(s), and 1135 cm^{-1} (w); nmr ($CDCl_3$) τ 7.90–9.30 (m, 7, C_3H_7), 7.83 (s, 3, $ArCH_3$), 7.75 (s, 3, $ArCH_3$), 5.08 [t, 1, $ArCH(CH_2)_2$], 4.00 (s, 1, OH, exchanges with D_2O), 2.88 (s, 1, C_3H), 1.99 (s, 1, C_6H).

Anal. Calcd for $C_{11}H_{17}NO_2$: C, 67.66; H, 8.75. Found: C, 67.63; H, 8.93.

Reaction of Pyridyl 1-Oxide Carbanion with Acetone.—Pyridine 1-oxide (1.35 g, 0.015 mol) in anhydrous tetrahydrofuran (70 ml) was treated with *n*-butyllithium (1.92 g in hexane, 0.03 mol) and the mixture was treated with acetone (1.74 g, 0.03 mol) for 3 hr. The product was a brown oil which crystallized to give **2,6-di(1-methyl-1-hydroxyethyl)pyridine 1-oxide** (0.534 g, 17.8%): mp 118° (chromatographed on alumina and recrystallized from acetone); ir (KBr) 3300–3200 (s), 1266 (w), 1195 (s), 1168 (s), and 1150 cm^{-1} (m); nmr ($CDCl_3$) τ 8.40 [s, 12, 2 $>C(CH_3)_2$], 2.60 (s, 3, C_3H, C_4H, C_5H), 2.50 (s, 2, OH, exchanges with D_2O).

Anal. Calcd for $C_{11}H_{17}NO_3$: C, 62.54; H, 8.11. Found: C, 62.40; H, 8.35.

4-(1-Hydroxycyclohexylmethyl)-3-methylpyridine 1-oxide had mp 217–219° (acetone); ir (KBr) 3240 (s), 1275 (s), 1185 (s), 1175 (s), and 1160 cm^{-1} (s).

Anal. Calcd for $C_{13}H_{19}NO_2$: C, 70.55; H, 8.65. Found: C, 70.35; H, 8.79.

Dimethyl (1-oxido-4,5-dimethyl-2-pyridyl)carbinol had mp 129° (acetone); ir (KBr) 3150 (s), 1250 (s), 1180 (s), and 1150 cm^{-1} (s); nmr ($CDCl_3$) τ 8.35 [s, 6, $>C(CH_3)_2$], 7.77 (s, 3, $ArCH_3$), 7.68 (s, 3, $ArCH_3$), 2.82 (s, 1, C_3H), 1.98 (s, 1, C_6H), 1.93 (s, 1, OH, exchanges with D_2O).

Anal. Calcd for $C_{10}H_{15}NO_2$: C, 66.27; H, 8.34; N, 7.73. Found: C, 66.00; H, 8.47; N, 7.89.

1-(1-Oxido-4,5-dimethyl-2-pyridyl)-1-phenylethanol had mp 141° (acetone); ir (KBr) 3200–3100 (w), 1245 (s), and 1155 cm^{-1} (s); nmr ($CDCl_3$) τ 8.17 (s, 3, $-CCH_3$), 7.82 (s, 3, $ArCH_3$), 7.70 (s, 3, $ArCH_3$), 2.70 (m, 6, C_3H, C_6H_5), 2.05 (s, 1, C_6H), 1.60 (s, 1, OH, exchanges with D_2O).

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04. Found: C, 73.97; H, 7.17.

α,6-Di(1-hydroxycyclohexyl)-2-methylpyridine 1-oxide had mp 111° (acetone); ir (KBr) 3300–3100 (s), 1275 (m), and 1200 cm^{-1} (s).

Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91. Found: C, 70.83; H, 9.11.

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Registry No.—1-(1-Oxido-2-pyridylmethyl)cyclohexanol, 34277-46-8; 2,6-di(1-hydroxyethyl)pyridine 1-oxide, 34277-47-9; 2-(1-hydroxyethyl)pyridine 1-oxide, 34277-48-0; 4-chloro-2-(1-hydroxy-2-benzyl)-5-methylpyridine 1-oxide, 34965-48-5; (4,5-dimethyl-1-oxido-2-pyridyl)-*n*-propylcarbinol, 34277-50-4; 2,6-di(1-methyl-1-hydroxyethyl)pyridine 1-oxide, 34277-51-5; 4-(1-hydroxycyclohexylmethyl)-3-methylpyridine 1-oxide, 34277-52-6; dimethyl (1-oxido-4,5-dimethyl-2-pyridyl)carbinol, 34277-58-2; 1-(1-oxido-4,5-dimethyl-2-pyridyl)-1-phenylethanol, 34277-59-3; 2,6-di(1-hydroxycyclohexyl)-2-methylpyridine 1-oxide, 34277-60-6.

Ring-Opening Reactions of the Pyrazolo[1,2-*a*]pyridazin-6-one System[1]

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The ring-opening reactions of 8-phenyl-1,4-methano-1,4-dihydropyrazolo[1,2-*a*]pyridazin-6-one (**4**) and 1,4,8-triphenyl-1,4-dihydropyrazolo[1,2-*a*]pyridazin-6-one (**5**) in dilute hydrochloric acid and potassium hydroxide solutions were found to give 1- and 2-nitrogen-substituted pyrazol-3-one derivatives in high yield. The ring-opening reactions of **5** yielded 1-(1,4-diphenyl-1,3-butadienyl)-3-hydroxy-5-phenylpyrazole in potassium hydroxide solution, 1-(4-hydroxy-1,4-diphenyl-2-butenyl)-3-hydroxy-5-phenylpyrazole in hydrochloric acid, and the corresponding trichloroacetate in trichloroacetic acid. The ring opening of **4** in hydrochloric acid gave 1-(4-hydroxy-2-cyclopentenyl)-5-hydroxy-3-phenylpyrazole but no ring opening of **4** was observed in potassium hydroxide solution. The hydrogenated adduct, 8-phenyl-1,4-methano-1,2,3,4-tetrahydropyrazolo[1,2-*a*]-pyridazin-6-one, did not open under acidic or basic conditions.

The Diels–Alder reaction has been known to yield pyridazine derivatives since 1925.[4] The majority of work in this area from 1925 until 1960 has dealt with adducts of acyclic azodicarboxylates. Since 1960 a number of workers have reported adducts of cyclic acyl[5–7] and diacyl-cis-azo compounds.[8–11] Although the azodicarboxylate adducts have been shown to undergo a number of useful reactions,[12–15] investigations of the potentially more interesting adducts of cyclic azo compounds have not been pursued. The following is a report of some ring-opening reactions of pyrazol-3-one adducts to give N-substituted pyrazolin-3-ones.

The oxidation of a 3-substituted 2-pyrazolin-5-one (**1**) with lead tetraacetate gave the pyrazol-3-one ring system (**2**). When the oxidation was carried out in the presence of a diene the pyrazol-3-ones were trapped as Diels–Alder adducts (**3**).[6] The adducts **4** and **5** of cyclopentadiene and of 1,4-diphenylbutadiene, respectively, with 5-phenylpyrazol-3-one (**2**, R = C_6H_5)[6] were investigated in the course of this work.

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(2) National Aeronautics and Space Administration Fellow, 1965–1968.

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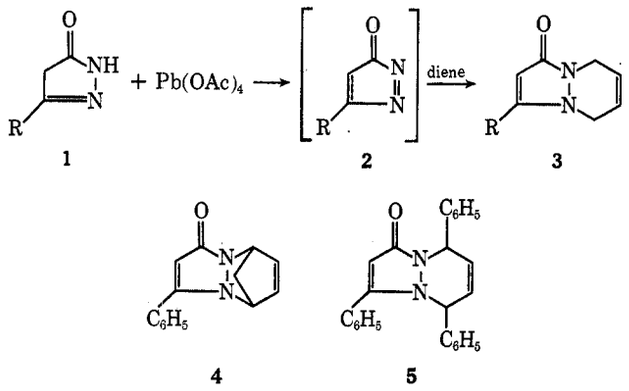
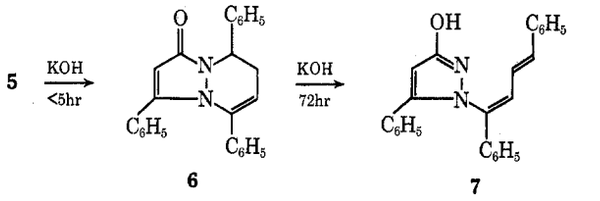


The 1,4-dihydropyrazolo[1,2-a]pyridazin-6-one ring system **3** contains both a *4-pyrazolin-3-one* and a *3,6-dihydropyridazine* moiety. The properties of the 4-pyrazolin-3-one ring system have not been investigated in much detail. Reactions carried out under acidic[16] and basic[17] conditions indicated that the ring system was stable to mild treatment. It has also been shown to be stable toward catalytic hydrogenation, as debenzylation of 1-benzyl-2,3-dimethyl-3-pyrazolin-5-one occurred rather than hydrogenation of the pyrazolinone ring.[16] The 3,6-dihydropyridazine ring system has been shown to undergo a number of reactions in the form of an ethyl azodicarboxylate adduct. Catalytic hydrogenation,[18] retro Diels–Alder reactions,[19] and acid-[20] and base-catalyzed[21] hydrolysis of *N*-acyl functions have been reported.

Results and Discussion

In this investigation it was found that widely different products were obtained from the alkaline and acidic reactions of the bicyclic system **3**. Further, all of the ring-opened products resulted from opening of the pyridazine rather than the pyrazolinone ring. Refluxing of **5** in 20% solution of potassium hydroxide in 80% aqueous ethanol results in rapid isomerization (<5 hr) of the pyridazine double bond to the 3 position (**6**) followed by slow ring opening (~72 hr) of this isomer to give the diene **7**. The isomer 1,4,8-tri-



phenyl-3,4-dihydropyrazolo[1,2-a]pyridazin-6-one (**6**) has an ultraviolet spectrum (Table I) which suggests that a styrene type chromophore [λ_{max}^{EtOH} 248 nm (ϵ 14,000), 282 (750), 291 (500)][22] is present along with the pyrazoline chromaphore of **5** (Table I). The mass spectrum of **6** showed intense peaks corresponding to loss of phenyl (*m/e* 273 and 77) and a peak at *m/e* 234 corresponding to $C_{16}H_{14}N_2$, probably a 3,6-diphenyldihydropyridazine. The mass spectrum of adduct **5** showed minor amounts of these fragments while cleaving primarily through a reverse Diels–Alder mechanism to give diphenylbutadiene (*m/e* 206). Each proton of the C-3 methylene group of **6** appeared as an eight-line pattern in the pmr spectrum with δ 2.63 (C_3H) and 3.08 ppm (C_3H') with the following coupling constants: J_{HH} = 17 (C_3H, C_3H'), 6.5 (C_3H, C_4H), 1 (C_3H, C_2H), 6.5 (C_3H', C_4H), and 3 Hz (C_3H', C_2H). The assignment of the pyridazine double bond of **6** to the two position was based primarily on the fact that it opened with cleavage of the ring at the amide nitrogen.

The difference in rates of isomerization of **5** to **6** and subsequent ring opening to **7** allowed complete isomerization of **5** to occur before the ring-opened product was detected. The ultraviolet spectrum of **7**, 1-(1,4-diphenyl-1,3-butadienyl)-3-hydroxy-5-phenylpyrazole, shows absorption at 335 and 238 nm (Table I) which may be attributed to the 1,4-diphenylbutadiene chromaphore [λ_{max}^{EtOH} 345 nm (ϵ 25,000), 328 (46,700), 314 (41,700), 232 (12,000)].[23] The pmr resonance for the 1-(1,4-diphenyl-1,3-butadienyl) vinyl protons on carbons 2, 3, and 4 appeared at 7.28, 6.68, and 7.03 ppm, respectively, with coupling constants J_{HH} = 9 (C_2H, C_3H), 1 (C_2H, C_4H), and 5 Hz (C_3H, C_4H). The mass spectrum of **7** showed intense peaks corresponding to loss of a styryl function (*m/e* 260 and 104) and a base peak at *m/e* 219 for $C_{16}H_{13}N$.

In order to determine that ring opening of **5** had occurred at the amide nitrogen, the ring-opened compound **7** was hydrogenated over palladium to give

TABLE I

ULTRAVIOLET ABSORPTION OF SUBSTITUTED PYRAZOLONES AND PYRAZOLES

Compd	Tautomeric form	Ultraviolet spectrum, nm (ϵ) 95% Ethanol	Cyclohexane
5	Oxo	245 (12,500)	245 (15,800)
6	Oxo	292 (10,200)	
		244 (24,700)	
7	Hydroxyl	335 (22,100)	
		255 (25,400)	
		sh 244 (3760)	
		238 (4380)	
7	Oxo		335 (34,600)
			267 (4120)
			sh 245 (4480)
			237 (5350)
8	Hydroxyl	sh 295 (2300)	
		254 (16,000)	
8	Oxo		307 (8000)
			265 (4100)
			sh 227 (8000)
9	Oxo	245 (9550)	245 (12,500)
10	Oxo	245 (6160)	244 (10,700)
4	Oxo	sh 305 (4500)	sh 326 (3780)
		271 (13,200)	257 (15,000)
11	Hydroxyl	300 (3860)	302 (7600)
		254 (18,800)	256 (18,500)
13	Hydroxyl	246 (11,800)	244 (7650)
14	Hydroxyl	255 (16,170)[a]	301 (12,190)
15	Oxo	256 (14,200)	

[a] Spectrum taken in water.

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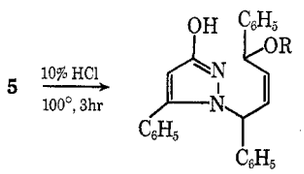
1-(1,4-diphenylbutyl)-3-hydroxy-5-phenylpyrazole (**8**) (*m/e* 368, $C_{25}H_{24}N_2O$). The ultraviolet spectrum of **8** was very similar to the model compound 1,5-diphenyl-3-hydroxypyrazole (**15**)[24] (Table I). The ultraviolet and infrared spectra of compounds **7** and **8** were influenced by solvent polarity. It appears that tautomerization between the hydroxyl form[25] (**7** as shown) and the oxo (amide O=CNH–) form occurs with the oxo form predominating in less polar solvents.

Acid-catalyzed ring opening of **5** occurred under somewhat milder conditions. Refluxing **5** in 10% hydrochloric acid for 13 hr yielded the ring-opened product 1-(4-hydroxy-1,4-diphenyl-2-butenyl)-5-phenyl-3-hydroxypyrazole (**9**), which was isolated and characterized as the monohydrate, $C_{25}H_{24}N_2O_3$. The chemical shifts of the side-chain methine and vinyl protons were similar and appeared as two broad peaks centered at 6.15 (2 H, $W_{1/2}$ = 3.5 Hz) and 6.19 ppm (2 H, $W_{1/2}$ = 4.0 Hz). The ultraviolet spectrum (Table I) showed no evidence of a styryl type chromophore, indicating that the pyridazine double bond did not migrate in the course of ring opening. The mass spectrum of **9** did not show a molecular ion at *m/e* 382, but did show a strong M − 18 peak at *m/e* 364. The fragmentation pattern of this ion was identical with that of **5**. This would indicate that loss of water from **9** occurs through ring closure to **5** rather than **6** or dehydration to **7**. Compound **9** was hydrogenated with loss of the benzylic hydroxyl group to give **8**, thus confirming that the position of ring attachment was the same as in compound **7**.



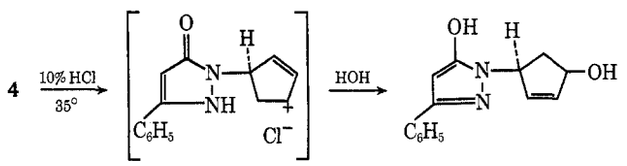
9

The product **9** can be viewed as resulting from nucleophilic displacement at the allylic–benzylic carbon which was bonded to the most electron-deficient nitrogen.[19] A bimolecular reaction was postulated, as unimolecular ring opening to give a carbonium ion at C-4 would be expected to lead to migration of the double bond into conjugation with the phenyl group. The same reaction pathway was followed on ring opening in trichloroacetic acid.

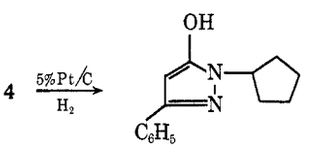
Heating **5** in trichloroacetic acid at 90° gave compound **10** ($C_{27}H_{21}N_2O_3Cl_3$), the trichloroacetate of **9**. The ultraviolet spectrum of **10** (Table I) was similar to that of **9** and showed two carbonyl absorptions at 5.65 and 6.10 μ in the infrared region for the trichloroacetate and pyrazolinone carbonyl groups, respectively. The methine and vinyl protons appeared as a broad, unsymmetrical peak between 6.00 and 6.14 ppm (4 H) in the pmr spectrum.

The trichloroacetate **10** underwent facile ring closure. Heating **10** at 117° gave the adduct **5** within 5 min. Attempts to hydrolyze **10** to **9** with 20% hydrochloric acid at 45° and with 20% potassium hydroxide at 80° yielded the ring closure product **5** and trichloroacetic acid. The facile ring closure of **9** in the mass spectrometer and of **10** on heating suggest that the double bond retained the cis configuration during ring opening, as this configuration should favor ring closure.

The two reaction pathways which led to ring opening of **5**, base-catalyzed double-bond migration followed by ring opening and acid-catalyzed nucleophilic displacement at the allylic carbon, should be effectively prevented by the 1,4-methano group of **4**. Nevertheless, the cyclopentadiene adduct **1** was found to open readily in acid solution. On stirring **4** with 10% hydrochloric acid for 5 hr, the ring-opened alcohol **11** was obtained (>90% yield). The ring strain of **4** and the stability of the hydroxypyrazole ring both facilitate unimolecular ring opening to the intermediate allylic cation **12**. The same N–C bond cleaved when **4** was hydrogenated over platinum to give 1-cyclopentyl-3-phenyl-5-hydroxypyrazole (**13**). The infrared and ultraviolet



12 **11**



13

spectra of **11** and **13** (Table I) were very similar to the reported values of 1-methyl-3-phenyl-5-hydroxypyrazole (**14**)[26] (Table I), thus indicating attachment of the alkyl group at the amide nitrogen as shown. The downfield resonance position of the methine hydrogens (δ >5 ppm) in the pmr spectrum of **11** indicates that they are both allylic. The mass spectrum of **11**, M^+ 242 (26% of *m/e* 160 = 100), shows ions from fragmentation of the cyclopentenol side chain (*m/e* 186, $M^+ - C_3H_4O$ and *m/e* 55, C_3H_3O); cleavage of the side chain (*m/e* 160 for phenylpyrazolinone and *m/e* 82 for cyclopentadienol ions) and subsequent fragmentation of these ions. The mass spectrum of **13** showed only two significant peaks, the molecular ion *m/e* 228 (22% of *m/e* 160 = 100) and *m/e* 160.

In contrast to the observed facile ring opening of the adduct **4**, no ring opening was observed with the hydrogenated derivative 8-phenyl-1,2,3,4-tetrahydro-1,4-methanopyrazolo[1,2-*a*]pyridazin-6-one (**16**).[6] Refluxing the hydrogenated adduct in 20% hydrochloric acid or in 20% potassium hydroxide solutions did not produce bond cleavage.

Base-catalyzed ring opening of the cyclopentadiene adduct **4** was also unsuccessful. Refluxing **4** in 20% potassium hydroxide solution for 100 hr under nitrogen led to partial decomposition of the adduct. The only identifiable compound isolated from this mixture was unreacted **4**.

Conclusion

The investigation of the acid- and base-catalyzed ring opening of the pyrazolo[1,2-*a*]pyridazine ring

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system has led to a number of interesting reactions and products. From the above data it appears that the pyridazine double bond was necessary to increase the reactivity of the ring system toward opening. After ring opening had occurred the resulting 1- or 2-substituted pyrazolin-5-ones underwent no further reactions under the conditions employed. A number of other pyridazine systems have been prepared[5,7,11] from *cis*-azodienophiles which may undergo ring opening through reaction pathways analogous to those presented here.

Experimental Section[27]

8-Phenyl-1,4-methano-1,4-dihydropyrazolo[1,2-*a*]pyridazin-6-one (4).—The title compound was prepared by the previously reported procedure.[6] The adduct was obtained in 70% yield and was recrystallized from cyclohexane to give the pure compound: mp 143–144° (lit.[6] mp 143–144°); pmr[28] ($CDCl_3$) δ 4.77 (s, C_1H), 5.75 (d, J = 5.5 Hz, C_2H, C_3H), 6.24 (d, C_3H), 5.15 (s, C_4H), 5.59 (s, C_7H), 7.43 (s, C_8 C_6H_5), 1.99 (d, J = 8 Hz, C_{1-4} methano CH, CH′), 2.99 (d, C_{1-4} methano CH′, CH).

1,4,8-Triphenyl-1,4-dihydropyrazolo[1,2-*a*]pyridazin-6-one (5).—The previously reported[6] general procedure for Diels–Alder reactions was followed. From a mixture of 0.05 mol of 1,4-diphenylbutadiene, 3-phenyl-2-pyrazolin-5-one, and lead tetraacetate was obtained 15.6 g (88%) of **5**. Recrystallization from cyclohexane–benzene mixtures gave the pure compound: mp 203–205° with darkening; pmr ($CDCl_3$) δ 5.12 (m, C_1H and C_4H), 6.78–7.47 (m, phenyl), 5.89 (m, C_2H and C_3H), 5.58 (s, C_7H); mass spectrum[29] m/e (rel intensity) 364 (72), 273 (13), 260 (2), 234 (9), 219 (8), 206 (100), 204 (91), 104 (13), 102 (40), 91 (49), and 77 (25).

Anal. Calcd for $C_{25}H_{20}N_2O$: C, 82.39; H, 5.54; N, 7.68. Found: C, 82.31; H, 5.35; N, 7.81.

1,4,8-Triphenyl-3,4-dihydropyrazolo[1,2-*a*]pyridazin-6-one (6).—A mixture of 1.0 g (0.0027 mol) of **5** in a 20% solution of potassium hydroxide in 50% ethanol was refluxed for 5 hr. The mixture was then poured into 300 ml of cold water with rapid stirring to give 1.0 g of a white solid, **6**. Recrystallization from a cyclohexane–benzene mixture gave an analytical sample: mp 250–250.5°; pmr ($CDCl_3$) 6.98–7.55 (m, phenyl), 5.28–5.43 (m, C_2H and C_4H), 2.63 (octet, J = 17, C_3H, C_3H', J = 6.5, C_3H, C_4H, J = 1 Hz, C_3H, C_2H), 3.08 (octet, J = 6.5, C_3H', C_4H, J = 3 Hz, C_3H', C_2H), 5.61 (s, C_7H); mass spectrum m/e (rel intensity) 364 (88), 273 (100), 260 (3), 234 (35), 220 (52), 219 (40), 206 (12), 204 (78), 115 (96), 104 (98), 102 (40), 91 (41), 77 (100).

Anal. Calcd for $C_{25}H_{20}N_2O$: C, 82.39; H, 5.54; N, 7.68. Found: C, 81.76; H, 5.61; N, 7.85.

1-(1,4-Diphenyl-1,3-butadienyl)-5-phenyl-3-hydroxypyrazole (7).—A mixture of 2.0 g (0.0054 mol) of **5** was refluxed in a 20% solution of potassium hydroxide in 80% ethanol for 72 hr. The mixture was then poured into 300 ml of cold water and neutralized with acetic acid to give 2.0 g of a white solid, **7**. Recrystallization from a benzene–95% ethanol mixture resulted in an analytical sample of the dihydrate, mp 217–218°. A recrystallization of **7** from a benzene–absolute ethanol mixture resulted in the nonhydrated form. The pmr assignments (DMSO-d_6) are δ 7.20–7.42 (m, phenyl), 6.12 (s, pyrazole C_4H), 7.82 (d of d, J = 9, C_2H, C_3H, J = 1 Hz, C_2H, C_4H), 6.68 (d of d, J = 15 Hz, C_3H, C_4H), 7.03 (d, C_4H); mass spectrum m/e (rel intensity) 364 (50), 273 (32), 260 (78), 234 (<3), 219 (100), 206 (9), 204 (32), 115 (80), 104 (41), 102 (7), 91 (59), 77 (56).

Anal. Calcd for $C_{25}H_{20}N_2O$: C, 82.39; H, 5.54; N, 7.68. Found: C, 82.25; H, 5.54; N, 7.52.

Catalytic Hydrogenation of 7 to 1-(1,4-Diphenylbutyl)-5-phenyl-3-hydroxypyrazole (8).—To a slurry of 0.1 g of 5% palladium on charcoal catalyst in 10 ml of absolute ethanol was added a solution of 1.0 g (0.0027 mol) of **7** in 50 ml of absolute ethanol. The slurry was stirred at 1 atm under hydrogen for 25 hr at 27°. After uptake of hydrogen ceased at 130 ml, the catalyst was removed by filtration and the solvent was evaporated to give 1.0 g of **8**. Recrystallization from an ethanol–benzene mixture furnished an analytical sample: mp 114.5–115°; pmr (DMSO-d_6) δ 6.88–7.68 (m, phenyl and pyrazole C_4H), 5.25 (t, J = 7 Hz, C_1H, C_2H_2), 1.42–2.20 (m, C_2H_2 and C_3H_2), 2.60 (t, J = 7 Hz, C_4H, C_3H_2). The infrared spectra of **8** showed a considerable difference in chloroform and ethanol solutions. In chloroform, a strong peak at 5.9 μ was present but was not observed in ethanol. The mass spectrum included ions at m/e (rel intensity) 368 (19), 248 (100), 221 (13), 220 (12), 207 (8), 160 (40), 131 (25), 117 (35), 104 (44), 91 (62), 77 (27).

Anal. Calcd for $C_{25}H_{24}N_2O$: C, 81.49; H, 6.49; N, 7.58. Found: C, 81.82; H, 6.73; N, 7.73.

Catalytic Hydrogenation of Compound 9 to 1-(1,4-Diphenylbutyl)-5-phenyl-3-hydroxypyrazole (8).—The above procedure for a catalytic hydrogenation was used with 0.5 g (0.0013 mol) of **9**. Hydrogen uptake stopped at 47 ml and 0.4 g (80%) of **8** was isolated. The product was shown to be **8** by means of its infrared spectrum, which was superimposable with the spectrum of the above sample (**8**).

1-(1,4-Diphenyl-4-hydroxy-*cis*-2-butenyl)-5-phenyl-3-hydroxypyrazole (9).—A mixture of 2.0 g (0.0054 mol) of **5** and 10% hydrochloric acid was refluxed and stirred for 13 hr. The mixture was cooled and filtered to give 2.0 g of a white solid **9**, mp 203–204°. Recrystallization from a benzene–95% ethanol mixture gave an analytical sample of the monohydrate: mp 203–205°; pmr ($CDCl_3$) δ 6.80–7.38 (m, phenyl), 6.67 (s, pyrazolone C_4H), 6.15–6.19 (m, C_1, C_2, C_3, and C_4 H's of butenyl side chain); mass spectrum m/e (rel intensity) 382 (0), 364 (76), 273 (10), 260 (2), 234 (1), 219 (8), 206 (80), 204 (72), 104 (25), 102 (100), 91 (90), 77 (45).

Anal. Calcd for $C_{25}H_{24}N_2O_3$: C, 74.98; H, 6.04; N, 6.99. Found: C, 75.28; H, 5.68; N, 6.86.

2-(1,4-Diphenyl-4-trichloroacetoxy-*cis*-2-butenyl)-3-phenyl-3-pyrazolin-5-one (10).—A mixture of 2.0 g (0.0054 mol) of **5** and 2.0 g of trichloroacetic acid was heated to 90° for 30 hr. The solution was poured into 300 ml of water with stirring to give 1.8 g (90%) of solid **10**. Recrystallization from benzene and cyclohexane gave an analytical sample: mp 117° dec with gas evolution; pmr ($CDCl_3$) δ 6.62–7.44 (m, phenyl), 5.71 (s, pyrazolone C_4H), 6.11 (m, C_1, C_2, C_3, and C_4 H's of butenyl side chain); mass spectrum ring closed thermally to **5**; ir 5.65 (ester C=O), 6.10 μ (pyrazolinone C=O).

Anal. Calcd for $C_{27}H_{21}N_2O_3Cl_3$: C, 61.43; H, 4.02; N, 5.31. Found: C, 61.38; H, 4.15; N, 5.17.

Acid-Catalyzed Ring Closure of 10.—A mixture of 0.6 g (0.0011 mol) of **10** and 15 ml of a 20% hydrochloric acid solution in an ethanol–water solvent was stirred at 45° for 30 hr. The reaction mixture was poured into 100 ml of water and neutralized with sodium carbonate. The solid which formed (0.5 g) was identified as **5** by means of its infrared spectrum which was superimposable with that of an authentic sample of **6**.

Base-Catalyzed Ring Closure of 10.—A mixture of 0.5 g (0.0011 mol) of **10** and 20 ml of a 20% potassium hydroxide solution in an ethanol–water solvent was heated to 80° for 1 hr. The reaction mixture was poured into 150 ml of water and neutralized with acetic acid. The solid which formed (0.5 g) was identified as **5** by means of its infrared spectrum, as in the acid-catalyzed closure.

1-(4-Hydroxycyclopent-2-enyl)-3-phenyl-5-hydroxypyrazole (11).—A mixture of 2.0 g (0.0090 mol) of **4** and 50 ml of 10% hydrochloric acid was stirred at 40° until homogeneous, *ca.* 10 hr. The reaction mixture was neutralized with sodium hydroxide to give 2.0 g of a white solid precipitate. Recrystallization from an ethanol–benzene mixture resulted in an analytical sample: mp 180–182°; pmr ($CDCl_3$) δ 7.25–7.75 (m, C_3 C_6H_5), 5.76 (s, pyrazole C_4H), 5.61 (m, J = 9, C_1H, C_5H, J = 5 Hz, C_1H, C_5H'), 5.78–6.28 (m, C_2H and C_3H), 5.15 (m, J = 7, C_4H, C_5H', J = 4 Hz, C_4H, C_5H), 2.63 (octet, J = 15 Hz,

(27) Boiling points and melting points are uncorrected. Microanalyses were performed by Alfred Berhardt, Mulheim, Germany, and Galbraith Laboratories, Inc. The infrared spectra were measured with a Perkin-Elmer Model 137 double-beam spectrophotometer. The ultraviolet spectra were measured on a Cary Model 14 spectrophotometer and the pmr spectra were obtained on a JOEL 4H-100 and Varian Model A-60 with deuteriochloroform and deuteriodimethyl sulfoxide as solvents and tetramethylsilane as an internal standard (TMS = 0.0 ppm). The mass spectrometer employed was an AEI MS-902.

(28) Pmr data follows the convention: pmr (solvent) δ in ppm downfield from TMS = 0.0 ppm (multiplicity, coupling constant in Hz when resolved, assigned proton, coupled proton). Integrated peak intensities are correct for the assigned proton.

(29) The mass spectral data is shown as the mass to charge ratio (m/e) with the intensity as the per cent of the base peak in parenthesis. The fragments reported are those considered important in comparison with other spectra reported herein and those peaks which have an intensity greater than 5% of the base peak.

C_5H, C_5H'), 3.08 (octet, C_5H'); the O and N are considered to be trans; mass spectrum *m/e* (rel intensity) 242 (26), 186 (22), 161 (98), 160 (100), 103 (90), 82 (46), 77 (49), 55 (19); ir 3.5–4.7 and 5.2–6.1 (H bond), 2.8 μ (OH).

Anal. Calcd for $C_{14}H_{14}N_2O_2$: C, 69.42; H, 5.79; N, 11.57. Found: C, 69.55; H, 5.93; N, 11.47.

1-Cyclopentyl-3-phenyl-5-hydroxypyrazole (13).—A mixture of 4.0 g (0.0018 mol) of **4** and 0.1 g of 5% platinum on charcoal was stirred in 95% ethanol under hydrogen at 1 atm and 23°. Hydrogen uptake ceased at 440 ml after 5 hr. After filtration of the catalyst and evaporation of the solvent, 3.8 g (95%) of the solid **13** was obtained. A recrystallization of the product from a benzene–ethanol mixture gave an analytical sample: mp 207–208°; pmr ($CDCl_3$) δ 7.20–7.84 (m, C_3 C_6H_5), 5.81 (s, pyrazole C_4H), 4.68 (m, cyclopentyl C_1H), 1.98 (m, cyclopentyl methylenes); mass spectrum *m/e* (rel intensity) 228 (22), 173 (73), 160 (100), 103 (7), 77 (7); ir 3.5–4.7 and 5.2–6.1 μ (H bond).

Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.68; H, 7.02; N, 12.28. Found: C, 73.87; H, 6.82; N, 12.08.

8-Phenyl-1,4-methano-1,2,3,4-tetrahydropyrazolo[1,2-*a*]-pyridazin-6-one (15).—The title compound was prepared by the previously reported procedure,[6] mp 149–151° (lit.[6] mp 148–149°).

Anal. Calcd for $C_{14}H_{14}N_2O$: C, 74.34; H, 6.29; N, 12.39. Found: C, 74.30, H, 6.30; N, 12.60.

Registry No.—**4**, 14181-57-8; **5**, 34347-69-8; **6**, 34347-70-1; **7**, hydroxyl, 34347-71-2; **7**, oxo, 34347-79-0; **8**, hydroxyl, 34347-72-3; **8**, oxo, 34347-80-3; **9**, 34347-73-4; **10**, 34347-74-5; **11**, 34347-75-6; **13**, 34347-76-7; **14**, 34347-81-4; **15**, 14181-60-3.

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Mechanism of the Transformation of 2,4-Dihydroxy-1,4-benzoxazin-3-ones and 2-Hydroxy-2-methyl-4-methoxy-1,4-benzoxazin-3-one to 2-Benzoxazolinone

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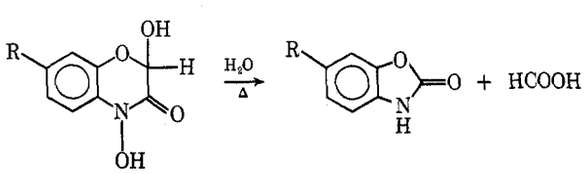
The formation of 2-benzoxazolinones from 2,4-dihydroxy-1,4-benzoxazin-3-ones and from 2-hydroxy-2-methyl-4-methoxy-1,4-benzoxazin-3-one is discussed. A previously proposed mechanism is criticized and a plausible mechanism is offered.

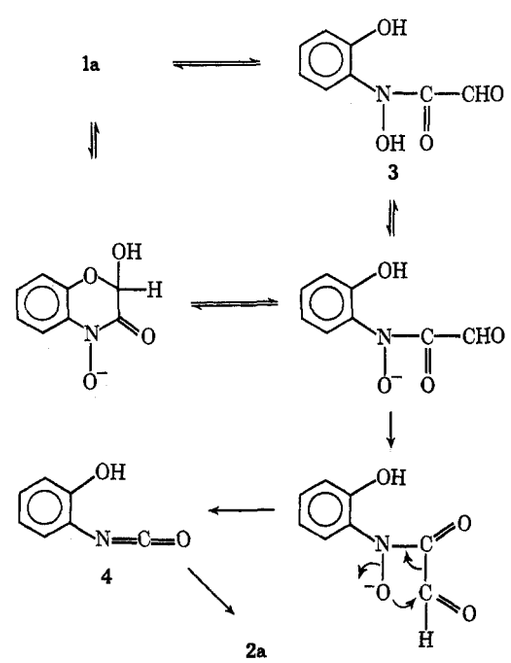
To date, the only reported hydroxamic acids from higher plants are those which are derivatives of 2,4-dihydroxy-1,4-benzoxazin-3-one (**1a**).[2] These compounds and products obtained from their rearrangement have been termed "Resistance Factors," since they are found in several varieties of crop plants and exhibit antifungal and insectistat properties.[3,4]



1 **2**

a, R = H
b, R = OCH_3

When **1** is heated in aqueous or alcoholic solution, the corresponding 2-benzoxazolinone (**2**) is rapidly formed with the liberation of formic acid, which has been established to arise from C-2.[5] The conversion of **1a** to **2a** was proposed to proceed *via* the isocyanate **4**.[6] This mechanism assigns no role to the phenolic hydroxyl group prior to the cyclization step (**4** → **2a**). Therefore, it would be assumed that isocyanate formation would occur independent of the presence of the phenolic hydroxyl function.



Under the conditions utilized for the formation of 2-benzoxazolinone (**2a**) from 2,4-dihydroxy-1,4-benzoxazin-3-one (**1a**), neither *N*-phenylglyoxylohydroxamic acid (**5**) nor *N*-phenyl-α,α-dichloroacetohydroxamic acid (**6**) gave the product expected from an isocyanate intermediate. *N*-Phenylglyoxylohydroxamic acid (**5**) could be transformed to aniline in 36% yield when it was refluxed with aqueous sodium bicarbonate solution, and a small amount of *sym*-diphenylurea (**7**) was isolated from *N*-phenyl-α,α-dichloroacetohydroxamic acid (**6**) after treatment with aqueous sodium hydroxide at room temperature. The products obtained would be

(1) Taken in part from the dissertation presented by M. D. Corbett, Nov 1970, to the Graduate School of the University of Kansas in partial fulfillment of the requirements for the Doctor of Philosophy Degree.

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