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REACTIONS OF PYRIDAZINE N-OXIDES WITH ORGANOMETALLIC COMPOUNDS[1)]

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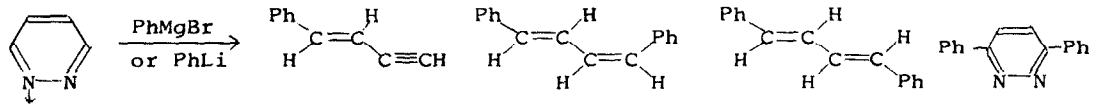
Although reactions of organometallic compounds with aromatic amines[2)] and their N-oxides[3)] have been investigated, similar reactions with pyridazines have only recently been examined[4,5)], and there are no reports of such reactions with pyridazine N-oxides.

We now report the formation of three kinds of hydrocarbons; monophenyl-substituted vinyl acetylene derivatives (II), all trans-1,4-diphenylbutadiene derivatives (III), and their geometrical isomers (IV). These are formed by elimination of nitrogen from the pyridazine ring by the reactions of phenylmagnesium bromide or phenyllithium with pyridazine N-oxide (Ia) and its monomethyl derivatives (Ib-e). Interestingly the formation of phenylated pyridazines, which are expected by analogy with other aromatic amine oxides[3)], is very minor in these reactions.

To pyridazine N-oxide (Ia) in benzene was added 1.5-2.0 mole phenylmagnesium bromide or phenyllithium in ether under vigorous stirring at 0-10°. After the usual work-up, the products were separated into two fractions, the hydrocarbon fraction and the pyridazine fraction by column chromatography on alumina with benzene. The hydrocarbon fraction was then subjected to vacuum distillation to afford trans-1-phenyl-1-butene-3-yne[6)] (IIa) (40%). The residue from the distillation was again chromatographed over alumina with hexane to afford a liquid hydrocarbon, IIIa (10%), and trans,trans-1,4-diphenylbutadiene, IVa (15%). Though the stereochemistry of IIIa has not been rigorously established, spectral evidence (mass, UV, IR, and nmr) indicate that this compound (IIIa) is a geometrical isomer

of IVa , and is probably cis, trans-1,4-diphenylbutadiene. The pyridazine fraction afforded 3,6-diphenylpyridazine[7] (Va) (5%).



Ia IIa IIIa IVa Va

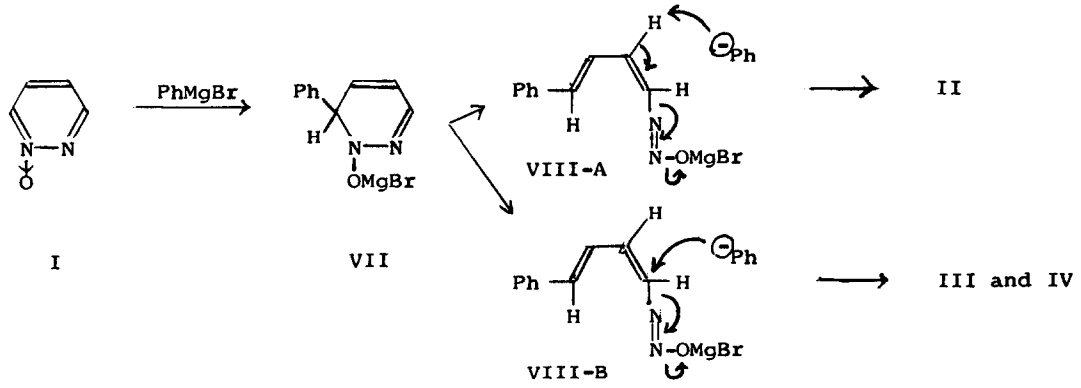
The products from various pyridazine N-oxides are listed in Table I. All of the products have elemental composition, molecular weight (mass), and IR, UV, nmr spectra consistent with the suggested structures. Some of the spectral data of these products are listed in Table II and III.

The IR spectra of IIa-e shown in Table II indicate clearly that IIa,d and e are the mono-substituted acetylenes, while IIb is di-substituted[8]. The nmr spectra of IIa-e are also consistent with the assigned structures and the large coupling constants (17 cps) between $H_{(1)}$ and $H_{(2)}$ in the nmr spectra of IIa and IIb show the presence of trans-ethylene function[9]. The assigned structures for IId and IIe are tentatively proposed from their UV spectra and are consistent with data shown in the Table.

The structure of IIIa was confirmed as trans,trans-1,4-diphenylbutadiene by mixture melting point with an authentic sample[10]. Since IVa changed to IIIa under the influence of room light, the structure of IVa is either the cis,trans-form or the cis,cis-form of 1,4-diphenylbutadiene. From mechanistic considerations, we prefer the cis,trans-form for IVa. Added to the spectral data indicated in the Table III, since the identical mass spectra were obtained from IIIa and IVa, IIIb and IVb, or IIIc and IVc, respectively, it can be concluded that IIIa-e are the more stable forms, and IVa-e are their geometrical isomers.

The following mechanism can be proposed as the most reasonable one for the formation of II-IV from I. The formation of these hydrocarbons (II, III, and IV) can easily be rationalized. The 1,6-dihydropyridazines (VII) presumably leads first to the ring-opened intermediate (VIII), which by the path indicated in formula VIII-A gives rise to the acetylenes (II), whereas the path indicated in formula VIII-B gives rise to the butadienes (III and IV). Since the ring-opened intermediate (VIIIc) from 4-methylpyridazine 1-oxide (Ic) lacks the hydrogen atom at the 4-position of the original ring, which plays an essential role in the non-

rearranged acetylene formation, the formation of the rearranged acetylene (IIb) from Ic should be considered as the exceptional case of this mechanism.



All the reactions mentioned so far were carried out in benzene-ether mixture. If tetrahydrofuran is used as a solvent, II is formed preferentially (50-60%), and the formation of III, IV and V is suppressed markedly.

The mechanistic rationalization for the solvent effect, and the formation of IIb from Ic are currently being investigated, together with the definite identification of the products (especially IV).

TABLE I

(1) R	(II) R_1	R_2	R_4	b.p.°C/mm (bath temp.)	(III) cis-trans R_1	R_2	R_3	R_4	(IV) trans-trans m.p.°C	Pyridazines (V)
a H	H	H	H	80-90/4	H	H	H	H	146-148	1*
b 3-CH_3	H	H	CH_3	100-105/3	H	H	H	CH_3	94-95	--
c 4-CH_3	same as b			" "	H	H	CH_3	H	76-77	--
d 5-CH_3	H	CH_3	H	90-95/4	same as c				"	--
e 6-CH_3	CH_3	H	H	90-95/4	same as b					2*
Yield	40-50%								10-15% 15-20%	ca.5%

1*) 3,6-diphenylpyridazine, m.p. 218-219°.

2*) 3-phenyl-6-methylpyridazine 1-oxide, m.p. 161-163°.[11]

TABLE II

$\overset{1}{>}C=C\overset{2}{<}C\equiv C-$ (3, 4)

	IR (CCl_4) cm^{-1}	NMR (CCl_4)
IIa	2100, 3320 (-C≡C-H)	$H_{(1)}$:3.06 τ (d), $H_{(2)}$:4.00 τ (d,d), $H_{(4)}$:7.17 τ (d) $J_{1,2}$=17 cps, $J_{2,4}$=1.8 cps
IIb	2230 (-C≡C-)	$H_{(1)}$:3.26 τ (d), $H_{(2)}$:4.05 τ (d,q), 4-CH_3:8.06 τ (d) $J_{1,2}$=17 cps, $J_{2,4}$=1.8 cps
IId	2100, 3320 (-C≡C-H)	$H_{(1)}$:3.0-3.4 τ (unassigned), $H_{(4)}$:7.21 τ (s), 2-CH_3:7.97 τ (d) J=1.8 cps
IIe	2100, 3320 (-C≡C-H)	$H_{(2)}$:4.29 τ (unresolved mc), $H_{(4)}$:6.93 τ (d), 1-CH_3:7.70 τ (s) J=1.8 cps

TABLE III

$\overset{1}{>}C=C-C=C\overset{4}{<}$ (1, 2, 3, 4)

IIIa	3.31 (4H, A_2B_2 type sym. mc)	IVa	2.9-3.8 τ (4H,unassigned ABCD type mc)
IIIb	$H_{(1)}$:3.40 τ (d), $H_{(2)}$:3.67 τ (d) $H_{(3)}$:3.75 τ (broad), 4-CH_3:7.83 τ $J_{1,2}$=17 cps	IVb	2.90-3.70 τ (3H,unassigned) 4-CH_3:7.79 τ (s)
IIIc	$H_{(4)}$:3.60 τ (broad), 3-CH_3:7.90 τ	IVc	$H_{(1)}$:3.11 τ (d), $H_{(2)}$:3.50 τ (d), $H_{(4)}$:3.43 τ (unresolved q), 3-CH_3:7.90 τ , $J_{1,2}$=17 cps

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