Reactions of Azines. 7. Synthesis and Thermal Rearrangement of 1-Oxo-3,4-diaza-2,4,6-heptatrienes and 1-Oxo-3,4-diaza-2,4,6,7-octatetraenes (Allenyl Azines)

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The preparation and "criss-cross" cycloaddition reactions of 1-oxo-3,4-diaza-2,4,6-heptatrienes **5** obtained from 1-substituted triphenylphosphonium 2-[(2-oxo-1,2-diphenylethylidene)hydrazono]propylides **23a–e** and formaldehyde, benzaldehyde, or *p*-nitrobenzaldehyde to give simple substituted pyrazoles **8** are examined (66–89% yield). The 1-benzoyl-substituted phosphorane **23f** fails in the olefination reaction, giving only the corresponding acetylene **24**. A similar allenylization reaction of **23a,d,e** gives the corresponding pyrazolo[5,1-*c*][1,4]oxazines **27** in 65–81% yield with ketene, phenylketene, and benzylketene via the intermediate 1-oxo-3,4-diaza-2,4,6,7-octatetraenes **25**. The benzoyl-substituted ylide **23f** only reacts with unsubstituted ketene **10a** to give **27d** in 21% yield.

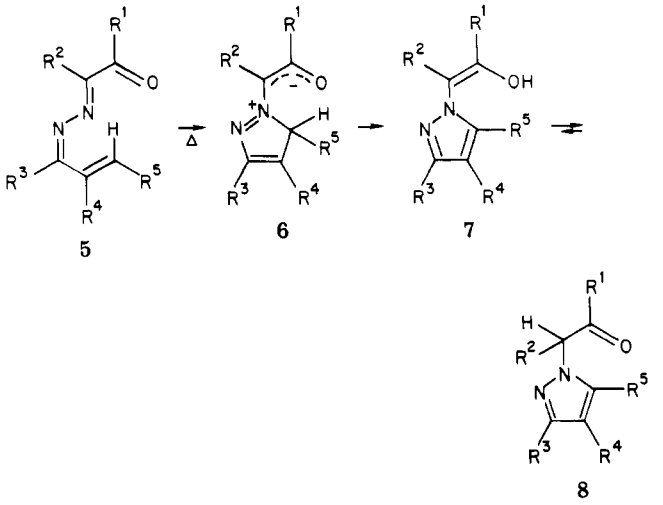
Electrocyclic cyclizations of azines and α,β-unsaturated azines are well-known in the literature.[1-3] We have previously shown[3] a simple, general synthesis of the pyrazole ring system based on the thermolysis of α'-oxo-α,β-unsaturated azines **5**, which were derived from the reactions of α-diketone monohydrazones **1**, with α,β-unsaturated aldehydes and ketones **2** or from the reactions of α-unsubstituted-phosphonium ylide **3**, with aldehydes **4** (Scheme I). We have also shown[2] that cumulated azines, of structure **11**, are excellent synthons for a variety of fused pyrazoles (Scheme II). Cyclization reactions via the azomethine imine **12** have been shown to give pyrazolo[5,1-*c*][1,4]oxazines **13**, 4,9-dihydropyrazolo[1,5-*b*]isoquinolines[2] **14** and 4,5-dihydropyrazolo[1,5-*a*]pyridines[4] **15**, as well as 4,9-dihydropyrazolo[1,5-*b*]isoquinolines[5] **16**. The cumulated azines **11** were prepared by allowing the corresponding phosphoranes **9** to react with ketenes **10**.

Our continued interest in cumulated azines as synthons for fused pyrazole ring systems led us to study the reaction of isocyanate **17** with the phosphorane **9a**.[6] As expected, the intermediate betaine **18** did not collapse to the hoped for ketimine **20** but transferred a proton to give the stabilized amide phosphorane **19** (Scheme III). Transformations of the type **18** to **19** are well-known in the literature.[7] However, early in this century Staudinger and Meyer[8] showed that phosphoranes without a proton on the α-carbon atom underwent normal olefination reactions. Therefore, a suitable α-substituted phosphorane was made for use in the preparation of unsaturated azines.

Alkylation and acylation of phosphorane **9a** and formation of the corresponding phosphoranes **23** have been reported.[9]

We now report the results of the reactions of α-substituted-phosphoranes **23** with aldehydes **4** and ketenes **10**. We report the study of the reactions of **23** with isocyanates **17** in the accompanying paper.

Scheme I



Results and Discussion

Phosphoranes **23a–d** were allowed to react with benzaldehyde and *p*-nitrobenzaldehyde under reflux in acetonitrile and gave colorless pyrazoles **8** in good yields (Table I). Attempted reactions of the benzyl-substituted phosphorane **23e** with benzaldehyde or *p*-nitrobenzaldehyde were unsuccessful even when higher boiling solvent (toluene) was employed. The reduced reactivity may be due to either the steric effect of the α-benzyl group or the stabilizing effect that the benzyl group may have on the phosphorane. In all cases except one, the starting material was recovered unchanged. A reaction occurred successfully only when gaseous formaldehyde was passed over the solution of **23e** in acetonitrile. An 88% yield of **8f** was obtained.

The benzoyl-substituted phosphorane **23f** did not give a pyrazole product in either polar (CH_3CN) or nonpolar (benzene) solvent under reflux conditions with any aldehyde, even formaldehyde. Only ylide **23f** was recovered. The benzoyl group diminishes the nucleophilicity of the α-carbon enough to prevent reaction. But at the higher temperature (toluene solvent) phosphorane **23f** gave the acetylenic azine **24** (Scheme IV). The formation of acetylenes from unsaturated betaines is a well-documented reaction.[9a,10] Attempted thermal rearrangement of the

(1) Wagner-Jauregg, T. *Synthesis* **1976**, 349.
(2) Schweizer, E. E.; Evans, S. *J. Org. Chem.* **1978**, *43*, 4328 and references cited therein.
(3) Albright, T. A.; Evans, S.; Kim, C. S.; Labaw, C. S.; Russiello, A. B.; Schweizer, E. E. *J. Org. Chem.* **1977**, *42*, 3691 and references cited therein.
(4) Schweizer, E. E.; Hayes, J. E.; Hirwe, S. N. unpublished results.
(5) Schweizer, E. E.; Hsueh, W.; Rheingold, A. L.; Durney, R. L. *J. Org. Chem.* **1983**, *48*, 3889.
(6) Evans, S. Ph.D. Thesis, University of Delaware, Newark, DE, June 1977.
(7) Ohshiro, Y. Mori, Y.; Komatsu, K.; Agawa, T. *J. Org. Chem.* **1971**, *36*, 2029. Froyen, *Acta. Chem. Scand., Ser. B* **1974**, *28B*, 586.
(8) Staudinger, H.; Meyer, J. *Chem. Ber.* **1920**, *53*, 72.
(9) (a) Schweizer, E. E. Lee, K. J. *J. Org. Chem.* **1982**, *47*, 2768. (b) Lee, K. J. Ph.D. Thesis, University of Delaware, Newark, DE, 1983.
(10) Trippett, S.; Walker D. M. *J. Chem. Soc.* **1959**, 3874. Gough, S. T. D.; Trippett, S. *Proc. Chem. Soc.* **1961**, 302. Gough, S. T. D.; Trippett, S. *J. Chem. Soc.* **1962**, 2333. Markl, G. *Chem. Ber.* **1961**, *94*, 3005. Bestmann, H. J.; Geismann, C. *Liebigs Annl. Chem.* **1977**, 282.

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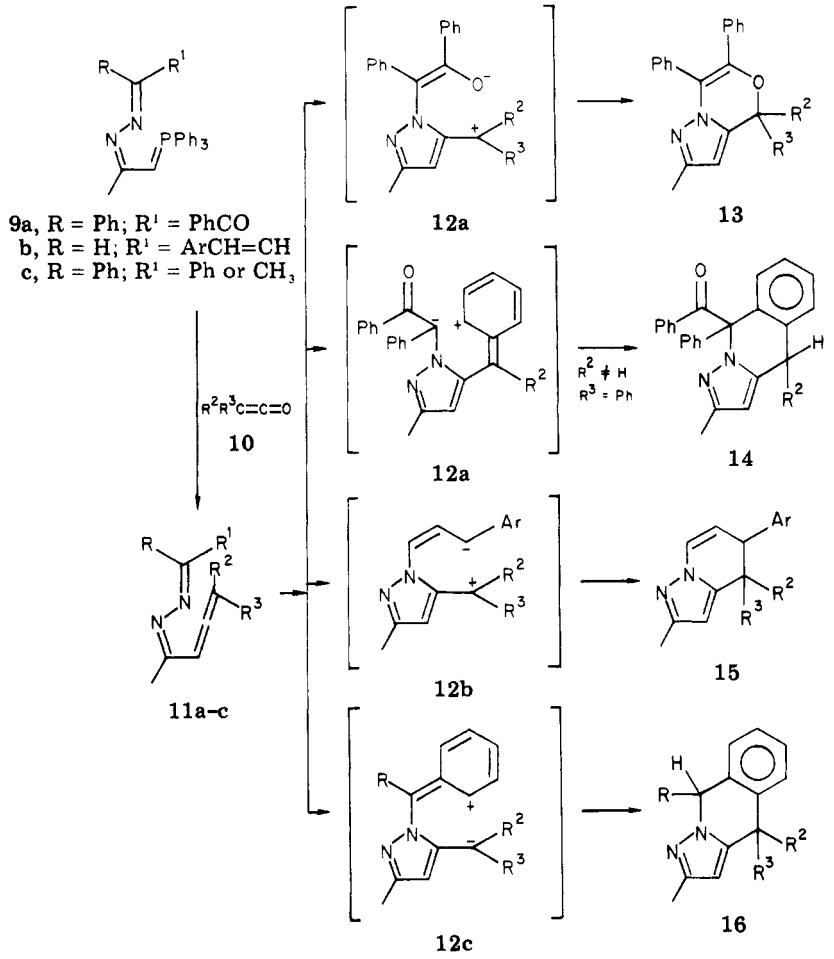
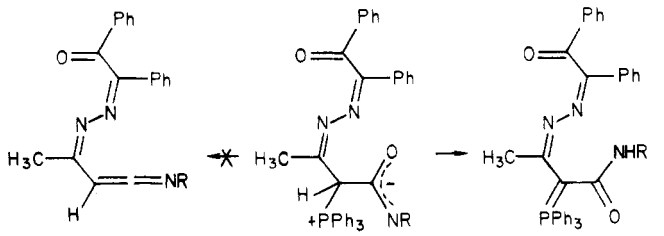
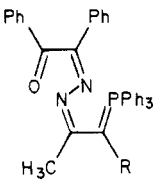
Scheme II



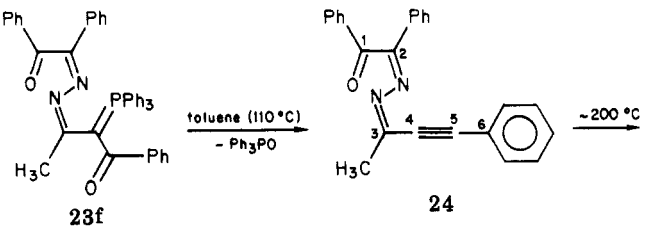
Scheme III





23a, R = CH_3
b, R = C_2H_5
c, R = n-C_3H_7
d, R = H_2C=$CHCH_2$
e, R = $PhCH_2$
f, R = PhCO

Scheme IV



acetylenic azine **24** was unsuccessful (up to 200 °C, 17 h).

The methyl- (**23a**), allyl- (**23d**), and benzyl-substituted (**23e**) azinephosphonium ylides reacted completely at room temperature in benzene with ketene (**10a**) and phenylketene (**10b**). Heating of the initial Wittig reaction mixture without isolation of **25** gave the corresponding pyrazolo[5,1-*c*][1,4]oxazines **27** in 65–73% yield (Scheme V).

The ylides **23a**, **23d**, and **23e** did not react at room temperature with benzylketene (**10c**); however, under refluxing conditions (benzene) the corresponding pyrazolo species **27** were obtained in 72–81% yield.

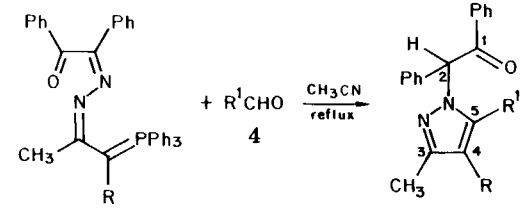
The attempted reaction of the benzoyl ylide **23f** with a variety of substituted ketenes failed. Only the parent ketene **10a** gave a reaction under the conditions employed. The pyrazolo[5,1-*c*][1,4]oxazine **27d** was obtained in only 21% yield.

Thus the utility of α-substituted keto azine phosphoranes **23a–f** for the preparation of allenyl keto azines **25** which undergo "criss-cross" cycloaddition[1] reactions under thermolysis to give pyrazolo[5,1-*c*][1,4] oxazines **27** has been demonstrated. The inhibiting effect of electrophilic groups on the reaction has also been demonstrated. Further utility of cumulated azines as synthons for the fused pyrazolo moiety will be demonstrated in forthcoming papers.

Experimental Section

Melting points were obtained on a Thomas-Hoover Unimelt capillary apparatus and were uncorrected. IR spectra were recorded on a Unicap SP 1100 infrared spectrophotometer and calibrated by comparison with a standard polystyrene film sample.

Table I. Yields, Physical Properties, and Spectroscopic Data of Pyrazoles 8

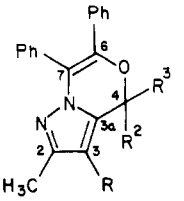


8

no.	R	R^1	rxn time h	% yld	mp, °C	formula[a]	IR,[b] cm^{-1}	^1H NMR,[c] δ	^{13}C NMR,[c] δ
8a	CH_3	Ph	40	66	121–122	$C_{25}H_{22}N_2O$	1705, 1595	1.90 (s, 3 H, C4 CH_3), 2.15 (s, 3 H, C3 CH_3), 6.56 (s, 1 H, C2 H), 7.22–7.38 (m, 13 H, Ar), 7.63 (m, 2 H, Ar ortho to C=O)	193.1 (Cl), 66.9 (C2), 148.1 (C3), 113.7 (C4), 141.7 (C5), 12.1 (C3 CH_3), 8.5 (C4 CH_3)
b	CH_3	*p*-O_2NPh	15	89	189–190	$C_{25}H_{21}N_3O_3$	1710, 1605	1.90 (s, 3 H, C4 CH_3), 2.18 (s, 3 H, C3 CH_3), 6.71 (s, 1 H, C2 H), 7.17–7.48 (m, 10 H, Ar), 7.66 (m, 2 H, Ar ortho to C=O), 8.16 (m, 2 H, Ar ortho to NO_2)	193.2 (Cl), 68.5 (C2), 147.6 (C3), 115.2 (C4), 139.9 (C5), 12.0 (C3 CH_3), 8.4 (C4 CH_3)
c	CH_3CH_2	*p*-O_2NPh	15	88	176–177	$C_{26}N_{23}N_3O_3$	1715, 1610	0.97 (t, J = 7.3, 3 H, CH_2CH_3), 2.23 (s, 3 H, C3 CH_3), 2.27 (q, J = 7.3, 2 H, CH_2CH_3), 6.70 (s, 1 H, C2H), 7.11–7.51 (m, 10 H, Ar), 7.66 (m, 2 H, Ar ortho to C=O), 8.16 (m, 2 H, Ar ortho to NO_2)	193.3 (Cl), 68.6 (C2), 147.6 (C3), 108.3 (C4), 139.6 (C5), 12.0 (C3 CH_3), 15.3 (CH_2CH_3), 16.6 (CH_2CH_3)
d	$CH_3CH_2CH_2$	*p*-O_2NPh	15	80	143–144	$C_{27}H_{25}N_3O_3$	1710, 1605	0.77 (t, J = 7.3, 3 H, $CH_2CH_2CH_3$), 1.36 (q, J = 7.5, 2 H, $CH_2CH_2CH_3$), 2.22 (t, J = 6.4, 2 H, $CH_2CH_2CH_3$), 2.23 (s, 3 H, C3 CH_3), 6.77 (s, 1 H, C2 H), 7.08–7.54 (m, 10 H, Ar), 7.67 (m, 2 H, Ar ortho to C=O), 8.12 (m, 2 H, Ar ortho to NO_2)	193.2 (Cl), 68.6 (C2), 147.5 (C3), 108.3 (C4), 140.0 (C5), 12.1 (C3 CH_3); 13.8 ($CH_2CH_2CH_3$), 23.7 ($CH_2CH_2CH_3$), 25.3 ($CH_2CH_2CH_3$)
e	CH_2=$CHCH_2$[d]	Ph	40	67	105–106	$C_{27}H_{24}N_2O$	1700, 1590	2.12 (s, 3 H, C3 CH_3), 3.04 (m, 2 H, CH_2CH=CH_2), 4.72 (d, J = 17.2, 1 H, Hc), 4.95 (d, J = 10.3, 1 H, Hb), 5.85 (m, 1 H, Ha), 6.53 (s, 1 H, C2H), 7.21–7.44 (m, 13 H, Ar), 7.60 (m, 2 H, Ar ortho to C=O)	193.1 (C1), 67.0 (C2), 148.5 (C3), 115.4 (C4), 142.4 (C5), 12.0 (C3 CH_3), 27.6 (CH_2CH=CH_2), 136.8 (CH_2CH=CH_2), 114.6 (CH_2CH=CH_2)
f	$PhCH_2$	H	15	88	105–106	$C_{25}H_{22}N_2O$	1700, 1600	2.13 (s, 3 H, C3 CH_3), 3.74 (s, 2 H, CH_2Ph), 7.09–7.51 (m, 15 H, C2 H + C5 H + Ar), 7.94 (m, 2 H, Ar ortho to C=O)	194.1 (C1), 69.9 (C2), 147.7 (C3), 118.3 (C4), 133.7 (C5), 11.9 (C3 CH_3), 30.1 (CH_2Ph)

[a] Parent peaks agree to within ±0.003. In **8d** no M^+ ion exists. [M^+ − 105] ion is major peak. [b] Carbonyl and pyrazole (C=N/C=C) frequencies. [c] $DCCl_3$ solution. [d] ^1H NMR assignment of allyl group is 

Table II. Selected ^{13}C NMR Parameters[a] for 4*H*-Pyrazolo[5,1-*c*][1,4]oxazines 27

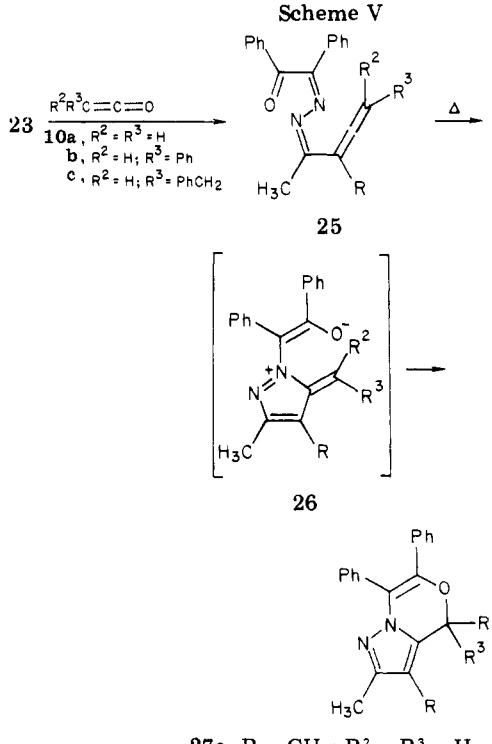


27

no.	R	R^2	R^3	C2	C3	C3a	C4	C6	C7	miscellaneous
27a	CH_3	H	H	148.9	109.3	139.4	62.4	133.9	120.8	12.0 (C2 CH_3), 7.5 (C3 CH_3)
b	CH_2=$CHCH_2$	H	H	148.7	111.4	139.6	62.4	133.7	120.8	12.1 (C2 CH_3), 27.3 (CH_2CH=CH_2), 136.0 (CH_2CH=CH_2), 115.4 (CH_2CH=CH_2)
c	$PhCH_2$	H	H	148.6	113.0	139.9	62.4	133.6	120.8	12.3 (C2 CH_3), 29.3 (CH_2Ph)
d	PhCO	H	H	150.9	116.1	142.4	63.1	133.4	120.1	14.3 (C2 CH_3), 213.6 (COPh)
e	CH_3	H	Ph	148.8	110.2	137.9	74.7	133.7	120.3	11.9 (C2 CH_3), 7.2 (C_3CH_3)
f	CH_2=$CHCH_2$	H	Ph	149.0	112.4	138.2	74.7	133.8	120.5	12.3 (C2 CH_3), 27.2 (CH_2CH=CH_2), 135.6 (CH_2CH=CH_2), 115.2 (CH_2CH=CH_2)
g	$PhCH_2$	H	Ph	149.1	113.7	138.1	74.6	133.7	120.4	12.5 (C2 CH_3), 28.9 (CH_2Ph)
h	CH_3	H	$PhCH_2$	148.5	110.0	136.9	73.7	134.1	119.7	12.0 (C2 CH_3), 6.9 (C3 CH_3), 40.2 (C4 CH_2Ph)
i	CH_2=$CHCH_2$	H	$PhCH_2$	148.6	111.5	137.0	73.4	133.9	119.7	12.2 (C2 CH_3), 27.0 (CH_2CH=CH_2), 135.7 (CH_2CH=CH_2), 115.3 (CH_2CH=CH_2), 40.1 (C4 CH_2Ph)
j	$PhCH_2$	H	$PhCH_2$	148.6	113.1	137.1	73.5	133.9	119.8	12.4 (C2 CH_3), 28.7 (C3 CH_2Ph), 39.9 (C4 CH_2Ph)

[a] Chemical shifts reported as parts per million vs. Me_4Si in $CDCl_3$ solution.

Scheme V



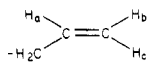
23 → 25 → 26 → 27

10a, $R^2 = R^3 = H$
b, $R^2 = H$; $R^3 = Ph$
c, $R^2 = H$; $R^3 = PhCH_2$

27a, R = CH_3; $R^2 = R^3 = H$
b, R = CH_2=$CHCH_2$; $R^2 = R^3 = H$
c, R = $PhCH_2$; $R^2 = R^3 = H$
d, R = PhCO, $R^2 = R^3 = H$
e, R = CH_3; $R^2 = H$; $R^3 = Ph$
f, R = CH_2=$CHCH_2$; $R^2 = H$, $R^3 = Ph$
g, R = $PhCH_2$; $R^2 = H$; $R^3 = Ph$
h, R = CH_3; $R^2 = H$; $R^3 = PhCH_2$
i, R = CH_2=$CHCH_2$; $R^2 = H$; $R^3 = PhCH_2$
j, R = $PhCH_2$; $R^2 = H$; $R^3 = PhCH_2$

Precise mass spectra were recorded by using a DuPont 21-492B instrument with a resolution of 3300 or 5000.

The ^1H and ^{13}C NMR spectra of approximately 10% (w/v) solutions in $CDCl_3$ were obtained on a Bruker Spectrospin Model WM 250. Chemical shifts are reported 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 hertz (J), singlet (s), doublet (d), doublet of doublets (dd), triplet (t), quartet (q), and multiplet (m). Selected ^{13}C NMR parameters for compounds **27** are collected in Table II. The assignment of the allyl group in the ^1H NMR is as shown below. The numbering system of the pyrazolo[5,1-*c*][1,4]oxazines **27** is as shown in Table II.



Dry nitrogen gas was routinely employed as the reaction atmosphere in all reactions. Acetonitrile was dried over calcium hydride, followed by its distillation over P_2O_5. Benzene was dried and distilled from sodium metal. In light of its toxicity, benzene should be replaced by toluene in any attempts to repeat or extend this work. All glassware was baked at 150 °C for a minimum of 4 h before use. Baker silica gel (60–200 mesh) and EM 7747 silica gel for column chromatography[11] were used throughout for product separation.

The following compounds were prepared by known methods: triphenyl[1-methyl-2-[(phenylphenacylidene)hydrazono]-propylidene]phosphorane (**23a**),[9a] triphenyl[1-ethyl-2-[(phenylphenacylidene)hydrazono]propylidene]phosphorane (**23b**),[9b] triphenyl[1-propyl-2-[(phenylphenacylidene)hydrazono]-propylidene]phosphorane (**23c**),[9b] triphenyl-[1-(2-propenyl)-2-[(phenylphenacylidene)hydrazono]propylidene]phosphorane (**23d**),[9a] triphenyl[1-benzyl-2-[(phenylphenacylidene)hydrazono]-propylidene]phosphorane (**23e**),[9a] and triphenyl[1-benzoyl-2-[(phenylphenacylidene)hydrazono]propylidene]phosphorane (**23f**).[9a]

Reactions of Triphenyl[1-alkyl-2-[(phenylphenacylidene)hydrazono]propylidene]phosphoranes 23 with Aldehydes 4. Preparation of 2-(3,4,5-Trisubstituted-1*H*-pyrazol-1-yl)-1,2-diphenylethanone (8a–e). General Method. A solution of phosphorane **23a–d** (4.00 mmol) and aldehyde **4** (4.40 mmol) in 30 mL of acetonitrile was stirred under reflux for the amount of time indicated in Table I. Removal of solvent in vacuo afforded an oil from which **8a–e** were isolated by column chromatography (silica gel, 7:3 *n*-Hex–EtOAc as eluent). An analytical sample was prepared by crystallization from ethanol. The pertinent physical properties and the spectroscopic data are listed in Table I.

Reaction of Triphenyl[1-benzyl-2-[(phenylphenacylidene)hydrazono]propylidene]phosphorane (23e) with Formaldehyde. Preparation of 2-(4-Benzyl-3-methyl-1*H*-pyrazol-1-yl)-1,2-diphenylethanone (8f). A two-necked,

(11) Taber, D. F. *J. Org. Chem.* **1982**, *47*, 1351.

round-bottomed flask (50 mL) containing paraformaldehyde (0.25–0.3 g) and equipped with a nitrogen inlet tube was heated in an oil bath at 185–190 °C. Formaldehyde thus generated was carried by a slow current of dry nitrogen over into a round-bottomed flask (100 mL) containing phosphorane **23e** (2.46 g, 4.0 mmol) in 30 mL of acetonitrile at room temperature. At the end of about 5 min, the reaction was complete, as indicated by a color change (red to yellow). The reaction mixture was then allowed to reflux for 15 h. Removal of the solvent in vacuo afforded an oil from which **8f** (1.29 g, 88%) was isolated by column chromatography [silica gel, CH_2Cl_2 as eluent]. An analytical sample was prepared by crystallization from petroleum ether. The pertinent physical properties and the spectroscopic data are listed in Table I.

Thermolysis of Phosphorane 23f. Preparation of 1-Phenyl-3-[(phenylphenacylidene)hydrazono]-1-butyne (24). A solution of phosphorane **23f** (1.59 g, 2.5 mmol) in 20 mL of toluene was stirred under reflux for 24 h. Removal of the solvent in vacuo afforded an oil from which **24** (0.86 g, 97%) was isolated by column chromatography (silica gel, 7:1 *n*-Hex–EtOAc as eluent). A yellow analytical sample was prepared by crystallization from ethanol: mp 103–104 °C; IR (KBr) 2220 (C≡C), 1680 (C=O), 1660, 1575 cm^{-1}; ^1H NMR δ 2.15/2.36 (s, 3 H, CH_3, syn/anti = 3/1 or vice versa), 7.24–7.61/7.78–7.95 (m, 15 H, Ar, syn/anti = 3/1 or vice versa); ^{13}C NMR[12] δ 197.2 (C1), 163.8/162.3 (C2), 149.7/151.8 (C3), 101.5 (C4), 84.0 (C5), 121.8 (C6), 23.9/20.2 (CH_3) [syn/anti or vice versa].

Precise mass calcd for $C_{24}H_{18}N_2O$: 350.142. Found: 350.140.

Reaction of Phosphorane 23a with Ketene (10a). Preparation of 2,3-Dimethyl-6,7-diphenyl-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27a). Ketene was generated by the pyrolysis of acetone according to the method of Williams and Hurd.[13] The ketene stream was bubbled through a solution of 1.08 g (2.0 mmol) of phosphorane **23a** in 20 mL of benzene for 5 min at room temperature. The resulting solution was stirred for 5 min at room temperature and 2 h under reflux. After removal of the solvent in vacuo, crude **27a** (0.44 g, 73%) was isolated as a slightly tan solid by trituration of the residue with cold ethanol. Recrystallization from ethanol afforded a colorless analytical sample: mp 163–164 °C; IR (KBr) 1652, 1605, 1505, 1480, 1450 cm^{-1}; ^1H NMR δ 1.99 (s, 3 H, C3 CH_3), 2.19 (s, 3 H, C2 CH_3), 5.25 (s, 2 H, C4 H_2), 7.15–7.43 (m, 10 H, Ar); mass spectrum, *m/z* (% base peak) 303 (22.1, $M^+ + 1$), 302 (100, M^+), 301 (22.1, $M^+ - 1$), 273 (17.3), 197 (37.7), 105 (16.9), 77 (20.6).

Precise mass calcd for $C_{20}H_{18}N_2O$: 302.142. Found: 302.142.

Reaction of Phosphorane 23d with Ketene (10a). Preparation of 6,7-Diphenyl-2-methyl-3-(2-propenyl)-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27b). Phosphorane **23d** (1.13 g, 2.0 mmol) was reacted as above (preparation of **27a**) with ketene. Column chromatography (silica gel, 7:1 *n*-Hex–EtOAc as eluent) of the reaction mixture yielded 0.44 g (68%) of **27b** as a solid. Recrystallization from ethanol afforded a colorless analytical sample: mp 144–145 °C; IR (KBr) 1650, 1602, 1580, 1500, 1470, 1450 cm^{-1}; ^1H NMR δ 2.18 (s, 3 H, C2 CH_3); 3.18 (d, J = 6.0, 2 H, $CH_2CH{=}CH_2$), 5.05 (dd, J_{trans} = 16.4 and J = 1.6, 1 H, H_c), 5.06 (dd, J_{cis} = 10.4 and J = 1.1, H_b), 5.25 (s, 2 H, C4 H_2), 5.89 (m, 1 H, H_a), 7.15–7.44 (m, 10 H, Ar); mass spectrum, *m/z* (% base peak) 329 (24.4, $M^+ + 1$), 328 (100, M^+), 327 (18.5, $M^+ - 1$), 299 (14.4), 223 (15.4), 105 (28.4), 77 (43.6).

Precise mass calcd for $C_{22}H_{20}N_2O$: 328.158. Found: 328.158.

Reaction of Phosphorane 23e with Ketene (10a). Preparation of 3-Benzyl-6,7-diphenyl-2-methyl-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27c). Phosphorane **23e** (1.23 g, 2.0 mmol) was reacted as above with ketene. Column chromatography (silica gel, 7:1 *n*-Hex–EtOAc as eluent) of the reaction mixture yielded 0.53 g (70%) of **27c** as a solid. Recrystallization from ethanol afforded a colorless analytical sample: mp 185–186 °C; IR (KBr) 1650, 1600, 1560, 1500, 1470, 1450 cm^{-1}; ^1H NMR δ 2.17 (s, 3 H, C2 CH_3), 3.79 (s, 2 H, CH_2Ph), 5.01 (s, 2 H, C4 H_2), 7.12–7.45 (m, 15 H, Ar); mass spectrum, *m/z* (% base peak) 379 (3.0, $M^+ + 1$), 378 (13.7, M^+), 261 (20.7), 105 (25.3).

Precise mass calcd for $C_{26}H_{22}N_2O$: 378.173. Found: 378.171.

(12) The numbering system used in the ^{13}C NMR is as shown in Scheme II.

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

Reaction of Phosphorane 23f with Ketene (10a). Preparation of 3-Benzoyl-6,7-diphenyl-2-methyl-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27d). The ketene stream was bubbled through a solution of 1.25 g (2.0 mmol) of phosphorane **23f** in 20 mL of benzene for 40 min at reflux temperature. After stirring for 25 h under reflux, the solvent was removed in vacuo and the residue chromatographed on silica gel column eluting with *n*-Hex–EtOAc (7:1). This procedure yielded 0.16 g (21%) of **27d** and 0.35 g of unreacted phosphorane **23f**. Recrystallization from ethanol afforded a colorless analytical sample: mp 142–143 °C; IR (KBr) 1650, 1600, 1545, 1495, 1460 cm^{-1}; ^1H NMR δ 2.29 (s, 3 H, C2 CH_3) 5.19 (s, 2 H, C4 H_2), 7.15–7.52 (m, 13 H, Ar), 7.72 (m, 2 H, Ar ortho to C=O); mass spectrum, *m/z* (% base peak) 393 (30.1, $M^+ + 1$), 392 (59.8, M^+), 391 (24.5, $M^+ - 1$), 363 (8.6), 287 (100, $M^+ - PhCO$), 105 (72.2), 77 (71.3).

Precise mass calcd for $C_{26}H_{20}N_2O_2$: 392.152. Found: 392.155.

Reaction of Phosphorane 23a with Phenylketene (10b). Preparation of 2,3-Dimethyl-4,6,7-triphenyl-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27e). To an orange solution of 2.15 g (4.0 mmol) of phosphorane **23a** and 1.28 g (12.70 mmol) of triethylamine in 30 mL of benzene was added dropwise over 10 min at room temperature 1.32 g (8.54 mmol) of phenylacetylchloride in 10 mL of benzene. There was a slight exotherm, the color faded to a pale orange, and a very fine precipitate formed. The hazy solution was stirred at ambient temperature for 1 h and under reflux for 2 h. After removal of solvent in vacuo, the crude reaction product was chromatographed on a silica gel column, eluting with methylene chloride, yielding 0.98 g (65%) of **27e** as a solid. Recrystallization from ethanol afforded a colorless analytical sample: mp 169–170 °C; IR (KBr) 1635, 1602, 1495, 1450 cm^{-1}; ^1H NMR δ 1.69 (s, 3 H, C3 CH_3), 2.19 (s, 3 H, C2 CH_3), 6.35 (s, 1 H, C4 H), 7.05 –7.44 (m, 15 H, Ar); mass spectrum, *m/z* (% base peak) 379 (11.6, $M^+ + 1$), 378 (40.6, M^+), 377 (3.8, $M^+ - 1$), 349 (8.3), 301 (10.5), 273 (100), 105 (35.4).

Precise mass calcd for $C_{26}H_{22}N_2O$: 378.173. Found: 378.175.

Reaction of Phosphorane 23d with Phenylketene (10b). Preparation of 2-Methyl-3-(2-propenyl)-4,6,7-triphenyl-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27f). Phosphorane **23d** (2.26 g, 4.0 mmol) was reacted as above with 1.28 g (12.70 mmol) of triethylamine and 1.32 g (8.54 mmol) of phenylacetyl chloride. Column chromatography (silica gel, 7:1 *n*-Hex–EtOAc) of the crude product yielded 1.05 g (65%) of **27f** as an oil. Crystallization from ethanol afforded a colorless analytical sample: mp 104–105 °C; IR (KBr) 1645, 1602, 1500, 1450 cm^{-1}; ^1H NMR δ 2.20 (s, 3 H, C2 CH_3), 2.83 and 2.96 (dd, J_{gem} = 16.3, J_{vic} = 6.0, 1 H each, $CH_2CH{=}CH_2$), 4.87 (dd, J_{trans} = 16.7 and J = 1.7, 1 H, H_c), 4.91 (J_{cis} = 9.8 and J = 1.4, 1 H, H_b), 5.66 (m, 1 H, H_a), 6.40 (s, 1 H, C4 H), 7.04–7.41 (m, 15 H, Ar); mass spectrum, *mz* (% base peak) 405 (5.6, $M^+ + 1$), 404 (14.4, M^+), 299 (31.9), 167 (76.9), 105 (28.1), 77 (57.5).

Precise mass calcd for $C_{28}H_{24}N_2O$: 404.189. Found: 404.186.

Reaction of Phosphorane 23e with Phenylketene (10b). Preparation of 3-Benzyl-2-methyl-4,6,7-triphenyl-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27g). Phosphorane **23e** (2.46 g, 4.0 mmol) was reacted as above with 1.28 g (12.70 mmol) of triethylamine and 1.32 g (8.54 mmol) of phenylacetyl chloride. Column chromatography (silica gel, CH_2Cl_2 as eluent) of the crude product yielded 1.21 g (67%) of **27g** as a solid. Recrystallization from ethanol afforded a colorless analytical sample: mp 138–139 °C; IR (KBr) 1650, 1602, 1495, 1450 cm^{-1}; ^1H NMR δ 2.16 (s, 3 H, C2 CH_3), 3.46 and 3.62 (d, J = 16.1, 1 H each, CH_2Ph), 6.18 (s, 1 H, C_4H), 6.95–7.42 (m, 20 H, Ar); mass spectrum, *m/z* (% base peak) 455 (5.9, $M^+ + 1$), 454 (13.8, M^+), 349 (30.5), 105 (47.2), 77 (81.8).

Precise mass calcd for $C_{32}H_{26}N_2O$: 454.204. Found: 454.204.

Reaction of Phosphorane 23a with Benzylketene (10c). Preparation of 4-Benzyl-2,3-dimethyl-6,7-diphenyl-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27h). To an orange solution of 1.08 g (2.0 mmol) of phosphorane **23a** and 0.60 g (6.0 mmol) of triethylamine in 20 mL of benzene was added dropwise over a 5-min period 0.68 g (4.0 mmol) of β-phenylpropionyl chloride in 10 mL of benzene. The resulting hazy solution was then stirred under reflux for 4 h. After removal of solvent in vacuo, the crude reaction product was chromatographed on a silica gel column, eluting with *n*-Hex–EtOAc (7:1), yielding 0.64 g (81%) of **27h** as an oil: IR (CCl_4) 1640, 1602, 1500, 1450 cm^{-1}; ^1H NMR δ 1.53 (s,

3 H, C3 CH_3), 2.14 (s, 3 H, C2 CH_3), 3.29 (d, J = 7.0, 2 H, C4 CH_2Ph), 5.58 (t, J = 7.0, 1 H, C4H), 7.04–7.36 (m, 15 H, Ar); mass spectrum, m/z (% base peak) 393 (7.5, $M^+ + 1$), 392 (13.6, M^+), 302 (24.7), 301 (100), 105 (85.4), 77 (50.3).

Precise mass calcd for $C_{27}H_{24}N_2O$: 392.189. Found: 392.187.

Reaction of Phosphorane 23d with Benzylketene (10c). Preparation of 4-Benzyl-6,7-diphenyl-2-methyl-3-(2-propenyl)-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27i). Phosphorane **23d** (1.13 g, 2.0 mmol) was reacted as above with 0.60 g (6.0 mmol) of triethylamine and 0.68 g (4.0 mmol) of β-phenylpropionyl chloride. Column chromatography (silica gel, 7:1 *n*-Hex–EtOAc) of the crude reaction product yielded 0.62 g (74%) of **27i** as an oil. Crystallization from hexane–ether afforded a colorless analytical sample: mp 118–120 °C; IR (CCl_4) 1642, 1602, 1500, 1450 cm^{-1}; ^1H NMR δ 2.15 (s, 3 H, C2 CH_3), 2.69 and 2.94 (dd, J_{gem} = 16.5, J_{vic} = 6.1, 1 H each, $CH_2CH{=}CH_2$), 3.20 and 3.31 (dd, J_{gem} = 13.6, J_{vic} = 6.6, 1 H each, C4 CH_2Ph), 4.97 (dd, J_{trans} = 16.9 and J = 1.7, 1 H, H_c), 5.01 (dd, J_{cis} = 10.1 and J = 1.6, 1 H, H_b), 5.65 (t, J = 6.6, 1 H, C4H), 5.68 (m, 1 H, H_a), 7.07–7.32 (m, 15 H, Ar); mass spectrum, m/z (% base peak) 419 (10.7, $M^+ + 1$), 418 (20.0, M^+), 328 (25.3), 327 (100), 105, (34.5), 91 (16.9), 77 (12.2).

Precise mass calcd for $C_{29}H_{26}N_2O$: 418.204. Found: 418.203.

Reaction of Phosphorane 23e with Benzylketene (10c). Preparation of 3,4-Dibenzyl-6,7-diphenyl-2-methyl-4*H*-pyrazolo[5,1-*c*][1,4]oxazine (27j). Phosphorane **23e** (1.23 g, 2.0 mmol) was reacted as above with 0.60 g (6.0 mmol) of triethylamine and 0.68 g (4.0 mmol) of β-phenylpropionyl chloride. Column chromatography [silica gel, 7:1 *n*-Hex–EtOAc] of the crude reaction product yielded 0.67 g (72%) of **27j** as an oil. Crystallization from ethanol afforded a colorless analytical sample: mp 138–139 °C; IR (KBr) 1650, 1610, 1500, 1455 cm^{-1}; ^1H NMR δ 2.15 (s, 3 H, C2 CH_3), 3.01 and 3.19 (dd, J_{gem} = 13.6, J_{vic} = 6.8, 1 H each, C4 CH_2Ph), 3.29 and 3.55 (d, J_{gem} = 16.4, 1 H each, C3 CH_2Ph) 5.41 (t, J = 6.8, 1 H, C4H), 7.05–7.35 (m, 20 H, Ar); mass spectrum, m/z (% base peak) 469 (8.0, $M^+ + 1$), 468 (20.7, M^+), 378 (31.9), 377 (100), 105 (18.8), 91 (58.6), 77 (31.9).

Precise mass calcd for $C_{33}H_{28}N_2O$: 468.220. Found: 468.220.

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Registry No. **8a**, 89849-20-7; **8b**, 89849-21-8; **8c**, 89849-22-9; **8d**, 89849-23-0; **8e**, 89849-24-1; **8f**, 89849-25-2; **10a**, 463-51-4; **10b**, 3496-32-0; **10c**, 87101-44-8; **23a**, 81724-92-7; **23b**, 89726-08-9; **23c**, 89726-09-0; **23d**, 81724-93-8; **23e**, 81724-94-9; **23f**, 81724-95-0; **24**, 89849-26-3; **27a**, 89849-27-4; **27b**, 89849-28-5; **27c**, 89849-29-6; **27d**, 89849-30-9; **27e**, 89873-79-0; **27f**, 89849-31-0; **27g**, 89849-32-1; **27h**, 89849-33-2; **27i**, 89849-34-3; **27j**, 89849-35-4; PhCHO, 100-52-7; *p*-$O_2NC_6H_4CHO$, 555-16-8; CH_2O, 50-00-0.

Reactions of Azines. 8. Rearrangement of 1-Oxo-3,4,8-triaza-2,4,6,7-octatetraenes to 2,3-Dihydro-1*H*-imidazo[1,2-*b*]pyrazol-2-ones and 4,9-Dihydropyrazolo[5,1-*b*]quinazolines

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Reactions of phosphoranes **1** with isocyanates **2** have given excellent yields of 4,9-dihydropyrazolo[5,1-*b*]-quinazolines **10** and 2,3-dihydro-1*H*-imidazo[1,2-*b*]pyrazol-2-ones **13** presumably via the intermediate 1-oxo-3,4,8-triaza-2,4,6,7-octatetraenes **3**. The ratios of the compounds **10** to **13** increased as the bulk of the substituents increase on the phosphoranes **1** and isocyanates **2** and were determined from the ^1H NMR data. The ratio of **10** to **13** decreased upon changing the para substituents on the phenyl isocyanate in the following order: CH_3O, CH_3, H, Cl, CF_3, and NO_2 (i.e., in order of increasing σ_p value). There was a linear relationship between σ_p value and the ratio of log [**10**/**13**], ρ = –0.5. The ratios of **10** to **13** in the reaction of α-ethylphosphorane with undistilled isocyanates were almost all the same, 65 ± 2/35 ± 2, and reversed compared to the results observed when freshly distilled isocyanates were used.

In this work we report[1] a new synthesis of 2,3-dihydro-1*H*-imidazo[1,2-*b*]pyrazol-2-ones **13** and 4,9-dihydropyrazolo[5,1-*b*]quinazolines **10** based on the thermal rearrangement of 1-oxo-3,4,8-triaza-2,4,6,7-octatetraenes **3**. The antitumor activity of the imidazo[1,2-*b*]pyrazole ring system has received considerable attention during the past few years.[2-4] We have found that 2,3-dihydro-1*H*-imidazo[1,2-*b*]pyrazol-2-ones may be readily converted into imidazo[1,2-*b*]pyrazoles.[5] The known medicinal activity of fused pyrazoles has also spurred considerable research into the synthesis of imidazo[1,2-*b*]pyrazoles[6-10] as well as the pyrazolo[5,1-*b*]quinazolines.[11-14]

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