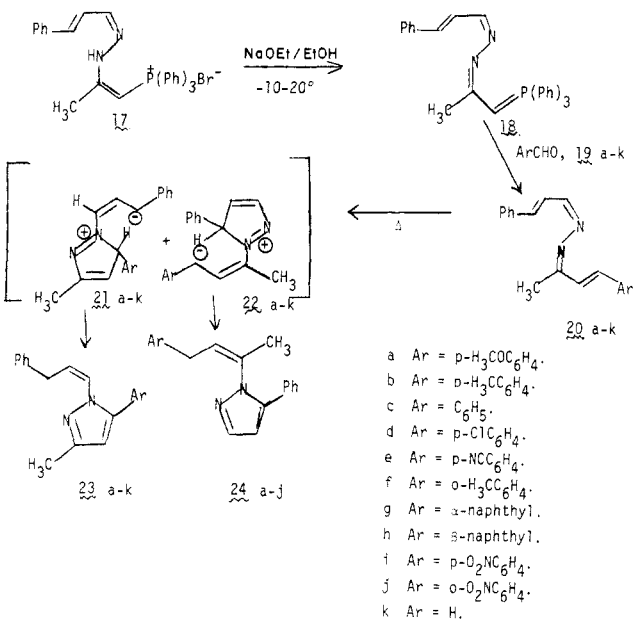
Scheme I



Scheme II



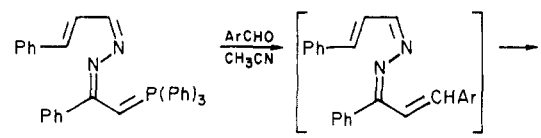
Scheme III



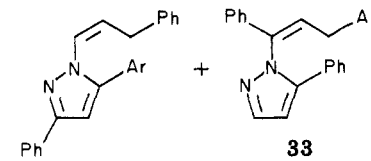
study the rearrangement product ratios by allowing the ylide **28** to condense with the appropriate aldehyde in refluxing acetonitrile over a 72-h period. These conditions gave us a solution containing pyrazoles and triphenylphosphine oxide on which the ratios of the pyrazoles (**32/33**) were determined by examining the proton NMR (see Table II).

Assuming comparable steric interactions of the phenyl and methyl groups, one would expect that the phenyl group would provide greater stabilization for the anionic moiety of intermediate **31**, thus giving a smaller **32/33** ratio than that found for **23/24**. The ratio of the unsubstituted phenylpyrazoles (where Ar = C_6H_5) is 66:34 **32/33**; whereas, in the comparable methyl case the **23/24** ratio (where Ar = C_6H_5) is 74:26. It is also found that in all of

Table II. Conversion of Ylide 28 and Aldehydes to Pyrazoles 32/33



28 29



32 33

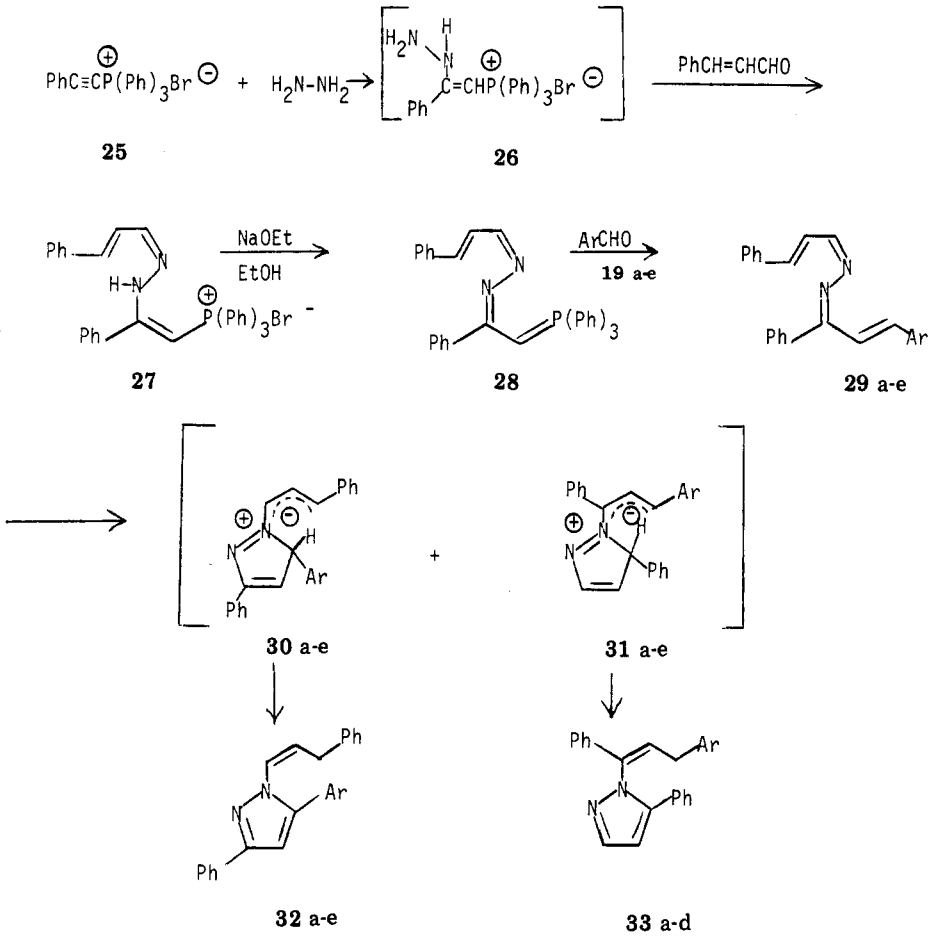
compd	Ar	mp,[a] °C	crude ratio of 32/33
32a	C_6H_5	91-92	66/34
33a	C_6H_5	*b*	
32b	*p*-$H_3COC_6H_4$	*b*	47/53
33b	*p*-$H_3COC_6H_4$	101-103	
32c	*p*-ClC_6H_4	*b*	44/56
33c	*p*-ClC_6H_4	95-97	
32d	*p*-NCC_6H_4	*b*	47/53
33d	*p*-NCC_6H_4	121-123	
32e	H	157 (0.2 mm)[c]	100/0
33e	H	*d*	

[a] Satisfactory exact mass and proton and carbon NMR data have been obtained for all of the compounds listed (see note *b*). [b] All liquids, probably due to slight impurities of the corresponding isomers. [c] Boiling point by micro boiling point technique. [d] Not formed.

the substituted (Ar substituted) species the **32/33** ratios are in the 45 ± 2–55 ± 2 range; i.e., all **32/33** ratios are <1. We recognize that the phenyl and methyl conditions of pyrazole formation are not comparable; however, the conditions within each pair of pyrazoles are identical, and the steric and electronic effects generally follow the trends expected.

Finally, when the ylides **18** and **28** were allowed to react with formaldehyde to yield **20k** and **29e**, where a terminal methylene (CH_2) has been substituted for CHAr, the only pyrazole species obtained were **23k** and **32e**. This, of course, is the expected result since the Ar stabilization of **22k** and **31e** is lost, and the steric effects of the confor-

Scheme IV [a]



[a] a, Ar = C_6H_5; b, Ar = p-$H_3COC_6H_4$; c, Ar = p-ClC_6H_4; d, Ar = p-NCC_6H_4; e, Ar = H.

mation related to **20b** is lessened even further.

On the basis of the work reported in this paper, we come to the conclusion that the steric effect is important in directing the ring closure of azines to pyrazoles. In the case of the diaryl methyl-substituted azines **20** it is overriding until the aryl group is substituted by a highly electron-withdrawing group. With the diaryl phenyl-substituted azine **29** the signals are not as clear-cut; however, the phenyl group seems to stabilize the intermediate **31** over **30** to a greater extent than the methyl group stabilizes **22** over **21**.

The methyl-substituted azine ylide **18** is more reactive than the phenyl-substituted azine ylide **28**. However, the phenyl-substituted azine **29** is more readily rearranged than the methyl-substituted azine **20**.

The reactions of unsaturated azines with and without cumulated conjugated bonds are being examined and will be reported at a future date.

Experimental Section

Proton NMR spectra of approximately 10% (w/v) solutions in $CDCl_3$ were obtained on a Bruker Spectrospin Model WM 250. Chemical shifts are recorded in parts per million (δ scale) vs. tetramethylsilane as an internal standard. In reporting the NMR data, the following abbreviations have been employed: coupling constant in herz (J), singlet (s), doublet (d), doublet of doublets (dd), triplet (t), quartet (q), multiplet (m). ^{13}C NMR spectra of approximately 15% (w/v) solutions in $CDCl_3/CHCl_3$ were obtained on the Bruker Spectrospin Model WM 250. Electron-impact mass spectra were recorded by using a Du Pont CEC21-110D instrument with a resolution of 5000.

Dry nitrogen was routinely used as a reaction atmosphere in all reactions. Eastman precoated (silica gel on polyethylene) chromatogram sheets impregnated with fluorescent indicator were employed in thin-layer chromatographic operations. Melting points were obtained with a Thomas-Hoover apparatus and are uncorrected. A Varian Aerograph Model 90-P gas chromatograph with a column (10 ft × 0.25 in.) packed with 10% GE SF-96 silicone firebrick and equipped with a thermal-conductivity detector was used to separate the mixture of pyrazoles. Elemental analyses were performed by Micro Analysis Inc., Wilmington, DE.

The aromatic aldehydes used were purchased from Aldrich Chemical Co. and were used without purification except for p-chlorobenzaldehyde which was crytallized prior to its use. Acetonitrile was dried over molecular seives followed by its distillation over P_2O_5. Ethyl alcohol was distilled over sodium metal and diethyl phthalate. All glassware was baked at 110–120 °C overnight.

The ^1H and ^{13}C NMR data in Tables IV–XI appear as supplementary material.

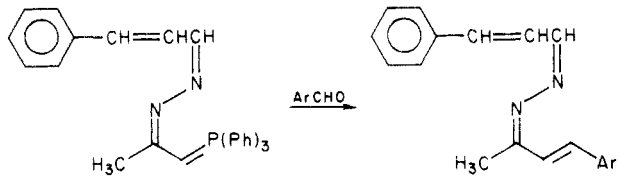
Preparation of (2-Propynyl)triphenylphosphonium Bromide (12). The salt was prepared according to the procedure of Eiter and Odinger.[9]

Preparation of (2-Methyl-7-phenyl-3,4-diaza-1,4,6-heptatrien-1-yl)triphenylphosphonium Bromide (17). Hydrazine (1 g, 0.03 mol) was added to a solution of salt **12** (11.5 g, 0.03 mol) in acetonitrile (40 mL) and stirred at room temperature for 1 h.

Cinnamaldehyde (9 g, 0.06 mol) was added, and stirring was continued at room temperature for an additional 16 h. The yellow compound precipitated, was filtered, and was washed with acetonitrile (~10 mL). A precipitate was formed which on filtration gave 13.1 g (87%) of the pure salt **17**: mp 184–185 °C; ^1H NMR δ 2.53 (s, 3 H, CH_3), 3.72 (d, 1 H, J_{P-H} 19.7, =CHP), 5.29 (dd, 1 H, J = 9.2, J = 16.0, CH=CHCH), 6.52 (d, 1 H, J = 16.0, PhCH=), 6.95–7.91 (m, 20 H, Ar), 8.17 (d, 1 H, J = 9.2, HC=N),

(9) Eiter, K.; Odinger, H. *Justus Liebigs Ann. Chem.* **1965**, *682*, 62.

Table III. Preparation of Azines 20a-j



18 20a-j

compd	Ar	yield, %	mp,[c] °C
20a	p-$H_3COC_6H_4$	62[a]	147-149
20b	p-$H_3CC_6H_4$	70[b]	148-149
20c	C_6H_5	59[a]	120-122
20d	p-ClC_6H_4	64[a]	154-154.5
20e	p-NCC_6H_4	81[b]	165-166.5
20f	o-$H_3CC_6H_4$	59[b]	107-108
20g	α-naphthaldehyde	65[b]	126-128
20h	β-naphthaldehyde	80[a]	148-150
20i	p-$O_2NC_6H_4$	66[a]	163-165
20j	o-$O_2NC_6H_4$	65[a]	133-135
20k	H	68[a]	*d*

[a] Ylide 18 isolated and then allowed to react with aldehyde. [b] Ylide 18 prepared and then allowed to react in situ with aldehyde. [c] Satisfactory exact mass and proton and carbon NMR data have been obtained for all of the compounds listed above. [d] Liquid; no boiling point since it rearranges on heating.

12.41 (s, 1 H, NH); ^{31}P NMR δ 16.35.

Anal. Calcd for $C_{30}H_{28}N_2PBr$: C, 68.31; H, 5.35. Found: C, 68.23; H, 5.17.

Preparation of (2-Methyl-7-phenyl-3,4-diaza-2,4,6-heptatrienylidene)triphenylphosphorane (18). The salt 17 (8.9 g, 0.016 mol) was added, with stirring, to a cold (-10 °C, ice/methanol) solution of sodium ethoxide prepared from sodium (0.50 g, 0.021 mol) in anhydrous ethanol (60 mL). The deep red solution was stirred at -10 °C for 30 min, during which time a yellowish orange solid precipitated. On filtration it afforded the ylide 18 (6.68 g, 88%). Precipitation from CH_2CCl_2/heptane gave yellow-orange crystals: mp 97-99 °C; ^1H NMR δ 2.23 (s, 3 H, CH_3), 2.72 (d, 1 H, J_{PH} = 29.2, CH=P), 5.44 (dd, 1 H, J = 16.5, J = 7.7, CH=CHCH), 6.17 (d, 2 H, J = 16.5), 6.88-7.66 (m, 20 H, Ar), 8.11 (d, 1 H, CH=N); ^{31}P NMR δ 12.14; mass spectrum, calcd for $C_{30}H_{27}N_2P$ m/e 446.191, found m/e 446.186.

General Preparation of Azine 20. (A) From Isolated Ylide 18. A solution of the ylide 18 (4.46 g, 10 mmol) and the desired aldehyde 19 (15 mmol) in 35 mL of dry acetonitrile was heated under reflux for 2 h. The product precipitated on cooling the reaction mixture. The precipitated azine 20 was recovered by filtration. The residue, azine 20, was recrystallized from methanol to give a yellow analytical sample. Pertinent data are found in Table III and NMR data in Tables IV and V (supplementary material).

(B) From Salt 17 via Ylide 18. The salt 17 (5.72 g, 0.01 mol) was added with stirring to a cold (-10 °C, ice/methanol) solution of sodium ethoxide, prepared from sodium (0.25 g, 0.01 mol) in anhydrous ethanol (35 mL). The deep red solution was stirred at -10 °C for 30 min. To the yellowish orange reaction mixture was added the desired aldehyde (0.015 mol), and the reaction mixture was allowed to boil under reflux for 2 h. The product precipitated on cooling of the reaction mixture. The precipitated 20 was recovered by filtration. The residue, azine 20, was recrystallized from methanol/ethanol to give a yellow-orange analytical sample. The pertinent data are found in Table III and NMR data in Tables IV and V.

General Preparation of Pyrazoles 23/24 from Azines 20. The azine 20 (1 g) was placed, under a nitrogen atmosphere, in a heavy-walled 4-in. glass reaction vessel sealed with a butyl rubber cap and heated in an oil bath (200 °C) for 1 h. The ratio of the pyrazoles 23/24 was determined by gas chromatographic analysis and by ^1H NMR. Table I shows the pertinent results. Tables VI and VII (supplementary material) contain the ^1H NMR parameters for the isolated (by preparative GC) pyrazoles 23 and 24, respectively. The exact mass data for the isolated pyrazoles 23 and 24 were satisfactory.

Preparation of (Phenylethynyl)triphenylphosphonium Bromide (25). (Phenylethynyl)triphenylphosphonium bromide (25) was prepared according to the procedure described by Dickstein and Miller.[10]

Preparation of (2,7-Diphenyl-3,4-diaza-1,4,6-heptatrien-1-yl)triphenylphosphonium Bromide (27). Hydrazine (2 g, 0.06 mol) was added to a solution of (phenylethynyl)triphenylphosphonium bromide (25; 25.9 g, 0.06 mol) in acetonitrile (120 mL) and stirred at room temperature for 1 h. Cinnamaldehyde (18.0 g, 0.12 mol) was added, and stirring was continued at room temperature for an additional 16 h. The yellow compound precipitated, was filtered, and was washed with acetonitrile (10 mL). The residue was dissolved in a minimum amount of methylene chloride and filtered. The filtrate was added dropwise to anhydrous ether (~1200 mL) which on filtration gave 26.3 g (75%) of the pure salt 27: mp 179-180 °C; ^1H NMR δ 4.09 (d, 1 H, J_{P-H} = 18.9, =CHP), 5.30 (dd, 1 H, J = 9.9, J = 15.9, CH=CHCH), 6.61 (d, 1 H, J = 15.9, PhCH=), 6.97-8.04 (m, 25 H, Ar), 8.80 (d, 1 H, J = 9.9, CH=N), 1215 (s, 1 H, NH); ^{31}P NMR δ 16.58.

Anal. Calcd for $C_{35}H_{30}N_2PBr$: C, 71.30; H, 5.09. Found: C, 70.39; H, 5.33.

Preparation of (2,7-Diphenyl-3,4-diaza-2,4,6-heptatrienylidene)triphenylphosphorane (28). The salt 27 (12.3 g, 20.9 mmol) was added, with stirring, to a cold (ice/methanol) solution of sodium ethoxide prepared from sodium (0.5 g, 22 mmole) in anhydrous ethanol (75 mL). The deep orange solution was stirred at room temperature for 30 min. A yellowish orange substance precipitated and was separated by filtration to give 10.1 g (95%) of ylide 28. Purification from CH_2Cl_2/heptane gave dark orange crystals: mp 209-211 °C; ^1H NMR δ 3.20 (d, 1 H, J_{Ph} = 26.6, CH=P), 5.51 (dd, 1 H, J = 16.33, J = 6.1, CH=CHCH), 6.22 (d, 1 H, J = 15.9), 6.92-7.95 (m, 25 H, Ar), 7.97 (d, 1 H, -CH=N-); ^{31}P NMR δ 11.87; mass spectrum, calcd for $C_{35}H_{29}N_2P$ m/e 508.207, found m/e 508.206.

General Preparation of Pyrazoles 32/33 from Ylide 28. Method A. A mixture or solution of ylide 28 (1 mmol) and aldehyde 19 (1 mmol) in acetonitrile/benzene (15 mL, 2/1 ratio) was placed in a heavy-walled reaction bottle and sealed with a butyl rubber cap. The contents were heated in an oil bath (150 °C) for 6.5 h. On completion of the reaction, the solvent was removed by using a rotary evaporator and the crude product dried overnight under vacuum. The ratio of pyrazoles thus obtained was determined by ^1H NMR (see Table II). The ^1H NMR data are found in Tables VIII and IX and the ^{13}C NMR data in Tables X and XI (supplementary material).

Method B. A solution of ylide 28 (1 mmol) and aldehyde (1 mmol) in acetonitrile (25 mL) was stirred at 105-106 °C (oil bath) for 72 h. On completion of the reaction, the solvent was evaporated on a rotary evaporator, and the resulting crude mixture of pyrazoles was dried overnight under vacuum. The ratio of pyrazoles was determined by ^1H NMR (see Table II).

Preparation of Azine 20k. A two-necked round-bottomed flask (50 mL) containing paraformaldehyde (0.3-0.4 g) and equipped with a nitrogen inlet tube was heated in an oil bath at 185-195 °C. Formaldehyde thus generated was passed into a round-bottomed flask (100 mL) containing ylide 18 (3.0 g, 6.7 mmol) in dry ethanol (40 mL) cooled with ice/salt. The reaction mixture was allowed to reflux for 2 h. The solvent was removed by using a rotary evaporator, and the crude product was triturated with boiling petroleum ether (3 × 50 mL) to remove most of the triphenylphosphine oxide. Evaporation of the petroleum ether gave azine (0.99 g, 75%). Pertinent data are listed in Table III and NMR data in Tables IV and V.

Preparation of Pyrazole 23e from Azine 20k. This was done as in the general preparation of pyrazoles: yield 84.0%; ^1H NMR, TLC, and GC indicate only one pyrazole, 23e; ^{13}C NMR δ 13.6 (CH_3), 33.2 (C-1), 106.1 (C-5), 117.6 (C-2), 126.1 (C-14), 126.4 (C-3), 128.3 (C-12), 128.5 (C-13), 130.6 (C-6), 140.2 (C-11), 149.7 (C-4).

Preparation of Pyrazole 32e from Ylide 28. A two-necked round-bottomed flask (50 mL) containing paraformaldehyde (0.25-0.3 g) and equipped with a nitrogen inlet tube was heated

(10) Dickstein, J. I.; Miller, S. I. *J. Org. Chem.* **1972**, *37*, 2168.

in an oil bath at 185–195 °C. Formaldehyde thus generated was passed into a round-bottomed flask (100 mL) containing ylide (1.8 g, 5.9 mmol) in dry acetonitrile (30 mL) cooled with ice/salt. The reaction mixture was allowed to reflux for 72 h. On removal of triphenylphosphine oxide in the usual manner, as described in the previous experiment, pyrazole **32e** was obtained (0.6 g, 75%). Compound **32e** was purified by column chromatography using silica gel and elution with a mixture of petroleum ether (85%) and ethyl acetate (15%). TLC, ^{1}H NMR, and GC indicated the presence of only one pyrazole. Pertinent ^{1}H NMR and ^{13}C NMR data are listed in Tables VIII and X.

Acknowledgment. The generous support of the National Institute of General Medical Sciences (Grant No. GM27620) is gratefully acknowledged. We also thank Dr. Roger Crecely of the University of Delaware for obtaining and discussing the ^{1}H, ^{31}P, and ^{13}C NMR spectra reported in this work with us. Purchase of the Brucker WM 250 was supported, in part, by a grant (GM 27616) from the National Institutes of Health.

Registry No. **12**, 2091-46-5; **13**, 104-55-2; **15**, 52372-79-9; **17**, 80890-24-0; **18**, 80878-43-9; **19a**, 123-11-5; **19b**, 104-87-0; **19c**, 100-52-7; **19d**, 104-88-1; **19e**, 105-07-7; **19f**, 529-20-4; **19g**, 66-77-3; **19h**, 66-99-9; **19i**, 555-16-8; **19j**, 552-89-6; **19k**, 50-00-0; **20a**, 80878-44-0; **20b**, 80878-45-1; **20c**, 80878-46-2; **20d**, 80878-47-3; **20e**, 80878-48-4; **20f**, 80878-49-5; **20g**, 80878-50-8; **20h**, 80878-51-9; **20i**, 80878-52-0; **20j**, 80907-72-8; **20k**, 80878-53-1; **23a**, 80878-54-2; **23b**, 80878-55-3; **23c**, 80878-56-4; **23d**, 80878-57-5; **23e**, 80878-58-6; **23f**, 80878-59-7; **23g**, 80878-60-0; **23h**, 80878-61-1; **23i**, 80878-62-2; **23j**, 80878-63-3; **23k**, 80878-64-4; **24a**, 80890-25-1; **24b**, 80878-65-5; **24c**, 80878-66-6; **24d**, 80878-67-7; **24e**, 80878-68-8; **24f**, 80878-69-9; **24g**, 80878-70-2; **24h**, 80878-71-3; **24i**, 80878-72-4; **24j**, 80878-73-5; **25**, 34387-64-9; **26**, 80878-75-7; **27**, 80890-26-2; **28**, 80878-76-8; **29a**, 80878-77-9; **29b**, 80878-78-0; **29c**, 80878-79-1; **29d**, 80878-80-4; 29e, 80878-81-5; **32a**, 80878-82-6; **32b**, 80878-83-7; **32c**, 80878-84-8; **32d**, 80878-85-9; **32e**, 80878-86-0; **33a**, 80878-87-1; **33b**, 80878-88-2; **33c**, 80878-89-3; **33d**, 80878-90-6.

Supplementary Material Available: The ^{1}H NMR parameters for azines **20** (Table IV), pyrazoles **23** (Table VI), pyrazoles **24** (Table VII), pyrazoles **32** (Table VIII), and pyrazoles **33** (Table IX) and the ^{13}C NMR parameters for azines **20** (Table V), pyrazoles **32** (Table X), and pyrazoles **33** (Table XI) (8 pages). Ordering information is given on any current masthead page.

Studies on the Pinacol Coupling Reaction

Bradford P. Mundy,* Ramanujan Srinivasa, Youseung Kim, and Thomas Dolph

Chemistry Department, Montana State University, Bozeman, Montana 59717

Ronald J. Warnet*[1]

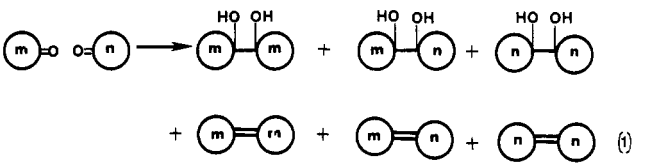
Chemistry Department, Simpson College, Indianola, Iowa 50125

Received May 26, 1981

The mixed pinacol coupling reaction has been carefully analyzed. Although a trend toward statistical distribution of products can be found, it is observed that true statistical distributions are rarely observed. Ring-size and alkyl substituent effects are examined. A through-space heteroatom influence on coupling is noted. By use of (*R*)-(+)-3-methylcyclohexanone, a very specific effect of coupling conditions on product stereochemistry is observed.

Question of Statistical Distribution in a Mixed Coupling. There has been a consensus that the mixed pinacol coupling reaction results in a statistical distribution of products; however, this has never been subjected to critical examination. Since products resulting from mixed couplings might provide useful intermediates for subsequent pinacol rearrangements,[2] we embarked on a careful analysis of this reaction.

Cycloalkanones have been well-characterized as exhibiting differential reactivity of the carbonyl group as a function of ring size, best demonstrated with the careful study by Brown[3] on the borohydride reduction of this series. The potential for differential formation and/or reactivity of anion radicals from these cycloalkanones prompted us to examine this system. Equimolar amounts of two cyclic ketones in THF were added to the [Mg–Hg]/$TiCl_4$ reduction mixture developed by Corey (eq 1).[4]



(1)

After workup of the reactions, the products were examined by GLC to determine product ratios; peak areas of the chromatograms were integrated electronically. Each coupling reaction was independently performed three times. The raw data from the combined experiments are found in the Experimental Section.

For ease of evaluation, the results are presented in graphical format (Figure 1). Examination of the *normalized* pinacol ratios show that although there is a trend toward a statistical distribution of products, even with a liberal 10% error limit arbitrarily placed about the 25% and 50% statistical region, rarely do the experimental

(1) Visiting Professor of Chemistry, Montana State University, 1979–1980.

(2) The problems of regio- and stereocontrol of pinacol rearrangements will be discussed elsewhere.

(3) (a) Brown, H. C.; Ichikawa, K. *Tetrahedron* **1957**, *1*, 22. (b) The reagent has also been used to examine steric effects in the methylcyclohexanones. Rickborn, B.; Wuesthoff, M. T. *J. Am. Chem. Soc.* **1970**, *92*, 6894.

(4) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S. *J. Org. Chem.* **1976**, *41*, 260.

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