Heterocyclic N-Oxides as Synthetic Intermediates. 5. Synthesis of 5-Aminopyridazine 1-Oxides[1]

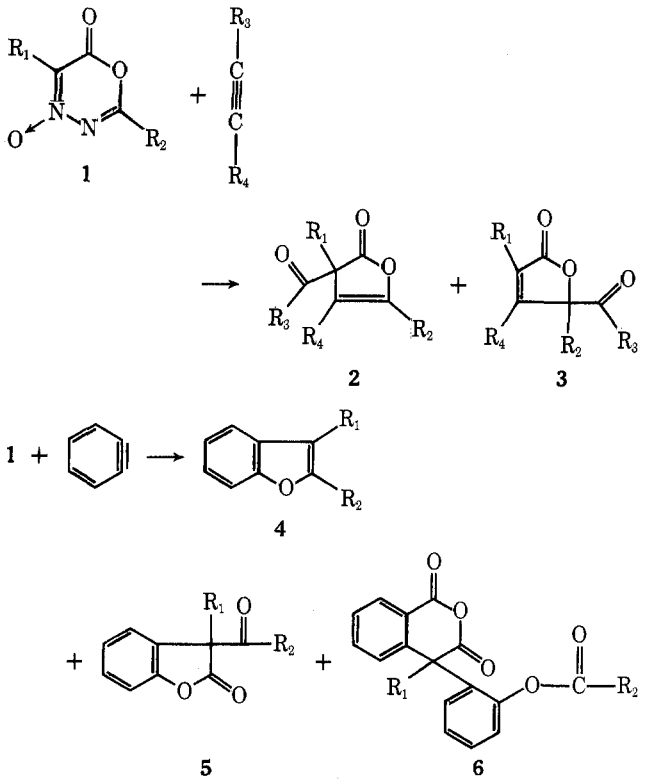
Jeremiah P. Freeman* and Raymond C. Grabiak[2]

Department of Chemistry, University of Notre Dame, Notre Dame, Indiana 46556

Received July 20, 1976

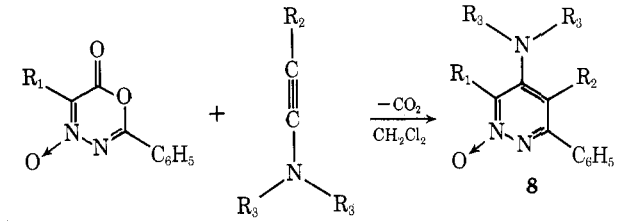
Condensation of 1,3,4-oxadiazin-6-one 4-oxides (1) with ynamines 7 produces 5-aminopyridazine 1-oxides 8 in good yields. The reaction is completely regiospecific and no 4-amino isomer is produced. Deoxygenation with phosphorus trichloride provides the parent 4-aminopyridazines 10. Mechanisms involving a concerted [2 + 4] cycloaddition or a two-step process initiated by attack of the ynamine at the imidate carbon of 1 are considered. In one case a pyrazole derivative, 1-dimethylcarbamyl-3,4,5-triphenylpyrazole, was isolated along with the 5-aminopyridazine 1-oxide 8c suggesting competition between 1,3 and 1,4 cycloaddition pathways.

We have recently reported the cycloadditions of 1,3,4-oxadiazin-6-one 4-oxides (1) with acetylenes[3] and benzyne.[4] The acetylene cycloadditions yielded acylbutenolides 2 and 3, while the benzyne cycloadditions produced benzofurans 4, benzofuranones 5, and homophthalic anhydrides 6.

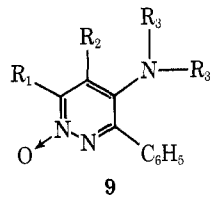


These products (2–6) result from deep-seated rearrangements which could be rationalized on the basis of first-formed 1,3-dipolar cycloadducts. These transformations are analogous to those proposed in the cycloaddition of 3,4-diazacyclopentadienone oxides with acetylenes.[5]

In continuation of our interest in this area, we now have investigated the cycloaddition of 1 with ynamines (7). Under very mild conditions an exothermic reaction accompanied by the evolution of carbon dioxide produced pyridazine oxides (8) in high yields (Table I). This transformation is analogous to the Diels–Alder reaction of α-pyrones with acetylenes[6] and occurs in a highly regioselective manner, since the isomeric pyridazine oxide (9) was not detected in any case (^{1}H NMR analysis). The structure of these pyridazine oxides (8) is based on elemental analysis, spectral information, chemical evidence, and mechanistic considerations.

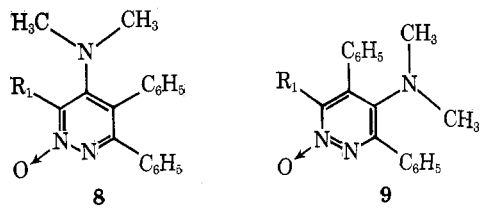


1a, C_6H_5 7a, $R_2 = CH_3$; $R_3 = C_2H_5$
b, CH_3 b, $R_2 = C_6H_5$; $R_3 = CH_3$
c, C_2H_5 c, $R_2 = H$; $R_3 = CH_3$, C_6H_5



9

Structure Proof. The molecular formulas of these derivatives were easily determined from the combustion analyses and the parent peaks in the mass spectra (see Table I for principal peaks). The infrared spectra, though compatible with the structural assignment, were of little use in distinguishing between structures 8 and 9. The ^{1}H NMR spectra, on the other hand, uncovered the first clue in support of structure 8. The chemical shifts of the N-methyl protons in the ^{1}H NMR spectra of 8c–e varied depending on the nature of R_1 as shown below. The shielding of the N-methyl protons



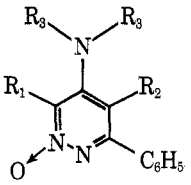
	N-CH_3, δ
8c, $R_1 = C_6H_5$	2.16
d, $R_1 = CH_3$	2.53
e, $R_1 = C_2H_5$	2.53

when R_1 is a phenyl group is consistent with structure 8c, since these protons may be situated in the shielding cones of the two adjacent phenyl rings. In the spectra of 9c–e the chemical shifts of the N-methyl protons should not change, since they are always flanked by the same substituents.

The chemical evidence accumulated firmly established 8 as the structure of these derivatives. Deoxygenation of 8 with phosphorus trichloride yielded pyridazines (10) in high yields (Table II). The physical properties of 10a ($R_1 = C_6H_5$; $R_2 = CH_3$; $R_3 = C_2H_5$) were in excellent agreement with those reported by Roffey and Verge[7] and thus substantiated the presence of the pyridazine ring system in 8.

Most aminopyridazine syntheses are quite tedious but it

Table I. 5-Aminopyridazine 1-Oxides

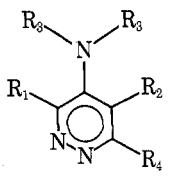


8

Compd	R_1	R_2	R_3	Procedure[a] and recrystn solvent[b]	Yield %	Mp, °C	Mass spectra, m/e (rel intensity)
8a	C_6H_5	CH_3	C_2H_5	I-A	94	153–156	333 (9), 317 (56), 316 (19), 302 (69), 160 (100)
8b	CH_3	CH_3	C_2H_5	I	88[c]		
8c	C_6H_5	C_6H_5	CH_3	II-B	57	241–243	367 (96), 351 (51), 350 (100)
8d	CH_3	C_6H_5	CH_3	II-C	71	173–174	305 (42), 289 (63), 288 (100)
8e	C_2H_5	C_6H_5	CH_3	II-C	74	147–148	319 (17), 303 (33), 302 (100)
8f	C_6H_5	H	C_6H_5, CH_3	II-B	84	166–168	353 (10), 337 (100), 336 (56)
8g	CH_3	H	C_6H_5, CH_3	II-C	95	151–153	291 (36), 275 (100), 274 (79)

[a] Procedure I requires stirring at room temperature for 0.5 h. Procedure II requires heating at reflux for 20 h. [b] A = cyclohexane, B = 95% ethanol, and C = benzene–hexane mixtures. [c] 8b was isolated as a pale yellow oil after chromatography on alumina; melting point of hydrochloride salt, 135–137 °C

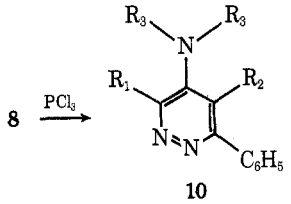
Table II. 4-Aminopyridazines



10

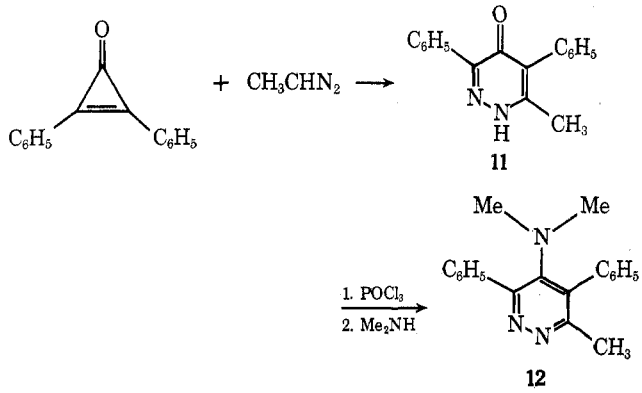
Compd	R_1	R_2	R_3	R_4	Yield, %	Mp (solvent),[b] °C	Partial NMR[c] R_1	R_2	R_3	R_4
10a	C_6H_5	CH_3	C_2H_5	C_6H_5	72	120–122[a] (A)		2.23	0.98 (t, 7 Hz) 2.93 (q, 7 Hz)	
10c	C_6H_5	C_6H_5	CH_3	C_6H_5	93	163–165 (B)			2.28	
10d	CH_3	C_6H_5	CH_3	C_6H_5	92	153–154 (B)	2.73		2.50	
10g	CH_3	H	CH_3, C_6H_5	C_6H_5	86	82–83 (B)	2.21	7.36	3.36	
12	C_6H_5	C_6H_5	CH_3	CH_3		127–128 (C)			2.23	2.42

[a] Lit.[7] mp 120–121 °C. [b] A = 2-propanol, B = cyclohexane, and C = hexane. [c] Measured in $CDCl_3$, Me_4Si standard, 60 MHz.



10

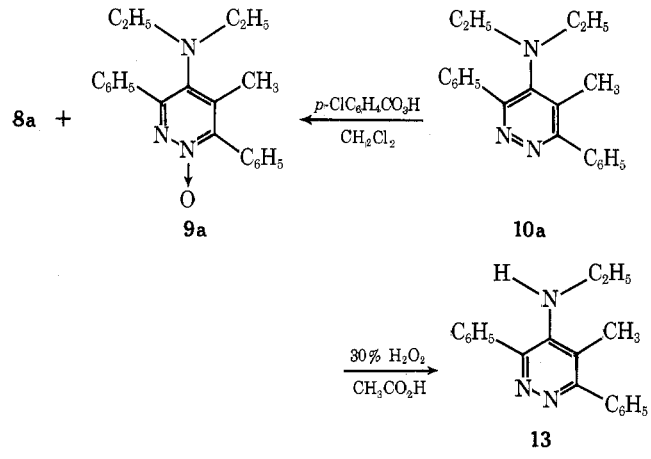
was possible to synthesize the alternative isomer of **10d** (R_1 = C_6H_5; R_2 = R_3 = CH_3), compound **12**, and show that it was not identical with the deoxygenation product of **8d**. This result indirectly proves the correctness of the structural assignments of **8**. Treatment of diphenylcyclopropenone with diazoethane according to the procedure of Breslow and co-workers[8] yielded the appropriate pyridazinone **11**. Successive treatment of **11** with phosphorus oxychloride and dimethylamine yielded **12**. The physical properties of **12** showed that it was not **10d** and confirmed the isomeric structural assignment for the latter. In addition, the *N*-methyl protons in the spectra of **10c,d** and **12** varied consistently in the manner described earlier for the *N*-oxides (Table II).



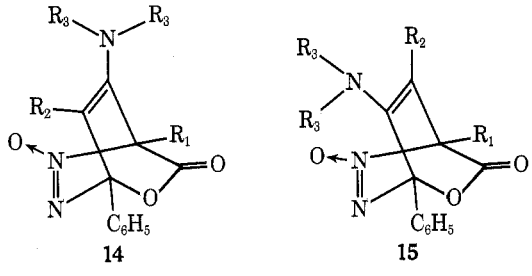
11

12

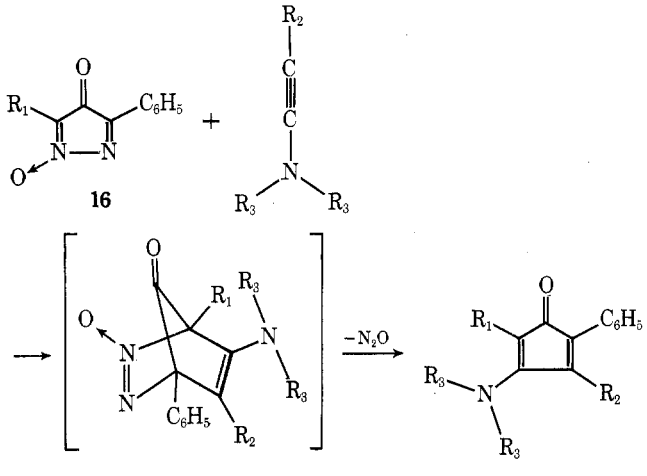
Attempts to oxidize pyridazine **10a** back to **8a** led to some interesting results. Peracetic acid treatment of **10a** yielded the dealkylated pyridazine **13** as the major product. The structure of **13** was deduced from spectral information and elemental analysis (Experimental Section), but its origin is uncertain. However, oxidation of **10a** with *m*-chloroperbenzoic acid yielded a yellow solid in high yield. The ^1H NMR spectrum of this solid suggested that it was a 1:1 mixture of **8a** and **9a**. Oxidation of the exocyclic nitrogen was ruled out, since there was no aliphatic N–O stretching band (950–970 cm^{-1}) in the infrared spectrum.[9] Attempts to separate the two isomers by fractional recrystaliization or thin layer chromatography were unsuccessful.



Mechanism. The [4 + 2] cycloaddition of **1** and **7** in principle can yield two cycloadducts, **14** and **15.**

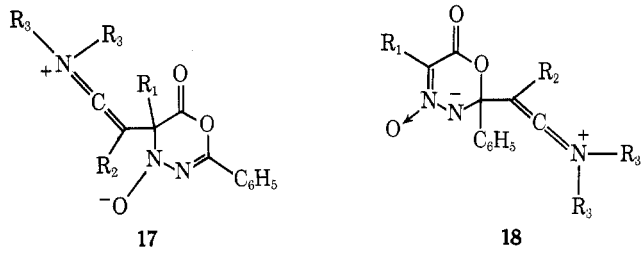


The preference for regioisomer **14**, the precursor of **8**, is analogous to that reported for the cycloadditions of oxazinones[10] and benzoxazinones[11] with ynamines. However, a more pertinent analogy is the cycloaddition of 3,4-diazacyclopentadienone 3-oxides (**16**) with ynamines, since the same mode of addition to the azine oxide moiety occurs there.[12]

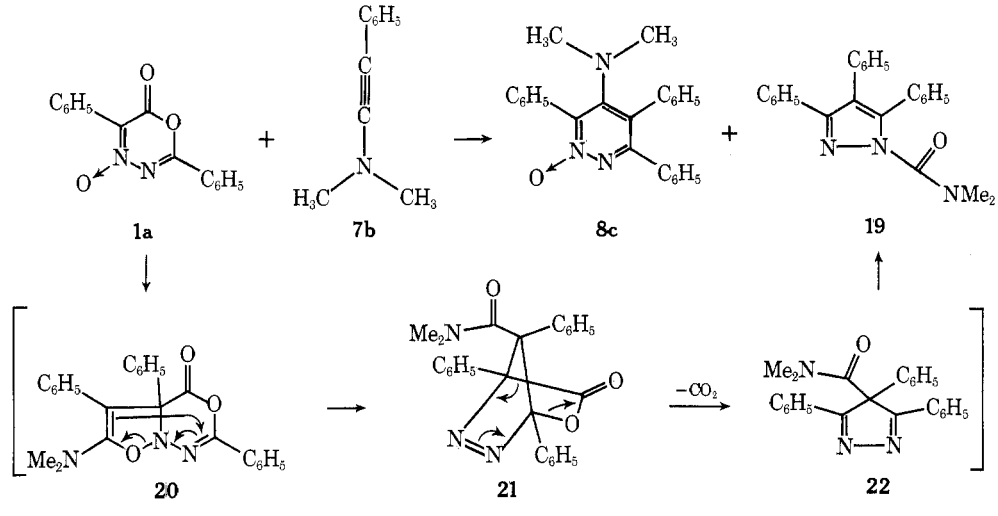


These inverse Diels–Alder cycloadditions might involve a concerted $[\pi 4_s + \pi 2_s]$ mechanism and the regiospecificity therefore explained on the basis of coulombic interactions between the heterocycle and the ynamine.

An attractive alternative is a two-step process involving an intermediate which could partition between a 1,3 cycloadduct, which is formed with most acetylenes, and a 1,4 cycloadduct. This would then help to explain the periselectivity of the ynamine cycloaddition. The regioisomer characterized from the 1,3-dipolar cycloaddition of simple nitrones and ynamines[13] suggests that the partitioning intermediate would have structure **17.** However, collapse of **17** to the 1,4 cycloadduct would yield the wrong regioisomer (**15**). Therefore nucleophilic attack of the ynamine (**7**) must occur at the imidate carbon, since cyclization of **18** would yield the correct regioisomer (**14**).



Although a 1,3 cycloaddition and a 1,4 cycloaddition must involve different interactions, competition between these two paths is still conceivable. Thus the reaction of oxidiazinone **1a** with ynamine **7b** yielded pyrazole **19** in addition to pyridazine **8c.** The structure of **19** was surmised from spectral information and by its hydrolysis to 3,4,5-triphenylpyrazole. This reaction may be an example of competing cycloadditions, since the formation of pyrazole **19** can be rationalized from a first-formed 1,3 cycloadduct **20.** Rearrangement of 4-isoxazoline **20** to intermediate **21** follows the path that has been suggested for the acetylene cycloadditions.[3] Loss of carbon dioxide from **21** would then yield isopyrazole **22,** although this step varies from that observed earlier[3] and violates the general trend reported for extrusion reactions ($N_2 > CO_2$).[14] Migration of the amido group in **22** to nitrogen would then yield **19.** Rearrangements of this type are known in the isopyrazole system,[15,16] but the migratory preference of the amido group over a phenyl group is interesting. The migratory preference of an ester group over a phenyl group has been noted.[15]



Experimental Section

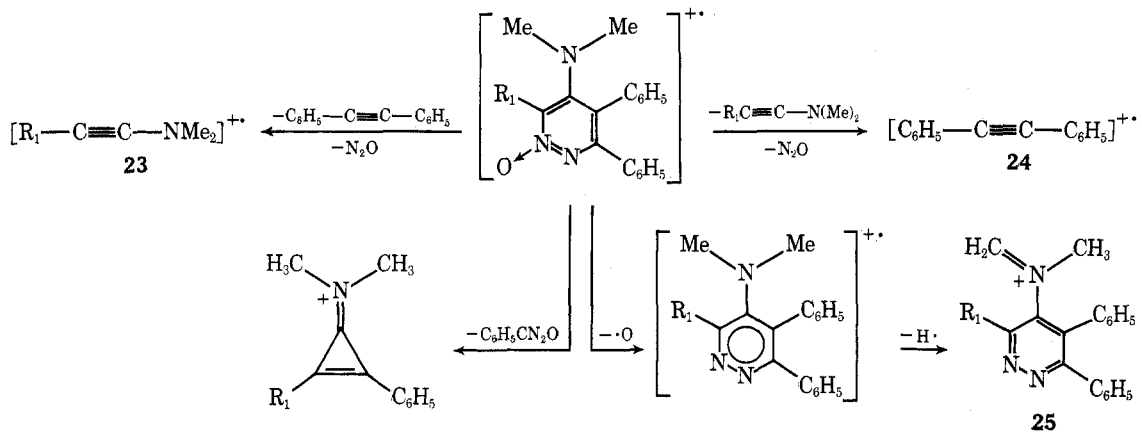
General. Infrared spectra were recorded on a Perkin-Elmer Model 137-A Infracord or a Perkin-Elmer 457. NMR spectra were measured on a Varian A-60A spectrometer; mass spectra were measured with an A. C. I. MS 902 mass spectrometer at 70 eV. We are indebted to Mr. Donald Schifferl for these measurements. The elemental analyses were done by Midwest Microlab.

1-Diethylamino-1-propyne (**7a**) was purchased from Fluka Chemicals. Phenyldimethylaminoacetylene (**7b**) was prepared from phenylchloroacetylene[17] and lithium dimethylamide according to the procedure of Viehe.[18] *N*-Methylanilinoacetylene (**7c**) was prepared from *N*-methyl-*N*-phenyl-1,2,2-trichlorovinylamine[19] according to the method of Ficini and Barbara.[20]

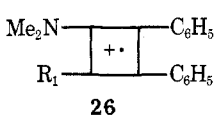
General Procedure for Ynamine Cycloadditions. A magnetically stirred solution of the oxadiazinone oxide (**1**, 4 mmol) in 20–30 ml of CH_2Cl_2 was treated with a solution of the ynamine **7** (4.4 mmol) in 5 ml of CH_2Cl_2. The reaction mixture was then subjected to the reaction conditions outlined in Table I and concentrated in vacuo, and the pyridazine oxide (**8**) was crystallized from the resulting residue with the appropriate solvent (Table I). Only pyridazine oxide **8b** could not be obtained crystalline by this method. Its isolation is described below.

Spectral Properties of Pyridazine Oxides, 8. The infrared spectra of these compounds possessed no special characteristics except a strong band in the region of 1350–1370 cm^{-1}, which is probably due to the N–O stretching vibration. The NMR spectra also were routine except as noted in the discussion.

The mass spectra of the pyridazine oxides were more useful and the cracking patterns for **8c–e** are representative of these derivatives and are illustrated below.

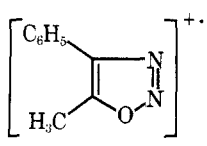


These spectra exhibited abundant parent ions, while the base ions were cations resulting from the loss of 17 mass units; they were assigned structure **25**. Formation of radical cations **23** and **24** might result from a common intermediate (**26**) analogous to that detected in the cracking pattern for simple pyridazines.[21]



26

The mass spectrum of **8a** was analogous to those of **8c–e**, except for the base ion which was observed at 160 mass units; it may be assigned structure **27**.



27

5-Diethylamino-4,6-dimethyl-3-phenylpyridazine 1-Oxide Hydrochloride. The oily residue obtained from oxadiazinone **1b** and ynamine **7a** was purified on a neutral alumina column with $CHCl_3$ as the eluant. **5-Diethylamino-4,6-dimethyl-3-phenylpyridazine 1-oxide (8b)** was isolated as a yellow, viscous oil (88% yield): ^1H NMR ($CDCl_3/Me_4Si$) δ 1.09 (t, J = 7 Hz, 6 H), 2.18 (s, 3 H), 2.53 (s, 3 H), 3.24 (q, J = 7 Hz, 4 H), 7.25–7.7 (m, 5 H).

The oil was dissolved in anhydrous Et_2O and anhydrous HCl was bubbled through the solution. Suction filtration yielded a yellow solid which was recrystallized from benzene to yield the hydrochloride salt as yellow needles: ir (Nujol) 2330, 1555, 1330 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.16 (t, J = 7 Hz, 6 H), 2.34 (s, 3 H), 2.79 (s, 3 H), 3.38 (q, J = 7 Hz, 4 H), 7.4–7.75 (m, 5 H), 15.3 (s, 1 H).

Anal. Calcd for $C_{16}H_{22}ClN_3O$: C, 62.45; H, 7.16; Cl, 11.53; N, 13.66. Found: C, 62.52; H, 7.20; Cl, 11.36; N, 13.62.

1-Dimethylcarbamyl-3,4,5-triphenylpyrazole (19). The ethanolic filtrate from the crystallization of **8c** was concentrated to one-half its original volume and treated with ether at 0 °C to precipitate a pale yellow solid, mp 205–240 °C.[16] Several fractional recrystallizations from absolute ethanol yielded 150 mg (4% yield) of **19** as colorless plates: mp 210–212 °C; ir (KBr) 1655, 1510, 1490, 1445, 1370, 773, 763, 695 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 2.71 [broad singlet, $(CH_3)_2NCO$]; MS *m/e* (rel intensity) 367 (43), 296 (100), 295 (19), 72 (75), 31 (18), 28 (20).

Anal. Calcd for $C_{24}H_{21}N_3O$: C, 78.47; H, 5.72; N, 11.44. Found: C, 77.92; H, 5.84; N, 11.72.

A stirred suspension of **19** (100 mg, 27 mmol) in 2 ml of 30% H_2SO_4 was heated under reflux for 6.5 h. After cooling, suction filtration yielded a white powder which was washed with H_2O. Recrystallization from 95% ethanol yielded **3,4,5-triphenylpyrazole** (62 mg, 78% yield) as long, feathery needles, mp 268–269 °C (lit.[22] mp 265 °C).

General Procedure of Deoxygenation. Formation of Pyridazines 10. A mixture of pyridazine oxide **8** (3 mmol) and 1 ml of phosphorus trichloride in 20 ml of $CHCl_3$ was stirred at room temperature overnight under a $CaSO_4$ drying tube. This mixture was then treated with 10% Na_2CO_3 until it was basic. The layers were separated and the aqueous phase was extracted with $CHCl_3$. The combined $CHCl_3$ layers were washed with H_2O and then with brine. The dried (K_2CO_3) $CHCl_3$ solution was concentrated in vacuo and the pyridizines **10** were obtained by crystallization with the solvents listed in Table II.

Peracetic Acid Oxidation of Pyridazine 10a. A solution of pyridazine **10a** (319 mg, 1 mmol) in 5 ml of glacial acetic acid was treated with a solution of 30% H_2O_2 (670 mg, 9.83 mmol) in 1 ml of acetic acid. This mixture was then heated at 72–74 °C for 15 h. Acetic acid was removed by distillation at aspirator pressures and the resulting residue was diluted with H_2O. The pH was adjusted to 10 with 10% Na_2CO_3 and the mixture was extracted with ether (3 × 10 ml). The ether solutions were washed with H_2O and then with brine. The dried (Na_2SO_4) ether solution was concentrated in vacuo and the residue was purified on a neutral alumina column (2 × 16 cm) with ethyl acetate as the eluent. The major component was recrystallized from benzene–hexane mixures to yield **5-ethylamino-3,6-diphenyl-4-methylpyridazine (13)** as biege prisms: 85 mg, 29% yield; ir (KBr) 3350, 1530, 1440, 1375, 1345, 1175, 1070, 768, 699 cm^{-1}; ^1H NMR ($CDCl_3/Me_4Si$) δ 1.05 (t, J = 7 Hz, 3 H), 2,22 (s, 3 H), 3.04 (broad quintet, 2 H), 3.92 (broad singlet, 1 H), 7.3–7.8 (m, 10 H); MS *m/e* (rel intensity) 289 (92), 288 (100), 274 (11), 260 (10), 245 (10), 231 (15), 78 (25).

Anal. Calcd for $C_{19}H_{19}N_3$: C, 78.89; H, 6.57; N, 14.53. Found: C, 78.61; H, 6.58; N, 14.48.

***m*-Chloroperbenzoic Acid Oxidation of Pyridazine 10a.** A stirred, ice-cold solution of pyridazine **10a** (275 mg, 0.87 mmol) in 10 ml of CH_2Cl_2 was treated dropwise with an ice-cold solution of *m*-chloroperbenzoic acid (1.26 mmol) in 10 ml of CH_2Cl_2. The mixture was allowed to equilibrate to ambient temperatures overnight. The solution was then washed with saturated $NaHCO_3$ (2 × 10 ml), H_2O (2 × 10 ml), and brine (2 × 10 ml). The dried ($MgSO_4$) CH_2Cl_2 solution was evaporated in vacuo and the yellow oil was passed through a short alumina column with ethyl acetate. Recrystallization from

benzene–hexane mixtures yielded yellow needles in two crops (255 mg, 88% yield), mp 143–144 °C. The ^{1}H NMR spectrum of this solid suggested that it was a 1:1 mixture of **8a** and **9a:** δ C(CH_3) 2.06 (**9a**), δ C(CH_3) 2.18 (**8a**).

3,5-Diphenyl-6-methyl-4-pyridazinone (11). Diazoethane was prepared according to the procedure of Wilds and Meader[23] with slight modification.

A 500-ml flask was fitted with an addition funnel and a distilling head set for simple distillation; a 500-ml receiver, immersed in an ice water bath, contained a small amount of anhydrous Et_2O.

A stirred solution of KOH (12.5 g, 0.22 mmol) in 50 ml of 1-propanol and 50 ml of anhydrous Et_2O was heated to 50 °C with a H_2O bath. When the Et_2O started to distill, *N*-nitroso-*N*-ethylurethane[23] (12.5 g, 85.6 mmol) in 40 ml of anhydrous Et_2O was added rapidly from the addition funnel. The bath was maintained at 50 °C and Et_2O was added portionwise until the distillate was colorless. Total volume of the ethereal diazoethane solution was 300 ml.

The diazoethane solution was treated in one portion with a solution of diphenylcyclopropenone[8a] (6.2 g, 30 mmol) in 150 ml of benzene. Precipitation occurred within a few minutes and the mixture was stirred overnight at ambient temperature. Suction filtration yielded a white powder which was recrystallized from methanol to yield 11 as small white needles in several crops (6.18 g, 79% yield): mp 304–305 °C; ir (KBr) 3300, 3080, 3000, 1525, 1290, 803, 756, 732, 695 cm^{-1}; ^{1}H NMR (Me_2SO-d_6/Me_4Si) δ 2.18 (s, 3 H), 7.39 (broad singlet, 8 H), 8.0–8.2 (m, 2 H), 13.65 (broad singlet, 1 H).

Anal. Calcd for $C_{17}H_{14}N_2O$: C, 77.86; H, 5.34; N, 10.69. Found: C, 77.78; H, 5.32; N, 10.80.

4-Dimethylamino-3,5-diphenyl-6-methylpyridazine (12). A stirred mixture of pyridazinone 11 (2.62 g, 10 mmol) in 20 ml of $POCl_3$ was heated on a steam bath for 30 min. After cooling, the mixture was slowly added to a mixture of ice (100 g) and $CHCl_3$ (100 ml). Na_2CO_3 (≈40 g) was added in small portions until the mixture was basic. The layers were separated and the aqueous phase was extracted with $CHCl_3$ (50 ml). The $CHCl_3$ solutions were washed with brine (3 × 25 ml), dried (K_2CO_3), and concentrated in vacuo. Crystallization from cyclohexane yielded **4-chloro-3,5-diphenyl-6-methylpyridazine** as biege plates in two crops (1.98 g, 71% yield): mp 127–128 °C; ir (KBr) 1475, 1425, 1380, 900, 762, 702 cm^{-1}; ^{1}H NMR ($CDCl_3$/Me_4Si) δ 2.53 (s, 3 H), 7.1–7.6 (m, 8 H), 7.7–7.9 (m, 2 H).

A mixture of the chloropyridazine (281 mg, 1 mmol) and anhydrous dimethylamine (1 g, 22.2 mmol) in 10 ml of Me_2SO was heated in a Fischer-Porter sealed tube for 5 days at 110–120 °C. The mixture was then added to 75 ml of H_2O and extracted with $CHCl_3$ (3 × 25 ml). The $CHCl_3$ solutions were washed with H_2O, then with brine, dried (K_2CO_3), and concentrated in vacuo to leave a pale yellow oil. Chromatography of this oil on alumina (1 × 29 cm) with CH_2Cl_2 yielded unchanged chloropyridazine as the first component. After a small amount of an unidentified material, pyridazine **12** was collected. Recrystallization from hexane yielded 65 mg of pale yellow plates (Table II).

Registry No.—**1a,** 28969-37-1; **1b,** 28969-38-2; **1c,** 28969-39-3; **7a,** 4231-35-0; **7b,** 4604-65-3; **7c,** 4231-31-6; **8a,** 60325-92-0; **8b,** 60325-93-1; **8b** HCl, 60325-94-2; **8c,** 60325-95-3; **8d,** 60325-96-4; **8e,** 60325-97-5; **8f,** 60325-98-6; **8g,** 60325-99-7; **9a,** 60326-00-3; **10a,** 23900-47-2; **10c,** 60326-01-4; **10d,** 60326-02-5; **10g,** 60326-03-6; **11,** 60326-04-7; **12,** 60326-05-8; **13,** 60326-06-9; **19,** 60326-07-0; 4-chloro-3,5-diphenyl-6-methylpyridazine, 60326-08-1.

References and Notes

(1) This research was sponsored in part by the National Cancer Institute, National Institutes of Health, Grant CA-10742.
(2) P. C. Reilly Fellow, 1973–1974; Arthur J. Schmitt Fellow, 1975–1976.
(3) J. P. Freeman, J. A. Kassner, and R. C. Grabiak, *J. Org. Chem.*, **40,** 3402 (1975).
(4) J. P. Freeman and R. C. Grabiak, *J. Org. Chem.*, **41,** 2531 (1976).
(5) (a) J. P. Freeman and M. J. Hoare, *J. Org. Chem.*, **36,** 19 (1971); (b) J. P. Freeman, E. G. Duthie, M. J. O'Hare, and J. F. Hansen, *ibid.*, **37,** 2756 (1972).
(6) For leading references, see J. A. Reed, C. L. Schilling, R. F. Tarvin, T. A. Retting, and J. K. Stille, *J. Org. Chem.*, **34,** 2188 (1969).
(7) P. Roffey and J. P. Verge, *J. Heterocycl. Chem.*, **6,** 497 (1969).
(8) (a) R. Breslow, T. Eicher, A. Krebs, R. A. Peterson, and J. Posner, *J. Am. Chem. Soc.*, **87,** 1320 (1965); (b) P. T. Izzo and A. S. Kende, *Chem. Ind. (London)*, 839 (1964).
(9) L. J. Bellamy, "The Infrared Spectra of Complex Molecules", Wiley, New York, N.Y., 1975, pp 343–344.
(10) W. Steglich, E. Buschmann and O. Hollitzer, *Angew. Chem., Int. Ed. Engl.*, **13,** 533 (1974).
(11) G. Höfle, O. Hollitzer, and W. Steglich, *Angew. Chem., Int. Ed. Engl.*, **11,** 720 (1972).
(12) J. P. Freeman and R. C. Grabiak, *J. Org. Chem.*, **41,** 1887 (1976).
(13) R. Fuks, R. Buijle, and H. G. Viehe, *Angew, Chem., Int. Ed. Engl.*, **5,** 585 (1966).
(14) B. P. Stark and A. J. Duke, "Extrusion Reactions", Pergamon Press, Elmsford, N.Y., 1967, p 174.
(15) R. K. Bransley, R. Grigg, G. Guilford, and P. Milner, *Tetrahedron,* **29,** 4159 (1973).
(16) It is probable that isopyrazole **22** was obtained from the reaction along with **19** but was gradually converted to **19** during the process of recrystallization (Experimental Section). The crude reaction product showed two distinct *N*-methyl signals in its NMR spectrum.
(17) L. Brandsma, "Preparative Acetylenic Chemistry", American Elsevier, New York, N.Y., 1971, p 97.
(18) H. G. Viehe, "Chemistry of Acetylenes", Marcel Dekker, New York, N.Y., 1969, p 906.
(19) A. J. Speziale and L. R. Smith, *J. Am. Chem. Soc.*, **84,** 1872 (1962).
(20) J. Ficini and C. Barbara, *Bull. Soc. Chim. Fr.*, 2787 (1965).
(21) J. H. Bowie, R. G. Cooks, P. F. Donaghue, J. A. Halleday, and H. G. Rodda, *Aust. J. Chem.*, **20,** 2677 (1967).
(22) W. E. Parham and W. R. Hasek, *J. Am. Chem. Soc.*, **76,** 799 (1954).
(23) A. L. Wilds and A. L. Meader, Jr., *J. Org. Chem.*, **13,** 763 (1948).