CMR SPECTRA OF *N*-OXYGENATED PYRAZOLES I. 3,5-DIALKYL- AND 3-ALKYL-5-PHENYL-4-OXO-4*H*-PYRAZOLE 1,2-DIOXIDES

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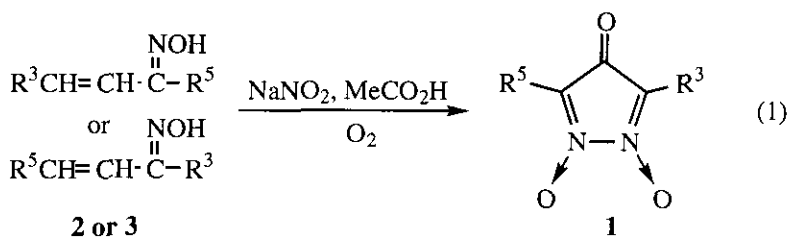
Abstract - The ^{13}C NMR spectra of a series of 3,5-dialkyl- and 3-alkyl-5-phenyl-4-oxo-4*H*-pyrazole 1,2-dioxides were determined. Signals for the carbonyl carbon, C4 of the pyrazole, appeared at δ 186.2 to 188.1 ppm, while the C3 and C5 signals were found in the region of 105.8 to 112.8 ppm. The effect of structural variation of the alkyl groups on the chemical shift of C3 in a selected series of these compounds was investigated using published electronic and steric parameters. Strong correlations were observed with electronic parameter sets σ* and E_s when augmented with a variety of published steric parameter sets.

In a recent signal publication, ^{13}C NMR data for over one thousand pyrazoles were tabulated,[2] and more recently, further magnetic resonance studies including ^{1}H, ^{13}C, and ^{15}N have been reported.[3] However, these reports did not include data on *N*-oxygenated pyrazoles, an area which has been of particular interest to us over the last several years. In view of this interest we have undertaken an examination of the ^{13}C NMR spectra of *N*-oxygenated pyrazoles. The 4-oxo-4*H*-pyrazole 1,2-dioxides (**1**) were targeted for our initial investigations in this area. To date we are aware of only a single report of ^{13}C NMR data for one compound in this series, dimethyl 4-oxo-4*H*-pyrazole-3,5-dicarboxylate 1,2-dioxide (**1**, $R^3 = R^5 = CO_2Me$).[4] We report herein the ^{13}C NMR properties of a series of thirteen compounds of this family and substituent effects of alkyl groups, R^3, on the chemical shift of the signal for the ring carbon C3, to which the substituents of interest are attached.



2 or 3 **1** (1)

The compounds (**1**) included in this study were prepared by nitrosation of α,β–unsaturated ketoximes (**2**) or (**3**) using a procedure described by Freeman, in which the oxime in acetic acid is treated with sodium nitrite under an oxygen atmosphere (equation 1).[5] Some of the compounds investigated have been previously reported by Freeman, others have been described by Unterhalt,[6] and additional new examples were prepared particularly for this study. The compounds (**1**) are brightly-colored solids, either yellow in the case of the 3,5-dialkyl derivatives, or red-orange for the 3-alkyl-5-phenyl-4-oxo-4*H*-pyrazole 1,2-dioxides.

The ^{13}C NMR spectral data for the thirteen 4-oxo-4*H*-pyrazole 1,2-dioxides included in this study are shown in Table 1. Routine ^{13}C NMR chemical shift values obtained at 75 MHz are normally reported to the nearest 0.1 ppm; however, particular care was taken to minimize random variations in this study. Spectra

were obtained on 0.10 *M* solutions of the pyrazoles in deuteriochloroform, with tetramethylsilane as an internal standard, and solvent taken from the same bottle was used throughout the study. All samples were run using the same instrument, a Varian Gemini 300 FT NMR system, with a probe temperature of 26°C. The data for all thirteen of the compounds were obtained without interruption over a 24 hour period. About two weeks later the spectra were repeated under the same conditions, using freshly prepared samples, and chemical shift values for the duplicate data sets agreed within ±0.01 ppm. On the basis of these observations we believe that, in terms of internal consistency within this study, we are justified in reporting the values in Table 1 to within 0.01 ppm.

Table 1. ^{13}C NMR Chemical Shifts (ppm Relative to Me_4Si at 26°C) for 4-Oxo-4*H*-pyrazole 1,2-Dioxides **1**

Cmpd	R^3	R^5	δ C3	δ C4	δ C5	δ Other
1a	Me	Ph	106.94	186.24	106.98	131.2, 129.3, 127.4, 122.1, 6.9
1b	Et	Ph	110.30	186.31	106.63	131.1, 129.3, 127.4, 122.2, 15.5, 9.4
1c	*n*-Pr	Ph	109.49	186.51	106.65	131.1, 129.3, 127.4, 122.2, 23.7, 18.8, 13.8
1d	*n*-Bu	Ph	109.66	186.50	106.66	131.1, 129.3, 127.4, 122.2, 27.1, 22.5, 21.5, 13.6
1e	*i*-Pr	Ph	112.03	186.37	106.17	131.0, 129.3, 127.4, 122.2, 23.6, 17.7
1f	*t*-Bu	Ph	112.16	187.01	105.88	130.9, 129.2, 127.5, 122.3, 33.2, 26.9
1g	Me	Me	107.26	186.43	107.26	6.8
1h	Et	Me	110.69	186.54	106.97	15.5, 9.4, 6.9
1i	*i*-Pr	Me	112.48	186.64	106.55	23.7, 17.8, 6.9
1j	*t*-Bu	Me	112.79	187.32	106.38	33.0, 26.8, 6.9
1k	Et	Et	110.34	186.63	110.34	15.5, 9.4
1l	*i*-Pr	*i*-Pr	111.69	186.78	111.69	23.7, 17.7
1m	*t*-Bu	*t*-Bu	111.67	188.04	111.67	33.0, 26.9

The possible effect of slight variations in concentration and in probe temperature were examined for 3,5-dimethyl-4-oxo-4*H*-pyrazole 1,2-dioxide (**1g**) and for 3,5-di-*tert*-butyl-4-oxo-4*H*-pyrazole 1,2-dioxide (**1m**). Samples which were 0.05 *M* and 0.20 *M* in **1g** or **1m** were compared with 0.10 *M* samples at 26°C. For **1m** no variation in chemical shifts greater than 0.01 ppm was observed over this concentration range. For **1g** identical chemical shift values were observed for 0.10 *M* and 0.20 *M* samples, although a 0.03 ppm upfield shift was seen for the C3-C5 signal in the spectrum of a 0.05 *M* sample.

The effect of variation in the probe temperature on chemical shift values was examined using 0.20 *M* samples of **1g** and **1m**. The temperature was varied in 5°C increments from 20°C to 45°C. Over this range a small upfield shift from 107.26 ppm at 20°C to 107.21 ppm at 45°C was observed for the C3-C5 signal of **1g**, while the corresponding signal in the spectrum of **1m** underwent a small downfield shift from 111.67 ppm to 111.70 ppm. The signal for C4 in **1g** was constant over the temperature range, while a slight downfield shift from 188.04 to 188.06 was observed at higher temperature for C4 in **1m**. In view of the small effect of temperature and concentration for the samples examined, we believe it is reasonable to

assume that the effect of any slight variations during the accumulation of the data shown in Table 1 would be inconsequential, particularly in view of the excellent agreement observed for the duplicate runs at 26°C.

Many parameter sets have been advanced to describe quantitatively the effects of substituents on reactivity, physical characteristics, and other properties of organic systems.[7] Part of our program in the examination of the ^{13}C NMR spectra of *N*-oxygenated pyrazoles involves the correlation of chemical shift data with known electronic (inductive, field, and resonance) and steric parameters. The existence of such correlations might prove useful in future investigations of the properties of these systems. Accordingly, several different dual substituent parameter (DSP) protocols were examined in an attempt to develop a predictive model for ^{13}C NMR chemical shifts based upon known substituent values and to assess the magnitude of the contributions to the shifts due to electronic and steric factors. In this paper we describe the parameter sets which thus far have provided the strongest correlations.

In this study particular attention was focused on compounds (**1a-1f**) (Table 1), and, more specifically, the effect of alkyl substituents R^3 attached to C3 upon the chemical shift of that ring carbon. Any resonance effects are generally assumed to be negligible for alkyl substituents, and therefore we have limited our initial investigations in this area to single and dual parameter treatments, with the dual parameter treatment utilizing one parameter to account for the electronic effect and one parameter to account for the steric effect of the alkyl substituent. The substituent parameters used in these initial studies are listed in Table 2 and Table 3.

Taft has presented what are commonly referred to as 'general' electronic substituent values, which are typically designated as σ^*,[8] and another set of electronic parameters E_σ was also put forward by Taft[9] in his initial treatment of *ortho* substituent effects (Table 2).

Table 2. Electronic Parameters Used

R^3	σ^* [a]	E_σ [b]
Me	0.0	0.0
Et	-0.1	-0.24
i-Pr	-0.19	-0.47
n-Pr	-0.115	-0.28
n-Bu	-0.13	-0.32
t-Bu	-0.30	-0.84

[a] Taft, see ref 8.
[b] Taft, see ref 9.

Table 3. Steric Parameters Used

R^3	E_s [a]	E_s^o [b]	E_s^c [c]	E_s' [d]
Me	0.0	0.0	0.0	0.0
Et	-0.07	-0.27	-0.376	-0.08
i-Pr	-0.47	-0.87	-1.082	-0.48
n-Pr	-0.36	-0.56	-0.666	-0.31
n-Bu	-0.39	-0.59	-0.696	-0.31
t-Bu	-1.54	-2.14	-2.458	-1.43

[a] Taft, see ref 9. [b] Palm, see ref 10.
[c] Hancock, see ref 11. [d] Dubois, see ref 12.

In the latter report, Taft also formulated parameters, E_s, to account for the steric effects of substituents. A variety of modifications of the original Taft E_s values have been advanced over the years, and three such modified parameter sets, E_s^o,[10] E_s^c,[11] and E_s',[12] (Table 3) were considered, along with E_s, in arriving at the best correlation between substituent effects and our spectral data.

The parameters E_s in Table 3 are those reported by Taft.[9] Hancock[11] and Talvik and Palm[10] submitted revised sets of steric parameters to account for the hyperconjugative effects of C-C and C-H bonds present

in branched alkyl substituents. Talvik and Palm[10] calculated E_s^o from equation 2, where n_H is equal to the number of α CH bonds and n_C is the number of α CC bonds in an alkyl substituent.

$$E_s^o = E_s + 0.33(n_H - 3) + 0.13n_C \qquad (2)$$

Hancock[11] calculated E_s^c from equation 3, where n is the number of α hydrogens in the substituent.

$$E_s^c = E_s - (0.306)(n - 3) \qquad (3)$$

Dubois[12] has provided an additional set of revised steric parameters based on standard esterification reaction conditions (carboxylic acids and methanol at 40°C, catalyzed by *p*-toluenesulfonic acid). The parameters of this set have been shown to account well for the steric effects of extremely hindered alkyl substituents.

Our initial examination of the C3 chemical shift data involved a single parameter treatment, in which chemical shift values calculated using the various parameters from Table 2 and Table 3 were plotted individually versus the chemical shifts of C3 for compounds (**1a**) to (**1f**) in Table 1. The results of the single parameter correlations are shown in Table 4, where $\boldsymbol{R^2}$ is a measure of the goodness of fit using a particular parameter. In the single parameter treatment the best fit, $\boldsymbol{R^2}$ = 0.8344, was observed with σ*, while much poorer single parameter correlations were observed for E_σ and for each steric parameter set.

Table 4. Goodness of Fit $\boldsymbol{R^2}$ for Single Parameter Correlations of C3 Chemical Shifts for **1a-1f**

Electronic Parameters	
σ*	$\boldsymbol{R^2}$ = 0.8344
E_σ	$\boldsymbol{R^2}$ = 0.7744

Steric Parameters	
E_s	$\boldsymbol{R^2}$ = 0.4807
E_s^o	$\boldsymbol{R^2}$ = 0.5998
E_s^c	$\boldsymbol{R^2}$ = 0.6318
E_s'	$\boldsymbol{R^2}$ = 0.5134

The ^{13}C NMR chemical shift data for C3 in this series of compounds was also subjected to analysis utilizing the dual substituent parameter equation 4, where x and y represent various electronic and steric parameters

$$\delta_{calc} = k[\boldsymbol{a}x + \boldsymbol{b}\ y] + \boldsymbol{c} \qquad (4)$$

taken from Tables 2 and 3, respectively. Proportionality constant k represents the slope of the best fit line and is a measure of the susceptibility of chemical shift to the electronic and steric parameters used in that treatment. Coefficients $\boldsymbol{a}$ and $\boldsymbol{b}$ represent the coefficients which give the best fit between the calculated and observed chemical shifts. Constant $\boldsymbol{c}$ represents the zero point of reference, which is the observed chemical shift of C3 for the methyl derivative (**1a**), which is 106.94 ppm.

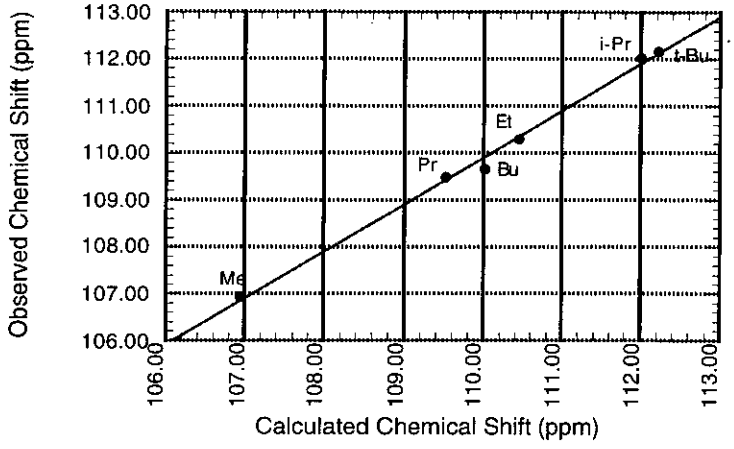
The data derived from equation 4 are summarized in Table 5. The calculated values for $\boldsymbol{R^2}$, the goodness of fit, were excellent for all of the parameter sets included in the Table. The best correlation between δ_{calc} and δ_{obs} was found for the combination of E_σ and E_s (entry *ii* in Table 5). A plot of δ_{calc} *vs* δ_{obs}, computed using values from Table 5, entry *ii* is shown in Figure 1.

Table 5. Optimized Values of k, a, and b in Best Fit Correlations for Predicted and Observed C3 Chemical Shift Values Using Electronic and Steric Parameters in Equation 4 [a]

Entry	k	a(Electronic Parameter)	b(Steric Parameter)	R^2 [b]
i	-37.457	$0.91\sigma^*$	$-0.09E_s'$	0.967
ii	-21.52	$0.75E_\sigma$	$-0.25E_s$	0.995
iii	-24.42	$0.79E_\sigma$	$-0.21E_s^\circ$	0.979
iv	-29.96	$0.80E_\sigma$	$-0.20E_s^c$	0.966
v	-21.706	$0.74E_\sigma$	$-0.26E_s'$	0.975

[a] $\delta_{calc} = k$ [a (electronic parameter) + b (steric parameter)] + 106.94
[b] Goodness of fit for plot of δ_{calc} *vs* δ_{obs}

Figure 1. Plot of δ_{obs} for C3 *vs* δ_{calc} Using Values from Entry *ii*, Table 5, in Equation 6



The predictive value of the equations developed as described in the foregoing discussion was tested by using the equations to predict chemical shift values for C3 in a series of 3-alkyl-5-methyl-4-oxo-4*H*-pyrazole 1,2-dioxides (**1g**-**1j**). Using the experimentally observed chemical shift value of 107.26 ppm for C3 in 3,5-dimethyl-4-oxo-4*H*-pyrazole 1,2-dioxide (**1g**) as the reference value in this series, the chemical shift values for C3 in **1h**, **1i**, and **1j** were calculated using parameters shown in Table 5. Equation 5 was used in these calculations (this is a modification of equation 4, using 107.26 ppm as the reference value, c, in place of the value of 106.94 used in equation 4).

$$\delta_{calc} = k\,[a\,(\text{electronic parameter}) + b\,(\text{steric parameter})] + 107.26 \qquad (5)$$

The form of equation 5 which gave the best agreement between δ_{calc} and δ_{obs} for **1g**-**1j** was that using values for E_σ (Table 2) and E_s (Table 3), along with a, b, and k shown in entry *ii* in Table 5. The comparison of δ_{calc} and δ_{obs} using this form of equation 5 is shown in Table 6. Similar calculations using other combinations of electronic and steric factors for the other four enteries in Table 5 also gave very good agree-

ment between calculated and observed chemical shift values for C3. At this point we have not investigated

Table 6. Comparison of Calculated and Observed Chemical Shift Values for C3 in Compounds **1g-1j**

Cmpd	R^3	δ_{calc} for C3 [a]	δ_{obs} for C3
1g	Me	---------	107.26
1h	Et	110.76	110.69
1i	*i*-Pr	112.32	112.48
1j	*t*-Bu	112.53	112.79

[a] $\delta_{calc} = -21.52[0.75\ E_\sigma + 0.25\ E_s] + 107.26$

quantitatively the nature of longer-range effects associated with the substituent at C5 on the chemical shift at C3. However, comparing the observed chemical shift values for C3 in **1a** (R^5 = Ph) and **1g** (R^5 = Me) and for similarly related compounds in Table 1 shows that this effect is not negligible. It is possible that further refinement beyond the dual parameter treatment could result in improved correlations.

Three additional compounds included in this study were 3,5-diethyl-, 3,5-diisopropyl-, and 3,5-di-*tert*-butyl-4-oxo-4*H*-pyrazole 1,2-dioxides (**1k**, **1l**, and **1m**). No attempt was made to include these examples in our calculations. However, an interesting observation for these compounds was that there is a slight upfield shift for the C3-C5 signal in the di-*tert*-butyl case (**1m**) compared with the C3-C5 signal in the diisopropyl compound (**1l**). It would appear that in **1m** the incremental shielding due to the steric compression shift[13] is more pronounced than in the other examples investigated, offsetting to a significant extent the increase in deshielding occasioned by the increased branching in the substituent when comparing the di-*tert*-butyl- and the diisopropylpyrazolones. In **1m** there is also a significant downfield shift in the signal for the carbonyl carbon, C4, when compared with that of the other compounds examined. This may also be a consequence of the particularly strong steric crowding in this compound.

CONCLUSIONS

The use of σ^*, E_s and E_σ values has been the subject of considerable debate and extensive inquiry. In this study it has not been our intent to provide overwhelming evidence in justification of any particular parameter scale. Our objective has been the determination of the parameters which provide the best correlations for our systems and which might prove useful in guiding further studies in the chemistry of *N*-oxygenated pyrazoles. On the basis of the current study with a series of 4-oxo-4*H*-pyrazole 1,2-dioxides, we have found that the Taft electronic and steric parameters E_σ and E_s serve well in providing a good correlation with our data. The ^{13}C NMR chemical shift data observed for C3 of this series of 4-oxo-4*H*-pyrazole 1,2-dioxides closely parallels the chemical shift data observed for C1 in substituted benzene derivatives.[14] It is our intent to extend future studies in this area to a wider range of substitutents, using ^{13}C NMR spectroscopy to evaluate other substituent effects (*i.e.*, inductive, field, and resonance effects) on *N*-oxygenated pyrazoles.

An understanding of substituent effects as revealed by ^{13}C NMR studies may, it is anticipated, lead to a better understanding of the chemical behavior of *N*-oxygenated pyrazoles and provide direction for further

investigations in this area. Correlations such as those using Taft or Hammett constants have contributed greatly to an understanding of diverse aspects of organic chemistry. In the chemistry of 4-oxo-4*H*-pyrazole 1,2-dioxides, one might consider their ability to participate as the dipolar components of 1,3-dipolar cycloaddition reactions[15] as an area where insight might be gained by a better understanding of substituent effects. In recent publications, calculations have been reported in which the electronic properties of the 4-oxo-4*H*-pyrazole 1,2-dioxide system have been assessed. On the basis of *ab initio* calculations, Harano has suggested that the system is antiaromatic.[16] However, Ramsden[17] has cited evidence from perturbation molecular orbital (PMO) calculations that are interpreted as indicating that the system is nonaromatic. It is possible that the ^{13}C NMR data may contribute to a better understanding of the nature of this system, and we are pursuing further investigations in this regard.

EXPERIMENTAL

IR spectra were run as neat liquids or nujol mulls using a Nicolet 5SXC FT-IR Spectrophotometer. NMR spectra were determined with a Varian Gemini-300 Spectrometer (^1H at 300 MHz; ^{13}C at 75 MHz) in deuteriochloroform with tetramethylsilane as an internal standard. Silica gel used for flash chromatography was Davisil, grade 633, 200-425 mesh. Elemental analyses were performed by Micro-Analysis, Inc., Wilmington, DE, USA. Melting point values were determined using a Thomas Hoover Uni-melt apparatus and are uncorrected.

Preparation of Known 4-Oxo-4*H*-pyrazole 1,2-Dioxides.

The method described by Freeman[5] was used, and known compounds were identified by comparison of infrared and pmr spectral properties and melting points with previously reported values. Previously described compounds in the series are **1a**, and **1b**;[5,6a] **1c** and **1d**;[6a] **1e**;[6b] **1f**;[6a,18] **1g**;[5] **1m**.[18]

4-Hexen-3-one Oxime.

A solution of 19.2 g (0.20 mole) of 4-hexen-3-one (Aldrich Chemical Co.) in 75 mL of ethanol (95%) was treated at rt with a solution of 21 g (0.25 mol) of sodium acetate (anhyd) in 20 ml of water, followed by a solution of 17.3 g (0.25 mol) of hydroxylamine hydrochloride in 20 mL of water. After stirring for 6 h at rt the mixture was filtered to remove NaCl, and the filtrate was extracted with 150 mL of ether, followed by two 50 mL portions of ether. The ether extract was washed with 50 mL portions of 10% Na_2CO_3 until the aqueous solution remained basic to litmus. After washing with 50 mL of saturated NaCl solution, the ether layer was dried (Na_2SO_4) and evaporated. The residual liquid was distilled at 6 torr, and the product was collected as a colorless liquid, 17.2 g (76%), bp 82-89°C. The ^1H NMR spectrum of the product showed a mixture, *ca.* 2:1, of the (*E*) and (*Z*) oximes. IR (neat): 3244 cm^{-1}, 3196, 1643 (wk), 1625 (wk), 966, 929. ^1H NMR (mixture) (*Z*): δ 6.81 ppm (dq, J = 16.5, 1.8 Hz, 1H), 6.21 (dq, J = 16.5, 6.5 Hz, 1H), 2.41 (q, J = 7.5 Hz, 2H), 1.89 (dd, J = 6.5, 1.8 Hz, 3H), 1.14 (t, J = 7.5 Hz, 3H); (*E*): 6.17-6.08 (m, 1H), 6.04 (d, J = 16.0 Hz, 1H), 2.52 (q, J = 7.5 Hz, 2H), 1.84 (d, J = 5.0 Hz, 3H), 1.10 (t, J = 7.5 Hz, 3H). *Anal.* Calcd for $C_6H_{11}NO$: C, 63.69; H, 9.80; N, 12.38. Found: C, 63.99; H, 9.50; N, 12.26.

4-Hepten-3-one Oxime.

Oximation of 4-hepten-3-one[19] was carried out as described above, giving 48% of the oxime, a colorless liquid, bp 111-118°C at 17 torr. The product was a mixture, *ca.* 3:2, of the (*E*) and (*Z*) oximes. IR (neat): 3264 cm^{-1}, 3204, 1647 (wk), 1628 (wk), 968. ^1H NMR (mixture) (*Z*): δ 6.77 (dt, J = 16.5, 1.5 Hz, 1H), 6.24 (dt, J = 16.5, 6.6 Hz, 1H), 2.41 (q, J = 7.5 Hz, 2H); (*E*): 6.13 (dt, J = 16.5, 6 Hz, 1H), 6.01 (d, J = 16.5 Hz, 1H), 2.52 (q, J = 7.8 Hz, 2H); unresolved multiplets at 2.28-2.14 and 1.16-1.01 included signals for the methyl groups of both isomers. *Anal.* Calcd for $C_7H_{13}NO$: C, 66.11; H, 10.30; N, 11.01. Found: C, 66.15; H, 10.38; N, 11.08.

2,6-Dimethyl-4-hepten-3-one Oxime.

A solution of 5.6 g (0.04 mol) of 2,6-dimethyl-4-hepten-3-one[20] in 50 mL of ethanol (95%) was treated with 5.04 g (0.06 mol) of sodium acetate in 10 mL of water and 4.2 g (0.06 mol) of hydroxylamine hydrochloride in 10 mL of water. After standing for 12 h at rt, the solution was concentrated under reduced pressure to about 30 mL. The residue was treated with 50 mL of water and 100 mL of ether. The ether layer was separated and washed with 5% $NaHCO_3$ solution until the wash solution remained basic to litmus, then it was washed with saturated NaCl solution, dried (Na_2SO_4), and evaporated. The residue was distilled at 87-92°C at 0.4 torr, giving 4.12 g (73%) of colorless distillate which partially crystallized in the condenser during distillation. Recrystallization from methanol gave large, rhombic plates of the major isomer, the (*Z*)-oxime, mp104-106°C. IR (nujol): 3256 cm^{-1}, 3212, 1644, 986, 940 (vs), 776. ^1H NMR: δ 9.10 ppm (br, 1H), 6.69 (dd, J = 16.5, 1.5 Hz, 1H), 6.20 (dd, J = 16.6, 6.6 Hz, 1H), 2.88 (septet, J = 7.0 Hz, 1H), 2.56-2.38 (m, 1H), 1.18 (d, J = 7.0 Hz, 3H), 1.08 (d, J = 6.6 Hz, 3H). An analytical sample was sublimed at 60°C and 0.4 torr, mp104-106°C. *Anal.* Calcd for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02 . Found: C, 70.02; H, 10.68; N, 9.01.

3-Ethyl-5-methyl-4-oxo-4*H*-pyrazole 1,2-Dioxide (**1h**).

A solution of 14.3 g (0.126 mol) of 4-hexen-3-one oxime in 250 mL of acetic acid-water (9:1) was stirred in ice and saturated with oxygen. Stirring under an oxygen atmosphere in the cold was continued while a solution of sodium nitrite, 24.5 g (0.35 mol) in 50 mL of water, was added over 6 h. Stirring in the cold under oxygen was continued for 1 h, then the solvent was removed without heating at 0.4 torr. The residue was partitioned between 5% Na_2CO_3 solution and ether. The ether solution was washed with saturated NaCl solution, dried (Na_2SO_4), and evaporated. The oily solid was crystallized from methanol at dry ice temperature to give 5.40 g of bright yellow flakes of the pyrazolone. The methanol filtrate was evaporated, and the residue was separated by flash chromatography on 80 g of silica gel with 5% acetone in hexane. A yellow fraction was collected which gave an additional 0.82 g of **1h**, total yield 6.22 g (32%). Recrystallization from hexane gave yellow flakes, mp 53-54°C; IR (nujol): 1688 cm^{-1} (str), 1645 (v str); ^1H NMR: δ 2.58 ppm (q, *J* = 7.8 Hz, 2H), 2.13 (s, 3H), 1.23 (t, *J* = 7.8 Hz, 3H). *Anal.* Calcd for $C_6H_8N_2O_3$: C, 46.15; H, 5.16; N, 17.94. Found: C, 46.32; H, 5.08; N, 17.80.

3-Isopropyl-5-methyl-4-oxo-4*H*-pyrazole 1,2-Dioxide (**1i**).

A solution of 12.7 g (0.1 mol) of 5-methyl-3-hexen-2-one oxime in 200 mL of acetic acid-water (9:1) was cooled in ice and saturated with oxygen. Stirring under oxygen in the cold was continued while a solution of 17.3 g (0.25 mol) of sodium nitrite in 40 mL of water was added over 3.5 h. Stirring in the cold under oxygen was continued for 1 h, then the solvent was evaporated at 0.4 torr without heating. The residue was partitioned between 5% sodium carbonate and ether, and the ether solution was washed with saturated NaCl, dried (Na_2SO_4), and evaporated. Crystallization from methanol at dry ice temperature gave the major portion of the desired pyrazolone, while an additional quantity was recovered from the methanol filtrate after evaporation and flash chromatography of the residue on 75 g of silica gel with 5% acetone-hexane. The total yield of **1i** was 6.4 g (38%). Recrystallization from pentane gave yellow needles, mp 31-32.5°C; IR (nujol): 1687 cm^{-1} (mod), 1637 (v str); ^1H NMR: δ 3.08 (septet, *J* = 7.0 Hz, 1H), 2.12 (s, 3H), 1.30 (d, J = 7.0 Hz, 6H). *Anal.* Calcd for $C_7H_{10}N_2O_3$: C, 49.41; H, 5.92; N, 16.46. Found: C, 49.76; H, 5.82; N, 16.40.

3-*tert*-Butyl-5-methyl-4-oxo-4*H*-pyrazole 1,2-Dioxide (**1j**).

A solution of 1.60 g (0.0113 mol) of 5,5-dimethyl-3-hexen-2-one oxime in 30 mL of acetic acid-water (9:1) was cooled in ice and saturated with oxygen. The solution was stirred in ice under an oxygen atmosphere while a solution of sodium nitrite, 1.9 g (0.027 mol), in 5 mL of water was added over 1.5 h. Stirring in the cold under oxygen was continued for 1 h, then the mixture was filtered, and the filtrate was diluted with 100 mL of water and extracted with three 50 mL portions of ether. The ether solution was washed with two 25 mL portions of water, then with portions of 5% $NaHCO_3$ until the wash solution remained basic. After washing with saturated NaCl, the ether solution was dried (Na_2SO_4) and evaporated. The residue was crystallized from methanol at dry ice temperature to give 0.23 g of the pyrazolone. Evaporation of the methanol filtrate and flash chromatography of the residue on 20 g of silica gel with 5% acetone in hexane gave an additional 0.28 g of the pyrazolone; total yield 0.51 g (29%). Recrystallization from methanol gave yellow needles, mp 69-70.5°C; IR (nujol): 1683 cm^{-1} (str), 1653 (v str); ^1H NMR: δ 2.09 ppm (s, 3H), 1.41 (s, 9H). *Anal.* Calcd for $C_8H_{12}N_2O_3$: C, 52.16; H, 6.56; N, 15.21. Found: C, 52.44; H, 6.53; N, 15.22.

3,5-Diethyl-4-oxo-4*H*-pyrazole 1,2-Dioxide (**1k**).

A solution of 5.08 g (0.04 mol) of 4-hepten-3-one oxime in 30 mL of acetic acid-water (9:1) was cooled in ice and saturated with oxygen. The solution was stirred in an ice bath under oxygen while a solution of 6.1 g (0.088 mol) of sodium nitrite in 10 mL of water was added over 2 h. Stirring under oxygen in the cold was continued for 1 h, then the solvent was removed without heating at 0.2 torr, and the residue was partitioned between 5% aqueous Na_2CO_3 and ether. The ether solution was washed with 25 mL of 5% Na_2CO_3, then with 25 mL of saturated NaCl solution, dried (Na_2SO_4), and evaporated. Flash chromatography on 30 g of silica gel with 10% acetone in hexane gave crude **1k**, which was rechromatographed and then recrystallized from pentane to give 0.71 g (10%) of **1k**, mp 39-40°C; IR (nujol): 1685 cm^{-1} (mod), 1639 (v str); ^1H NMR: δ 2.57 (q, J = 7.5 Hz, 4H), 1.23 (t, J = 7.5 Hz, 6H). *Anal.* Calcd for $C_7H_{10}N_2O_3$: C, 49.41; H, 5.92; N, 16.46. Found: C, 49.52; H, 5.79; N, 16.30.

3,5-Diisopropyl-4-oxo-4*H*-pyrazole 1,2-Dioxide (**11**).

A solution of 4.12 g (0.029 mol) of 2,6-dimethyl-4-hepten-3-one oxime in 40 mL of acetic acid-water (9:1) was saturated with oxygen, cooled in ice, and stirred under an oxygen atmosphere while a solution of 4.5 g (0.064 mol) of sodium nitrite in 10 mL of water was added over 2 h. After stirring for an additional 1 h under oxygen in the cold, the mixture was evaporated without heating at 0.4 torr, and the residue was partitioned between 5% Na_2CO_3 and 150 mL of ether. The ether solution was washed with 20 mL of 5% Na_2CO_3, 20 mL of water, and 20 mL of saturated NaCl, dried (Na_2SO_4), and evaporated to give an oily yellow solid. Recrystallization from methanol at dry ice temperature gave 0.78 g (14%) of yellow solid. Further recrystallization from hexane gave yellow needles, mp 70-71°C; IR (nujol): 1680 cm^{-1} (str), 1632 (v str); ^1H NMR: δ 3.06 ppm (septet, J = 7.0 Hz, 2H), 1.30 (d, J = 7.0 Hz, 12H). *Anal.* Calcd for $C_9H_{14}N_2O_3$: C, 54.53; H, 7.12; N, 14.13. Found: C, 54.73; H, 6.92; N, 14.21.

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