Compound **11** was in every respect identical with an authentic sample of 8-chloro-1-methyl-6-phenyl-3,4-dihydro-1,5-benzodiazocin-2(1H)-one provided by Fryer (Hoffmann-La Roche, Inc.).[12]

3-(3-Hydroxypropyl)-4-phenyl-1,2,3,4-tetrahydroquinazoline.—To a solution of 528 mg (2 mmol) of 1,5-methane-6-phenyl-3,4,5,6-tetrahydro-1,5-benzodiazocin-2(1H)-one in 25 ml of 95% ethanol and 10 ml of methylene chloride was added at room temperature 200 mg of sodium borohydride. After standing for 1 hr the excess sodium borohydride was decomposed by addition of a few drops of acetic acid. The reaction mixture was concentrated *in vacuo* and distributed between methylene chloride and water. The organic phase was dried and evaporated and the residue crystallized from diethyl ether to yield 150 mg (28%) of 3-(3-hydroxypropyl)-4-phenyl-1,2,3,4-tetrahydroquinazoline in white prisms: mp 102–104°; nmr ($CDCl_3$) δ 4.78 s (methine hydrogen) multiplets for the methylene groups at δ 1.75, 2.80, 3.83.

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.0; H, 7.5; N, 10.4; O, 6.0. Found: C, 75.8; H, 7.6; N, 10.4; O, 6.2.

Analogously prepared was 6-chloro-3-(3-hydroxypropyl)-4-phenyl-1,2,3,4-tetrahydroquinazoline (**13**) (oil), characterized by tlc and nmr (very similar to the nmr spectrum of the deschloro compound above).

7-Chloro-1,4-methano-5-phenyl-1,3,4,5-tetrahydro-2H-1,4-benzodiazepin-2-one (15).—A mixture of 7.0 g (29 mmol) of 6-chloro-4-phenyl-3,4-dihydroquinazoline (**3**), 70 ml of ethanol, 7 ml of triethylamine and 4.1 ml of ethyl bromoacetate was refluxed for 1.5 hr. The volatile parts were thoroughly removed *in vacuo* and the obtained residue was distributed between methylene chloride and water. On drying and evaporating the solvent, 6-chloro-3-carbethoxymethyl-4-phenyl-3,4-dihydroquinazoline resulted as an oil (8 g, 85% of theory). This crude ester was dissolved in 100 ml of ethanol and 45 ml of 2 *N* sodium hydroxide and heated for 1.5 hr to 60°. After evaporation of the alcohol *in vacuo* the alkaline solution was extracted with ethyl acetate to remove nonacidic material. The aqueous layer was neutralized with 2 *N* hydrochloric acid to pH 6–7 and then extracted with methylene chloride to yield 5.0 g (68%) of crude 6-chloro-3-carboxymethyl-4-phenyl-3,4-dihydroquinazoline as a colorless oil. This crude amino acid was dissolved in 70 ml of ethanol and 20 ml of 2 *N* sodium hydroxide and reduced with 2.0 g of sodium borohydride at 60° within 1.5 hr. The excess sodium borohydride was decomposed with 2 *N* hydrochloric acid. The ethanol was removed *in vacuo*, the aqueous solution neutralized and extracted with methylene chloride. After drying and evaporating the organic solvent, 4.25 g (85%) of 6-chloro-3-carboxymethyl-4-phenyl-1,2,3,4-tetrahydroquinazoline (**14**) resulted as a colorless oil, which was practically pure in tlc.

To a solution of 3.65 g of compound **14** in 50 ml of dry dioxane and 3.5 ml of triethylamine was dropwise added at 10° 2 ml of ethyl chloroacetate. After standing for 15 min at room temperature, the volatile parts were removed *in vacuo*, the resulting residue was dissolved in methylene chloride and this solution was extracted with dilute sodium bicarbonate and with water. The organic phase was dried over sodium sulfate and evaporated at 30° *in vacuo*. 7-Chloro-1,4-methano-5-phenyl-1,3,4,5-tetrahydro-2H-1,4-benzodiazepin-2-one (**15**) crystallized from ether (1.43 g, 42%) in white prisms: mp 150–152°; ir (CH_2Cl_2) 1780 (C=O).

Anal. Calcd for $C_{16}H_{13}ClN_2O$: C, 67.5; H, 4.6; Cl, 12.5. Found: C, 67.0; H, 4.7; Cl, 12.2.

Registry No.—**3**, 17954-62-0; **4a**, 17954-63-1; **4b**, 17954-64-2; **6**, 17952-93-1; **7**, 17954-65-3; **8**, 17954-66-4; **10**, 14098-46-5; **11**, 17954-18-6; **15**, 17954-69-7; 1,5-methano-6-phenyl-3,4,5,6-tetrahydro-1,5-benzodiazocin-2(1H)-one 17954-70-0; 6-(4-chlorophenyl)-1,5-methano-3,4,5,6-tetrahydro-1,5-benzodiazocin-2(1H)-one, 17954-71-1; 6-phenyl-3,4,5,6-tetrahydro-1,5-benzodiazocin-2(1H)-one, 17954-72-2; 6-(4-chlorophenyl)-3,4,5,6-tetrahydro-1,5-benzodiazocin-2(1H)-one, 17954-73-3; 1-methyl-6-phenyl-3,4,5,6-tetrahydro-1,5-benzodiazocin-2(1H)-one, 17954-74-4; 3-(3-hydroxypropyl)-4-phenyl-1,2,3,4-tetrahydroquinazoline, 17954-75-5.

Acknowledgment.—We are indebted to Mr. U. Stoeckli and his staff for the spectral data and the microanalyses. We also wish to thank Dr. R. I. Fryer of Hoffmann-La Roche, Inc., Nutley, N. J., for providing us with a sample of compound **14** prepared by his procedure for comparative purposes.

The Nitrosation of α,β-Unsaturated Oximes. IV. The Synthesis and Structure of 3,4-Diazacyclopentadienone Derivatives[1,2]

JEREMIAH P. FREEMAN,[3] JOHN J. GANNON, AND DONALD L. SURBEY

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

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β-Alkyl or aryl α,β-unsaturated oximes are converted by nitrous acid under oxygen or by a mixture of nitrous and nitric acids into 3,4-diazacyclopentadienone dioxides (**3**). Some negatively substituted methylene ketones are oxidized by nitrous acid to the same heterocycles. Nitrosation of the oximes under nitrogen produced the corresponding heterocyclic oxime. Nitrosation of 1-hydroxypyrazole 2-oxides (**10**) yielded 4-nitropyrazolenine 1,2-dioxides (**11**) that decomposed thermally to **3**. Reduction of the dioxides **3** with zinc in acetic acid furnishes a new and general route to 4-hydroxypyrazoles. Reduction of **3** with sodium dithionite yields 1,4-dhydroxypyrazoles, a new class of organic compounds. Oxidation of these latter compounds yields 3,4-diazacyclopentadienone oxides (**6**). A general mechanism for the nitrosation of α,β-unsaturated oximes is presented.

Nitrosation of β-aryl-α,β-unsaturated oximes produces a mixture of compounds which appear to be heterocyclic ketones and their corresponding oximes.[4] Since we have previously shown that mesityl oxide oxime is converted upon nitrosation into a pyrazolenine derivative[5] and, in an accompanying paper, that α-substituted α,β-unsaturated oximes yielded pyrazole derivatives,[6] we were led to suspect a five-ring structure for these compounds also.

Synthesis.—Previous investigators[4] reported that heterocyclic oximes were obtained from treatment of β-aryl-α,β-unsaturated oximes with nitrous acid while

(1) Part of these results have been described previously: paper III, J. P. Freeman and D. L. Surbey, *Tetrahedron Lett.*, 4917 (1967).

(2) Based in part on the Ph.D. dissertations of Donald L. Surbey and John J. Gannon. We are indebted to the donors of the Petroleum Research Fund, the Alfred P. Sloan Foundation, and the National Institutes of Health, National Cancer Institute, Grant No. CA 10742-01, for support of this research.

(3) Alfred P, Sloan Fellow, 1966–1968.

(4) (a) For some historical background on different structures proposed see ref 1. (b) Evidence for the presence of ketone and oxime functions is provided by G. Ponzio, *Gazz. Chim. Ital.*, **66**, 479 (1936), and G. Longo, *ibid.*, **66**, 815 (1936).

(5) Paper I, J. P. Freeman, *J. Org. Chem.*, **27**, 1309 (1962).

(6) J. P. Freeman and J. J. Gannon, *J. Org. Chem.*, **34**, 194 (1969). For a preliminary report, see J. P. Freeman and J. J. Gannon, *J. Heterocycl. Chem.*, **3**, 544 (1966).

TABLE I
3,4-DIAZACYCLOPENTADIENONE DIOXIDES

R	R′	Registry no.	Yield,[a] % A	B	C	Mp, °C	Uv spectra λmax	εmax	Calcd, % C	H	N	Found, % C	H	N	Oxime mp, °C
C_6H_5	CH_3	16901-38-5	40	18		164–165	256	20,900	58.82	3.95	13.72	58.65	4.28	14.04	218–219[b]
							303	5,950							
							418	720							
C_6H_5	C_2H_5	16858-30-3	30	15		83.5	254	20,300	60.55	4.62	12.84	60.42	4.88	12.88	198–199[c]
							301	5,500							
							420	630							
C_6H_5	C_6H_5	17952-96-4	14	5	26	191–192	256	39,100	67.67	3.79	10.52	67.68	4.38	10.13	212–213[d]
							330	4,180							
							452	1,700							
CH_3	CH_3	17952-97-5	15	Trace		109–110	280	12,100	42.26	4.26	19.71	42.34	4.36	19.93	205–206[e]
							358	160							
$CO_2C_2H_5$	$CO_2C_2H_5$				20	118[f]	229	14,400							
							285	5,500							
							368	740							
CO_2CH_3	CO_2CH_3	17952-98-6			22	168–169	233	15,800	36.53	2.63	12.17	36.86	2.66	12.37	
							285	6,870							
							362	170							
C_6H_5	$CO_2C_2H_5$	17952-99-7			22	129–130	254	19,000	54.79	3.84	10.68	55.08	4.30	10.46	
							290	4,750							
							424	1,200							

[a] A, B, and C refer to the different experimental methods. See Experimental Section. [b] Lit.[4b] mp 215°. [c] Lit. mp 195°: C. Harries and H. Tietz, *Ann.*, **330**, 237 (1904). [d] Lit.[4b] mp 208°. [e] *Anal.* Calcd for $C_5H_7N_3O_3$: C, 38.22; H, 4.49; N, 26.74. Found: C, 38.44; H, 4.74; N, 25.95. [f] Lit. mp 117–118°: P. Henry and H. von Pechmann, *Ber.*, **26**, 997 (1893). These authors described the oxidation of acetonedicarboxylic ester with red fuming nitric acid.

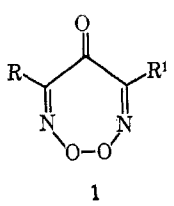
the corresponding ketones were produced in low yields when dilute nitric acid–nitrous acid mixtures were employed. Although it has been claimed that the oximes can be converted into ketones by nitric acid oxidation, we have not been able to effect this conversion to any useful extent. Attempts to convert the ketones into oximes with hydroxylamine leads to reduction of the heterocycle.[4b]

It has now been found that small amounts of the ketone are produced in the nitrosation reaction and that the yield of ketone can be increased by carrying out the reaction in the presence of molecular oxygen.[7] Pertinent data are summarized in Table I.

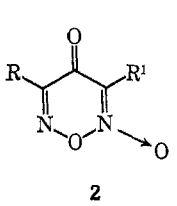
Some ketones of this series also may be obtained in low yield by oxidative nitrosation of the corresponding dialkyl ketone.[8] Presumably the 1,3-dioxime is first formed and then undergoes oxidative ring closure. Such a ring closure of diphenyl triketone 1,3-dioxime has been effected.

Because of the relative insolubility of the oximes of this series, the chemical studies on these compounds have been restricted to the ketones. The structure of the corresponding oximes has been inferred from that of the ketones.

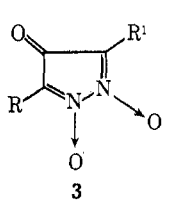
Structure.—Three structures may be considered for the compounds obtained in these reactions. Structures **1** and **2** have been considered earlier[4b] and structure **1** was favored. Wieland[9] independently suggested structure **2** based upon his work with furoxans but presented no experimental support.



1



2



3

The brightly colored ketones showed intense absorption in the infrared spectrum at 1640 cm^{-1} with a shoulder on the high frequency side at 1660 cm^{-1} and a strong band at 780 cm^{-1}. This latter band was present in all the compounds of this series regardless of whether an aromatic ring was present and probably is due to an N–O vibration. A band found in nitrones in the 1170–1280-cm^{-1} region is probably analogous to that present in this series of compounds at 1080–1140 cm^{-1}. The absence of a normal ketone carbonyl band coupled with the lack of ordinary carbonyl reactivity requires that any structural proposal incorporates a functional group adjacent to the carbonyl function which can reduce its carbonyl character. Structures **2** and **3** meet this requirement.

$$-N(\rightarrow O)=CC=O \leftrightarrow -N^{+}(=O)C=CO^{-}$$

From a structural viewpoint the nuclear magnetic resonance spectrum of the ketone obtained from 3-penten-2-one oxime was most revealing. Only one sharp signal was observed at δ 2.12 indicating that both methyl groups are in identical environments. Thus a structure such as **2** (R = R′ = CH_3) was ruled out.[10,11] In the corresponding oxime two signals for

(7) The actual effect of the oxygen is not understood, but the ketones could be obtained in up to 40% yield in its presence. In addition, small amounts of other products were obtained—the parent unsaturated ketone (formed presumably by deoximation), pyrazoles, isoxazoles, and isoxazolidine derivatives. Complete details may be found in the Experimental Section.

(8) See Table I, footnote *f*.

(9) H. Wieland, *Ann.*, **424**, 112 (1921).

(10) Many previous studies have established that a methyl group adjacent to an N-oxide function will have a different chemical shift than that of such a group adjacent to unoxidized nitrogen: *cf.* R. K. Harris, A. R. Katritzky, S. Øksne, A. S. Bailey, and W. C. Patterson, *J. Chem. Soc.*, 197 (1963); J. P. Freeman, *J. Org. Chem.*, **28**, 2508 (1963). While a rapid intramolecular exchange would lead to the same result, it has been shown in the benzofuroxan system, which might be expected to be more mobile since an aromatic structure is generated in the exchange, that a 15-kcal barrier exists to isomerization: F. B. Mallory, S. L. Manatt, and C. S. Wood, *J. Amer. Chem. Soc.*, **87**, 5433 (1965).

(11) Further inferential evidence against structure **2** is the fact that no isomers have been observed when the two groups attached (R) were different. In both cases when a methyl group was present its chemical shift (nmr spectrum) was the same, suggesting the same electronic environment. In addition both 4-phenyl-3-buten-2-one and 1-phenyl-2-butenone oximes gave the same ketone.

the methyl groups appeared due to the dissymmetry introduced by the orientation of the N-hydroxy group.

While these nmr data are consistent with the seven-membered-ring structure **1**, the bright colors of the compounds are not accommodated by such a structure. There would seem to be no reason for compounds containing such a ring system to be any more highly colored than acyclic 1,3-dioximino ketones which have a pale yellow color. Also the carbonyl groups of these dioximino ketones exhibit normal carbonyl absorption in the infrared spectrum at about 1735 cm^{-1} with no absorption in the 1600–1700-cm^{-1} region. The ultraviolet maxima and other data are recorded in Table I.

The 3,4-diazacyclopentadienone structure containing adjacent N-oxide functions (**3**) is the only structure consistent with all the spectral data.[12,13]

Reactions.—Reduction of ketones **3** with zinc and acetic acid produced the 4-hydroxypyrazoles **5** (Table II).

Previous syntheses of 4-hydroxypyrazoles have involved complicated starting materials, low yield reactions, or highly specific methods. A recent review[14] characterizes these compounds as "relatively inaccessible." Some of these methods are the reductive condensation of *vic*-triketones with hydrazine,[15] the alkylation of malonic ester with diazoacetic esters,[16] and the condensation of hydrazines with 2,2,3-trichlorobutyraldehyde.[17] Although the over-all yields are low in the present synthesis, the two-step process from readily accessible starting materials makes it useful and attractive.

Reduction of **3** with sodium hydrosulfite yielded the corresponding 1,4-dihydroxypyrazole **4** (Table III); reduction of the latter with zinc in acetic acid also produced the 4-hydroxypyrazoles **5** (Scheme I).

SCHEME I

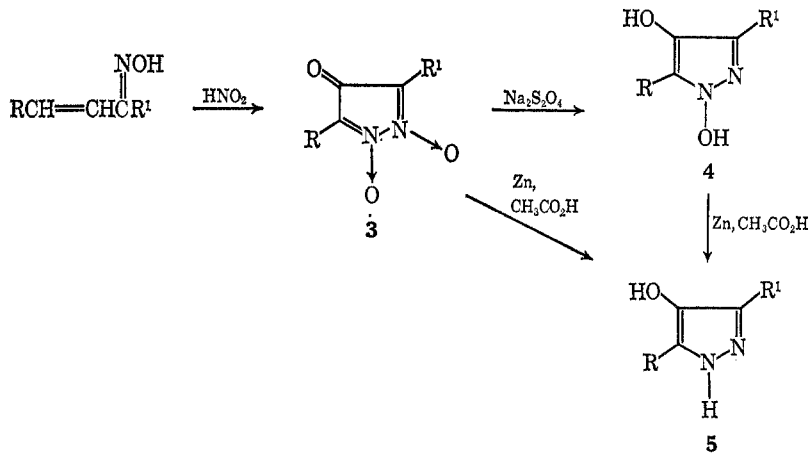


TABLE II

4-HYDROXYPYRAZOLES **5**

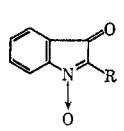
R	R¹	Registry no.	Mp, °C	Lit. mp, °C	Yield, %
C_6H_5	C_6H_5	17953-06-9	235[a]		68
C_6H_5	CH_3		194–195	188[b]	82
C_6H_5	C_2H_5	17953-07-0	178–179[c]		81
C_6H_5	$CO_2C_2H_5$		170–171	162[d]	85
$CO_2C_2H_5$	$CO_2C_2H_5$		138, 151[e]	137, 151[e]	57
CO_2CH_3	CO_2CH_3		243–244	232[f]	35

[a] *Anal.* Calcd for $C_{15}H_{12}N_2O$: C, 75.25; H, 5.12; N, 11.86. Found: C, 75.97; H, 5.16; N, 11.50. [b] F. Sachs and A. Röhmer, *Ber.*, **35**, 3307 (1904). [c] *Anal.* Calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.56; H, 6.73; N, 14.92. [d] A. Bertho and H. Nüssel, *Ann.*, **457**, 288 (1927). [e] Bertho and Nüssel (footnote *d*) reported that this compound changed from plates to needles at 137° and then remelted at 151°. [f] O. Dimroth and E. Eberhardt, *Ann.*, **355**, 29, 107 (1904).

The 1-hydroxypyrazole derivatives are the second reported members of that class.[18] Because of their ready oxidation (see below) they must be protected from the air and other adventitious oxidizing agents.

The structure of these 1,4-dihydroxypyrazoles rests on their elemental analyses, their nmr spectra which exhibit two low field, one-proton signals [*e.g.*, compound **4** (R = R¹ = C_6H_5) δ 12.5, δ 8.42], their enolic properties, the identity of their ultraviolet spectra with those of 4-hydroxypyrazoles, and their ready reduction to 4-hydroxypyrazoles. The relative position of groups R and R¹ cannot be settled with certainty, however (see below). In addition these compounds were readily oxidized by Fremy's salt with the loss of two

(12) The bright red and orange colors of the compounds encountered in this investigation are reminiscent of the brick orange isatogens which also contain a similar chromophore: P. Pfeiffer, *Ber.*, **45**, 1819 (1912).



(13) Recently, B. Unterhalt [*Arch. Pharm.*, **300**, 822 (1967); *Tetrahedron Lett.*, 1841 (1968)] suggested structure **3** for these compounds, but the data he cited did not distinguish clearly between a five- and six-membered ring. He appears to have been unaware of the previous suggestion of the six-membered ring structure and of the work of Ponzio and Longo.[4b]

(14) A. N. Kost and I. I. Grandberg, *Advan. Heterocycl. Chem.*, **6**, 327 (1966).

(15) See Table II, footnote *b*.

(16) See Table II, footnote *d*.

(17) F. D. Chattaway and G. D. Parkes, *J. Chem. Soc.*, 1005 (1935), and prior papers.

(18) For one previous example, see ref 6. Undoubtedly the compound assigned structure i by Henry and Von Pechmann (footnote *f*, Table I) for the sodium bisulfite reduction product of 2,5-dicarbethoxy-3,4-diazacyclopentadienone 3,4-dioxide, **3** (R = R¹ = $CO_2C_2H_5$), was actually the 1,4-dihydroxypyrazole derivative, **4** (R = R¹ = $CO_2C_2H_5$).

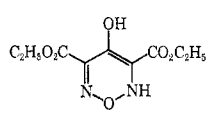


TABLE III

1,4-DIHYDROXYPYRAZOLES 4

R	R¹	Registry no.	Mp, °C	Yield, %	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
C_6H_5	C_6H_5	17953-00-3	171–172	91	71.42	4.79	11.10	71.59	5.04	10.64
C_6H_5	CH_3	17953-01-4	171–172	86	63.15	5.30	14.73	63.20	5.47	14.75
C_6H_5	C_2H_5	17953-02-5	165–166	87	64.69	5.92	13.72	64.82	6.26	13.74
C_6H_5	$CO_2C_2H_5$	17953-03-6	180–181	32[a]	58.06	4.87	11.28	58.12	5.02	11.42
CH_3	CH_3	17953-04-7	149–150	39[b]	46.87	6.29	21.86	47.00	6.82	22.39
$CO_2C_2H_5$	$CO_2C_2H_5$		165[c]	37[b]						
CO_2CH_3	CO_2CH_3	17953-05-8	167–168	35[b]	38.90	3.73	12.96	39.09	3.71	12.85

[a] Large quantities of the 4-hydroxypyrazoles were also obtained from these reactions. [b] Isolated by extraction of the reaction mixture with 1:1 ether–ethyl acetate. [c] Lit.[8] mp 169°.

TABLE IV

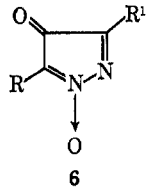
3,4-DIAZACYCLOPENTADIENONE MONOXIDES 6

Compound R¹	Compound R	Registry no.	Mp, °C	Yield, %	Ultraviolet spectra (C_2H_5OH) λ_{max}	Ultraviolet spectra (C_2H_5OH) ϵ_{max}	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
C_6H_5	C_6H_5	17953-08-1	165	95	250	18,940	71.99	4.03	11.19	71.61	4.32	11.30
					303	5,720						
					333	5,960						
					483	1,370						
C_6H_5	CH_3	17953-09-2	154–155	95	238	7,290	63.83	4.28	14.89	63.76	4.46	14.98
					323	6,720						
					415	800						
C_6H_5	C_2H_5[a]	17953-10-5	90–91	94	240	7,550	65.34	4.98	13.85	65.41	5.05	14.14
					325	6,240						
					418	850						
CH_3	CH_3	17953-11-6	98–100	90			47.62	4.80	22.21	47.50	5.06	22.46

[a] Depending upon the conditions used for recrystallization, this compound was sometimes obtained as a dimer. The properties of this dimer are described in the Experimental Section.

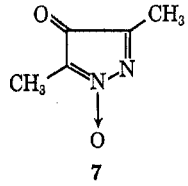
hydrogen atoms to deeply colored solids which could in turn be reduced to the dihydroxypyrazole.[19]

Structure **6** is proposed for these compounds (Table IV). It is based upon elemental composition, the



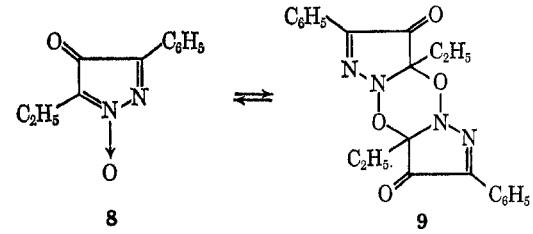
6

reduction products,[20] color, and other spectral properties (an intense band at 1555 cm^{-1}, a medium band at 1700 cm^{-1}, and the absence of absorption in the 3-μ region of their infrared spectra). As expected[14] the nmr spectrum of the dimethyl derivative **7** showed two methyl signals at δ 2.04 and 2.28.



7

It is not possible at this time to establish absolutely the structure of the unsymmetrical derivatives of **6** (and in turn of **4**), but some inferential evidence is available. During purification of the red ketone **8**, small amounts of yellow needles were isolated. These reverted to **8** upon heating or dissolution. It is believed that this new compound is a dimer of structure **9**.



8 **9**

The evidence for dimer formation is as follows: the presence in **9** of two carbonyl bands at 1730 and 1750 cm^{-1} compared to 1715 cm^{-1} in **8**; absorption in the ultraviolet spectrum of **9** at 246 mμ which slowly changed on standing to the spectrum of the monoxide **8** (Table IV); the presence in the nmr spectrum of **9** (−20°) of two sets of signals for the ethyl groups (δ CH_3 0.53 and 0.93) which changed on warming to room temperature to one set (δ CH_3 1.20) identical in all respects with that of **8**. The change in the ethyl group chemical shift suggests that it is associated with the nitrone function and therefore suggests structure **8** rather than the alternative for the monomer.[21]

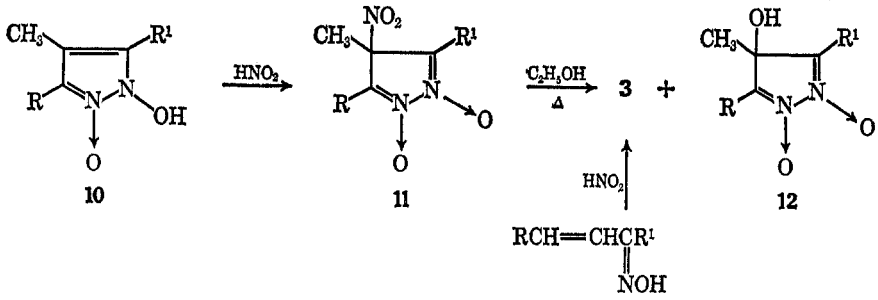
While all these reductions lead to five-membered-

(19) Oxidation of the 1,4-dihydroxypyrazoles **4** (R = R¹ = CO_2CH_3 or $CO_2C_2H_5$) could not be effected with a variety of oxidizing agents. It is possible that the reduced form is stablized by internal hydrogen bonding.

(20) Compound **6** (R = R¹ = C_6H_5) was readily reduced electrochemically to produce a stable radical anion whose esr spectrum was measured. This spectrum was identical with the spectrum previously reported (J. P. Freeman and D. L. Surbey, Abstracts, 151st National Meeting of the American Chemical Society, Pittsburgh, Pa., April 1966, p 38K) for the reduction of the dioxide **3** (R = R¹ = C_6H_5). The esr spectrum was very complex with apparent unequal coupling to both nitrogens as well as to hydrogen atoms in the benzene rings. Further work on this and other radical anions from these heterocycles is in progress in collaboration with Dr. K. J. Martin, Rohm and Haas Co., Huntsville, Ala. At this time it is not possible to relate the spectra to the structures proposed.

(21) Preliminary investigation of the mass spectra of these compounds also supports the structures within. For example, the spectrum of **6** (R = CH_3; R¹ = C_6H_5) shows peaks at M − 103 (loss of C_6H_5CN) and at 85 ($C_3H_3NO_2$), 57 (C_2H_3NO), and 41 (C_2H_3N) all indicating association of the methyl group and not the phenyl group with the nitrone function: M. J. Hoare, unpublished work.

SCHEME II



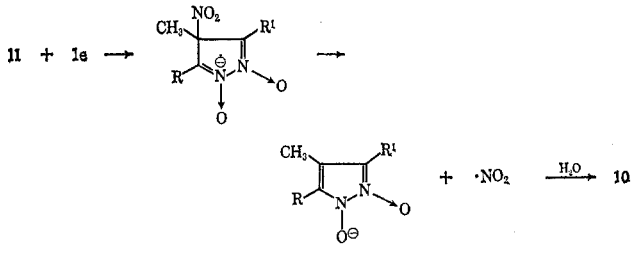
a, $R = R^1 = C_6H_5$
b, $R = C_6H_5$; $R^1 = CH_3$

ring protons consistent with a precursor such as **3**, it is not possible to rule out other structures by these reactions alone, since they could proceed by ring opening and reclosure. It has not been possible to reduce directly compound **3** to **6**, for example. Treatment of **3** ($R = R^1 = C_6H_5$) with triphenylphosphine in benzene led to an intractable tarry mixture. When triphenylphosphine in ethanol was employed, a mixture of compounds **4** and **5** ($R = R^1 = C_6H_5$) was obtained. However, the reduction studies are consistent with the nmr, infrared, and ultraviolet evidence and support structure **3** and its analogs for the products of these nitrosation reactions.[18]

Independent Synthesis.—In a preliminary study of the substitution reactions of 4-alkyl-1-hydroxypyrazole 2-oxides (**10**),[6] it was found that these compounds reacted with nitrous acid to produce intermediate nitro compounds **11** which decomposed upon heating in ethanol to yield the same ketones **3** produced by nitrosation of the appropriate unsaturated oxime under oxygen (Scheme II).

The structures of the intermediate nitro compounds were inferred from their elemental analyses, their infrared and nmr spectra, and their ready reduction back to the 1-hydroxypyrazole 2-oxide with sodium dithionite.[22] The infrared spectrum of **10a** showed strong bands at 1640 [$C_6H_5C{=}N(\rightarrow O)-$], and 1545 and 1345 cm^{-1} (asymmetric and symmetric NO_2 stretching). The infrared spectrum of **10b** showed bands at 1680 [$CH_3C{=}N(\rightarrow O)-$], 1640 [$C_6H_5C{=}N(\rightarrow O)-$], 1545 and 1340 cm^{-1} (NO_2 group). The infrared spectra of 1-hydroxypyrazole 2-oxides[6] showed no strong bands in these regions. The nmr spectra reveal the absence of the low field proton present in the hydroxypyrazole oxides and the shift of the methyl resonance (at position 4) to lower field.

(22) The reduction of **11** back to **10** can be understood in the following terms.

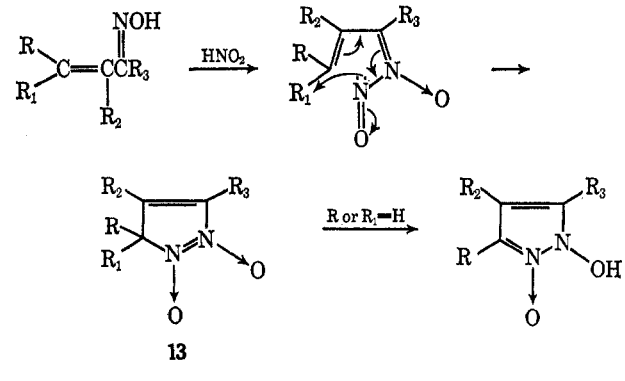


The loss of the nitrogen dioxide radical from a radical anion has been postulated: G. A. Russell and W. C. Danen, *J. Amer. Chem. Soc.*, **90**, 347 (1968).

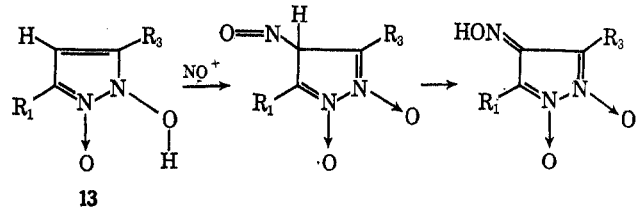
The details of the decomposition of the nitro compound to ketone **3** are unknown. In addition to the ketone an alcohol presumed by analogy to have structure **12** was also produced. Presumably these products arise from the corresponding oxy radical which can fragment to ketone or abstract hydrogen from solvent to form alcohol. While several uncertainties remain, the direct formation of ketone **3** from a five-membered-ring precursor lends support to a similar ring structure for the ketones themselves.

Mechanism of Formation.—The assignment of structure **3** to the products of these reactions allows the suggestion of a common reaction path for at least the early stages of all the nitrosation reactions of α,β-unsaturated oximes (Scheme III).[23]

SCHEME III



A compound of structure **13** ($R = R_1 = R_3 = CH_3$; $R_2 = H$) was obtained from mesityl oxide oxime.[5] When R_2 is an alkyl group the reaction can be stopped at the hydroxypyrazole stage.[6] However, when $R_2 = H$, the next step, apparently an electrophilic substitution, may proceed readily in the absence of oxygen. When



excess nitrous acid is not present and the reaction is run under oxygen, oxime formation is almost eliminated

(23) An ionic mechanism is preferred since only traces of the heterocycle and large amounts of nitro compounds were obtained when the nitrosations were carried out in ether with dinitrogen tetroxide. We are indebted to Dr. T. E. Stevens, Rohm and Haas Co., Huntsville, Ala., for these experiments (see Experimental Section).

and the ketone is the predominant product. The steps leading to ketone under these conditions are not known, but since it has not been possible to obtain ketone **3** from its oxime under the conditions of the reaction, we believe that ketone **3** arrives by a separate series of reactions which may involve free-radical intermediates.

While this mechanism accounts for the production of the diazacyclopentadienone dioxides from the unsaturated oximes, it does not explain their production from the 1,3-dioximes. In these cases the nitrogen–nitrogen bond must be formed during the oxidation step. Formation of a nitrogen–nitrogen bond rather than a nitrogen–oxygen bond finds precedence in the work of Hörner and coworkers,[24] who showed that aldoximes are oxidized to azine bisoxides, and by the recent disclosure that dehydration of certain 1,3-dioximes produced pyrazolenine monoxides[25] rather than 1,2,6-oxadiazines as previously claimed.[26] There does not appear to be substantial evidence for the existence of the 1,2,6-oxadiazine nucleus at this time.

The compounds reported here are the first examples of 3,4-diazacyclopentadienone derivatives. The parent diazacyclopentadienone oximes have been implicated in the ring opening of 4-nitrosopyrazoles.[27] Efforts to deoxygenate completely these compounds to the parent diazacyclopentadienones have so far been unsuccessful but experiments are continuing.

Experimental Section[28]

Synthesis of 3,4-Diazacyclopentadienone 3,4-Dioxides (3).—Three procedures were used. The first two, illustrated with benzalacetone oxime, are applicable to all the unsaturated oximes studied while the third is restricted to ketones activated by an electronegative group, *i.e.*, carbethoxy or phenyl. Since the condition of method C varied considerably, several examples are included. The analysis and properties of these compounds may be found in Table I.

Method A. 2-Phenyl-5-methyl-3,4-diazacyclopentadienone 3,4-Dioxide.—A solution of 5.0 g (0.03 mol) of benzalacetone oxime in 100 ml of 90% CH_3CO_2H was saturated with oxygen using a bubbler while stirring at 0–5°. A solution of 4.5 g (0.065 mol) of $NaNO_2$ in 40 ml of water was added over a 3-hr period to the closed system under a slight positive pressure of oxygen. After stirring for 1 additional hr, the reaction mixture was diluted with 300 ml of water, cooled to 0° and filtered.

The bright orange precipitate was slurried with 200 ml of CH_2Cl_2 and filtered to remove 0.15 g (2.2%) of oxime. The filtrate was concentrated to about 25 ml and chromatographed on silica gel using CH_2Cl_2 eluent. Recrystallization of these eluates from CH_2Cl_2–*n*-C_6H_{14} yielded 2.5 g (40%) of ketone **3**, R = CH_3, R^1 = C_6H_5, mp 164–165°. Table V shows a comparison of reactions conducted under N_2 and O_2.

Method B.—To 200 ml of cold 25% nitric acid was added 20 g (0.12 mol) of benzalacetone oxime. While this mixture was stirring at ice bath temperatures, crystals (0.1 mg) of $NaNO_2$ were added periodically. After 6 hr a red-orange solid was removed by decantation and washed thoroughly with water. Recrystallization from CH_3OH yielded 4.5 g (18%) of ketone **3** (R = CH_3; R^1 = C_6H_5).

Method C. 2,5-Diphenyl-3,4-diazacyclopentadienone 3,4-Dioxide.—A solution of 10 g of $NaNO_2$ on 50 ml of water was added in 1 hr to a solution of 30 g (0.14 mol) of dibenzyl ketone in a mixture of 300 ml of CH_3CO_2H and 100 ml of ethanol and the resulting mixture was stirred at room temperature for 24 hr. Another 5 g of $NaNO_2$ was added and stirring was continued for another 24 hr. An additional 5 g of $NaNO_2$ was added every day for 5 days. At the end of this week the mixture was filtered and the solid was washed with water and ethanol to yield 11.0 g (26%) of ketone **3** (R = R^1 = C_6H_5), mp 191–192°.

Oxidation of Diphenyl Triketone 1,3-Dioxime.—To a solution of 1 g of the dioxime[29] in 50 ml of 5% NaOH was added slowly with stirring at room temperature 5% NaOCl. An orange precipitate started to form soon after addition was started and addition was continued until the precipitation ended. The mixture was diluted with 100 ml of water and filtered. Recrystallization yielded 0.35 g (35%) of ketone **3** (R = R′ = C_6H_5), mp 192°.

2,5-Dicarbethoxy-3,4-diazacyclopentadienone 3,4-Dioxide.—To 30 g of red fuming nitric acid cooled in an ice bath was added dropwise with stirring 20 g (0.1 mol) of diethyl acetone-1,3-dicarboxylate over 30 min. After stirring for an additional 30 min at 0° the reaction mixture was poured with vigorous stirring into 200 ml of ice water. The yellow product was collected by filtration, washed with water and recrystallized from methanol: mp 118°; yield 5 g (20%).

2-Phenyl-5-carbethoxy-3,4-diazacyclopentadienone 3,4-Dioxide.—A solution of 10 g (0.145 mol) of $NaNO_2$ in 25 ml of water was added over a 30-min period at 0–5° to a solution of 5 g (0.024 mol) of ethyl 4-phenylacetoacetate[30] in 25 ml of CH_3CO_2H. The resulting solution was stirred for 1 additional hr at 0° and for 30 min at 25°. A bright yellow precipitate formed after about 45 min. At the end of the reaction period the mixture was poured into 250 ml of ice water, and the solid reaction product was recovered by filtration. Recrystallization from ethanol yielded 1.1 g (17%) of glistening red needles, mp 129–130°.

Synthesis of 3,4-Diazacyclopentadienone 3,4-Dioxide Oximes.—The following general procedure was developed mainly in experiments with benzalacetone and benzalacetophenone oximes, but is generally applicable to all the oximes studied (see Table V).

Benzalacetone Oxime.—The nitrosation of this oxime was carried out in exactly the same way as for the preparation of the ketone (method A above) except that deaerated solvents were employed and the reaction was run under nitrogen.

From 5 g (0.03 mol) of benzalacetone oxime there was obtained 5.8 g (85%) of the oxime of ketone **3** (R = CH_3; R^1 = C_6H_5) when the orange reaction product was slurried with methylene chloride and filtered. Chromatography of the filtrate on silica gel yielded 0.3 g (5%) of ketone **3** (R = CH_3; R^1 = C_6H_5).

Preparation of 4-Hydroxypyrazoles (Table II). Method A. 3,5-Diphenyl-4-hydroxypyrazole (5, R = R^1 = C_6H_5).—Zinc dust (5 g) was added to a solution of 1.0 g (3.9 mmol) of **3** (R = R^1 = C_6H_5) in 100 ml of CH_3CO_2H and the resulting mixture was stirred at 25° for 30 min. The mixture was filtered and the solid filter cake was washed with methanol. The combined washings and filtrate were evaporated to dryness in a rotary evaporator under vacuum. The residue was recrystallized from *n*-C_6H_{14}–CH_2Cl_2–CH_3OH: mp 235°, yield 0.60 g (68%). This compound proved to be identical with a sample prepared by the reaction of hydrazine with diphenyl triketone.[15]

Treatment of this product with acetic anhydride in pyridine produced a white crystalline product, mp 149°, which proved to be **1-acetyl-3,5-diphenyl-4-acetoxypyrazole**: ir (Nujol) 1710 (amide C=O), 1745 cm^{-1} (ester C=O); nmr ($CDCl_3$) δ 2.0, 2.5 (CH_3CO).

Anal. Calcd for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.04; N, 8.75. Found: C, 71.80; H, 5.14; N, 8.45.

Method B.—A mixture of 1 g of the 1,4-dihydroxypyrazole **4** (R = R^1 = C_6H_5) and 5 g of zinc dust in 50 ml of CH_3CO_2H was

TABLE V

NITROSATION OF α,β-UNSATURATED OXIMES. EFFECT OF OXYGEN

R	R^1	—% yield of nitrogen— Ketone	Oxime	—% yield of oxygen— Ketone	Oxime
C_6H_5	CH_3	4.7	85	40	2.2
C_6H_5	C_2H_5	6.5	63	30	10.5
C_6H_5	C_6H_5	18.5	40	13.5	Trace
CH_3	CH_3	<1.0	65	15	17.5

(24) L. Hörner, L. Hockenburger, and W. Kirmse, *Chem. Ber.*, **94**, 290 (1961). Although the conclusions of this work have been challenged [H. Kröpf and R. Lambeck, *Ann.*, **700**, 18 (1966)], the new evidence is not compelling.

(25) H. Gnichtel and H. S. Schönherr, *Chem. Ber.*, **99**, 618 (1966).

(26) N. Tokura, R. Tada, and K. Yokojama, *Bull. Chem. Soc. Jap.*, **34**, 270 (1961).

(27) R. Fusco and S. Rossi, *Tetrahedron*, **3**, 209 (1958).

(28) All nmr spectra were measured on a Varian A-60A spectrometer. This spectrometer was acquired under National Science Foundation equipment grant GP-6875.

(29) H. Wieland, *Ber.*, **37**, 1145 (1904).

(30) G. R. Ames and W. Davey, *J. Chem. Soc.*, 3483 (1957).

stirred at room temperature for 30 min and filtered. The solid filter cake was washed with methanol. The filtrate and washings were concentrated under vacuum and crystallized from methanol–water to yield 0.8 g (85%) of **5** (R = R^1 = C_6H_5).

Preparation of 1,4-Dihydroxypyrazoles (Table III). 3,5-Diphenyl-1,4-dihydroxypyrazole (4, R = R^1 = C_6H_5).—To a solution of 25 g of $Na_2S_2O_4$ in 150 ml of 25% ethanol was added 5.0 g (18.8 mmol) of **3** (R = R^1 = C_6H_5). The resulting red reaction mixture was stirred for 2 hr at 25° at which time the color had disappeared and a fine, white solid was floating in the solution. The mixture was diluted with 150 ml of water, cooled in ice, and filtered to yield 4.0 g of white needles, mp 170–172°. (Extraction of the filtrate and washings with ether yielded an additional 0.5 g of the desired product.) Recrystallization from methanol–water or CH_2Cl_2–*n*-C_6H_{14}–CH_3OH gave white plates, mp 171–172°. This recrystallization must be conducted carefully and preferably under nitrogen to avoid air oxidation.

The infrared spectra of the 1,4-dihydroxypyrazoles are characterized by a strong double band at 2600 and 3000 cm^{-1} due to the hydroxyl groups.

In reductions in which the dihydroxypyrazole did not precipitate from the reaction mixture, it was extracted with 1:1 ether–ethyl acetate.

Preparation of 3,4-Diazacyclopentadienone Monoxides (Table IV). 2,5-Diphenyl-3,4-diazacyclopentadienone 3-Oxide (6, R = R^1 = C_6H_5).—A solution of 1 g (4 mmol) of the dihydroxypyrazole **4** (R = R^1 = C_6H_5) in a mixture of 100 ml of CH_2Cl_2 and 15 ml of CH_3OH was shaken vigorously for 2 min in a separatory funnel with a solution of 2.5 g (9.3 mmol) of Fremy's salt[31] in 100 ml of water. The layers were separated and the water layer was washed with a 50-ml portion of CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$) and concentrated to yield ketone **6**, (R = R^1 = C_6H_5), a purple solid which was recrystallized from *n*-C_6H_{14}–CH_2Cl_2: yield 0.95 g (95%); mp 165°.

2-Ethyl-5-phenyl-3,4-diazacyclopentadienone 3-Oxide and Dimer.—Following the directions above, 3-ethyl-5-phenyl-1,4-dihydroxypyrazole was oxidized to the deep red monoxide **8** in 94% yield. It was recrystallized from CH_2Cl_2–*n*-C_6H_{14}, mp 90–91°.

If the mother liquors from this recrystallization were chilled and concentrated, light yellow needles, mp 86–88°, separated. Upon heating at its melting point or upon solution in CH_2Cl_2 this material reverted to the red monoxide. When the monoxide was allowed to stand in a concentrated CH_2Cl_2–*n*-C_6H_{14} solution for several days, it slowly was converted into the yellow compound.

Preparation of 3-Phenyl-4,5-dimethyl-4-nitropyrazolenine 1,2-Dioxide (11b).—To a solution of 8.0 g (0.045 mol) of 3-methyl-4-phenyl-3-buten-2-one oxime in 25 ml of 80% CH_3CO_2H was added with stirring and cooling a solution of 10 g (0.14 mol) of $NaNO_2$ in 17 ml of water. After stirring for 30 min the mixture was filtered to remove a cream-colored solid that was purified by careful recrystallization from cold (−20°) CH_2Cl_2–*n*-C_6H_{14}: mp 98–104° dec; yield 6.3 g (55%).

Anal. Calcd for $C_{11}H_{11}N_3O_4$: C, 52.63; H, 4.99; N, 16.84. Found: C, 52.84; H, 5.04; N, 16.95.

The same compound could be obtained in 72% yield by similar treatment of 1-phenyl-2-methyl-2-buten-1-one oxime.

3,5-Diphenyl-4-methyl-4-nitropyrazolenine 1,2-Dioxide (11a).—Similar treatment of 8 g (0.034 mol) of 1,3-diphenyl-2-methylpropenone oxime with 7 g (0.1 mol) of $NaNO_2$ in aqueous CH_3CO_2H produced 9.5 g (90%) of **11a**, mp 115° dec (CH_2Cl_2–*n*-C_6H_{14}).

Anal. Calcd for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.50. Found: C, 61.62; H, 4.46; N, 13.52.

Reduction of 3,5-Diphenyl-4-methyl-4-nitropyrazolenine 1,2-Dioxide.—A 2-g (0.0064 mol) sample of **11a** was added to a solution of 25 g of $Na_2S_2O_4$ in water. The mixture was shaken for 24 hr and filtered to yield 1.6 g (94%) of 1-hydroxy-3,5-diphenyl-4-methylpyrazole 2-oxide, mp 213–214°, identical with an authentic sample prepared by the nitrosation of 1,3-diphenyl-2-methylpropenone oxime.[6]

Thermal Decomposition of 3,5-Diphenyl-4-methyl-4-nitropyrazolenine 1,2-Dioxide.—Attempted recrystallization of **11a** from hot ethanol resulted in the evolution of brown fumes (NO_2, N_2O_3) and the development of a deep red color in the solution. Upon concentration and cooling, red needles of ketone **3** (R = R^1 = C_6H_5) separated. The yield of this product varied with temperature and concentration and was of the order of 40%.

Evaporation of the filtrate yielded a cream-colored solid which was identical with the product obtained by thermal decomposition of **11a** in chloroform (see below).

3,5-Diphenyl-4-methyl-4-hydroxypyrazolenine 1,2-Dioxide (12a).—A solution of 1 g (0.0032 mol) of **11a** in 7 ml of chloroform was heated under reflux on a steam bath for 15 min. Brown fumes were evolved. The solution was cooled and hexane was added to precipitate a cream-colored solid. Recrystallization of this solid from ethanol gave 0.7 g (70%) of **12a**: mp 215° dec; ir (Nujol) 3300 (OH), 1625 cm^{-1} [C_6H_5C=N(→O)—]; nmr ($CDCl_3$) δ 1.78 (s, 3), 5.28 (s, 1), 7.84 (m, 10).

Anal. Calcd for $C_{16}H_{14}N_2O_3$: C, 68.01; H, 5.00; N, 9.92. Found: C, 67.80; H, 5.09; N, 10.01.

Reaction of Benzalacetone Oxime and N_2O_4.—To a solution of 5 g of benzalacetone oxime in 50 ml of ether was added, at 25° under nitrogen, gaseous N_2O_4 swept into the solution with nitrogen until the brown color persisted. This mixture was stirred for 30 min at 25° and at 30° for 1 hr. The solvent was evaporated to yield 6.5 g of crude solid that was chromatographed on silica gel. Elution with 5:1 *n*-C_6H_{14}–CH_2Cl_2 furnished 1.2 g of an oil.

Anal. Calcd for $C_{10}H_{10}N_2O_4$: C, 54.05; H, 4.50; N, 12.61. Found: C, 53.04; H, 4.44; N, 11.67.

This compound probably is **3,3-dinitro-1-phenyl-1-butene**: ir (Nujol) 1650 (C=C), 1570; 1325 cm^{-1} (NO_2); nmr (CCl_4) δ 2.32 [s, 3, $CH_3C(NO_2)_2$–], 6.60, 7.13 (AB q, J = 16 Hz, —CH=CH—), 7.4 (s, 5, C_6H_5). Elution with 1:1 hexane–CH_2Cl_2 removed 0.7 g of a yellow solid, mp 56–57°.

Anal. Calcd for $C_{10}H_9N_3O_6$: C, 44.94; H, 3.37; N, 15.73. Found: C, 44.91; H, 3.71; N, 14.80.

This compound probably is **2,3,3-trinitro-1-phenyl-1-butene**: ir (Nujol) 1575 [$C(NO_2)_2$], 1540 cm^{-1} (C=CNO_2); nmr (CCl_4) δ 1.9 [s, 3, $CH_3C(NO_2)_2$–], 8.0 (s, 1, —CH=C<), 7.5 (m, 5, C_6H_5). Continued elution with CH_2Cl_2 furnished 0.8 g of ketone **3** (R = C_6H_5; R^1 = CH_3). No other characterizable materials were obtained.

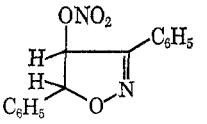
Other Products from Oxidative Nitrosation of Benzalacetone Oxime.—Further elution of the silica gel column used for the isolation of ketone **3** (R = C_6H_5; R^1 = CH_3, method A above) with 20:1 ethyl acetate–CH_2Cl_2 produced 0.2 g (4.4%) of **benzalacetone** (identified by comparison of infrared spectra). Elution with 3:1 $CH_3CO_2C_2H_5$–CH_2Cl_2 yielded 0.5 g of a solid that crystallized as white needles from *n*-C_6H_{14}–CH_2Cl_2, mp 117–119°. This compound was identified as **3-methyl-5-phenylpyrazole** by comparison with an authentic sample.[32]

Other Products from the Oxidative Nitrosation of Benzalacetophenone Oxime.—Treatment of benzalacetophenone oxime by method A above produced an insoluble high melting reddish solid when the reaction product was taken up in CH_2Cl_2 for chromatography. This solid could not be completely resolved but gave small amounts of ketone **3** (R = R^1 = C_6H_5) when heated in organic solvents.

Elution with CH_2Cl_2–*n*-C_6H_{14} mixtures as in method A yielded ketone **3** (R = R^1 = C_6H_5) contaminated with another compound. These two were separated by rechromatographing the mixture on silica and eluting with 1:1 benzene–hexane. This solvent eluted 0.75 g of a white solid that crystallized as white needles from *n*-C_6H_{14}–CH_2Cl_2 chloride: mp 29–93°; ir (KBr disk) 1640, 1270, 860 cm^{-1} ($CONO_2$); nmr ($CDCl_3$) δ 7.70 (m, 2), 7.40 (m, 3), 6.42 (d, 1, J = 3.5 Hz), 5.75 (d, 1, J = 3.5 Hz).

Anal. Calcd for $C_{15}H_{12}N_2O_4$: C, 63.37; H, 4.25; N, 9.85. Found: C, 63.12; H, 4.46; N, 9.77.

Treatment of this compound with base yielded 3,5-diphenylisoxazole (see below). The structure of the compound is suggested to be that of **3,5-diphenyl-4-nitrato-2-isoxazoline**.



Continued elution of the main column (after removal of the mixture above) with CH_2Cl_2 yielded a trace of **3,5-diphenylisoxazole**, mp 139–140°, identical with an authentic sample. No other characterizable compounds were obtained.

(31) D. J. Cram and R. A. Reeves, *J. Amer. Chem. Soc.*, **80**, 3099 (1958).

(32) B. Sjollema, *Ann.*, **279**, 248 (1894).

Registry No.—**8**, 17953-12-7; **11a**, 17953-13-8; **11b**, 17953-14-9; **12a**, 17953-15-0; diphenyl triketone, 643-75-4; 1-acetyl-3,5-diphenyl-4-acetoxypyrazole, 17953-16-1; 3,3-dinitro-1-phenyl-1-butene, 17953-17-2; 2,3,3-trinitro-1-phenyl-1-butene, 17953-18-3; 3,5-diphenyl-4-nitrato-2-isoxazoline, 17953-19-4.

The Nitrosation of α,β-Unsaturated Oximes. V. The Synthesis and Chemistry of 1-Hydroxypyrazole 2-Oxides[1]

JEREMIAH P. FREEMAN[2] AND JOHN J. GANNON

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

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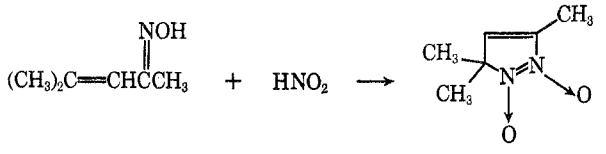
Nitrosation of α-substituted α,β-unsaturated oximes with sodium nitrite in acetic acid produces 1-hydroxypyrazole 2-oxides (**3**). These compounds are relatively strong organic acids and form chelates with a variety of transition metals. Reduction yields the corresponding N-hydroxypyrazoles or the parent pyrazoles. Acylation leads to a molecular rearrangement and production of 3-acyloxypyrazolenine 1-oxides (**10**). Nitrosation converts the 4-alkyl derivatives into 4-nitro-1,2-diazacyclopentadiene 1,2-dioxides (**16**).

Previous investigations of the action of nitrosating agents on α,β-unsaturated oximes involved oximes unsubstituted in the α position. Mesityl oxide oxime, a β-substituted derivative, was converted into 3,5,5-trimethylpyrazolenine 1,2-dioxide (**1**)[3] while a variety of other oximes were converted into 3,4-diazacyclopentadienone 3,4-dioxides (**2**).[4]



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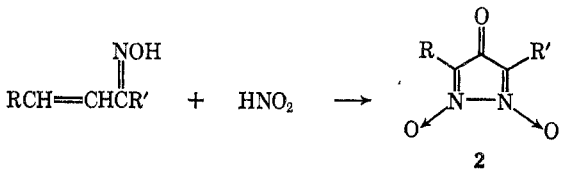

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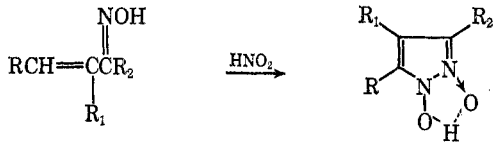
In 1904, Harries and Tietz[5] reported the nitrosation of 3-methyl-4-phenyl-3-buten-2-one oxime to a high-melting white solid of composition $C_{11}H_{12}N_2O_2$, to which they assigned a nitrimine[6] structure.

In a previous communication[7] we proposed that the structure of this product is analogous to that of compound **2** and actually is 1-hydroxy-3-phenyl-4,5-dimethylpyrazole 2-oxide (**3**, R = C_6H_5, R_1 = R_2 = CH_3). This reaction is rather general and a series of these compounds has been made (Table I).



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(1) We are grateful to the donors of the Petroleum Research Fund of the American Chemical Society and to the National Cancer Institute of the National Institutes of Health (Grant No. 1 RO1-CA10742-01) for support of this research.

(2) Alfred P. Sloan Fellow, 1966–1968.

(3) J. P. Freeman, *J. Org. Chem.*, **27**, 1309 (1962).

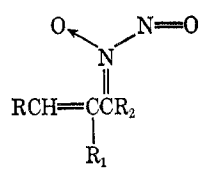
(4) J. P. Freeman and D. L. Surbey, *Tetrahedron Lett.*, 4917 (1967); J. P. Freeman, J. J. Gannon, and D. L. Surbey, *J. Org. Chem.*, **34**, 187 (1969).

(5) C. Harries and H. Tietz, *Ann.*, **330**, 237 (1904).

(6) J. P. Freeman, *J. Org. Chem.*, **26**, 4190 (1961).

(7) J. P. Freeman and J. J. Gannon, *J. Heterocycl. Chem.*, **3**, 544 (1966).

Structure.—The assignment of the hydroxypyrazole oxide structure to these compounds is based upon their elemental analyses, analogy to the structure of pernitrosomesityl oxide[3] from which these structures are derived by a prototropic shift, their acidity, spectral properties, and chemical reactions. While taken individually, none of these unequivocally proves the assigned structure; collectively they rule out alternative structures such as **4**, **5**, or **6**.



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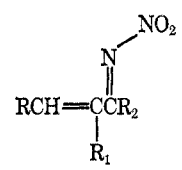

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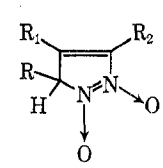

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Physical Properties.—All of these compounds are characterized by high melting points and limited solubility in most solvents. However, all are soluble in dilute sodium hydroxide from which they can be recovered by acidification. Their sodium salts can be isolated and are stable, crystalline materials. The acidity of one of these compounds, 1-hydroxy-3-phenyl-4,5-dimethylpyrazole 2-oxide (**8**), was measured by the method of Calvin[8a] and Bjerrum[8b] and its pK_a was 6.3.

The infrared spectra of these compounds showed no distinctive band associated with O–H stretching but were characterized by broad diffuse absorption between 4 and 6 μ. At longer wavelengths the bands were sharp and distinguishable. The hydroxyl proton was not observed in the nmr spectrum of the 1-hydroxypyrazole 2-oxide previously reported,[7] but it has been found at low fields in the other examples listed in Table I. Both the nmr chemical shift of this proton and the infrared data are suggestive of a highly chelated proton (*cf.* OH chemical shift of enolic β diketones and their infrared spectra). The ultraviolet spectra of these compounds and their sodium salts are rather similar suggesting a highly polar O–H bond.

The nmr spectrum of 1-hydroxy-3,4,5-trimethylpyrazole 2-oxide (**7**) consists of two sharp singlets at δ 1.95 (3 H) and 2.20 (6 H) in addition to a singlet at

(8) (a) M. Calvin and M. K. Wilson, *J. Amer. Chem. Soc.*, **67**, 2003 (1945); (b) J. Bjerrum, "Metal Ammine Formation in Aqueous Solution," P. Haase & Sons, Copenhagen, 1941, p 121.