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PREPARATION AND CHEMISTRY OF PYRAZOLINE-3,5-DIONES AND THEIR CYCLOADDUCTS

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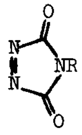
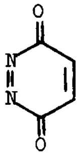
Cyclic di-α-carbonyl azo compounds, I-IV, are the most reactive dienophiles in the Diels-Alder reaction.[1] The 4-substituted-1,2,4-triazoline-3,5-diones (I)[2] are far more stable than the others (II-IV have been used in situ generally below 0°)[3] and are widely utilized. Our studies involving I[4] encouraged us to consider the chemistry of its analog V.[5] We anticipated that the pyrazoline-3,5-diones (V) would be isolable but reactive with unsaturated compounds forming easily hydrolyzable adducts.



I



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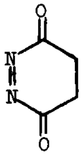
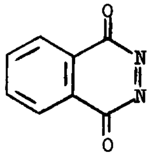
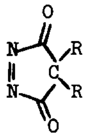


III

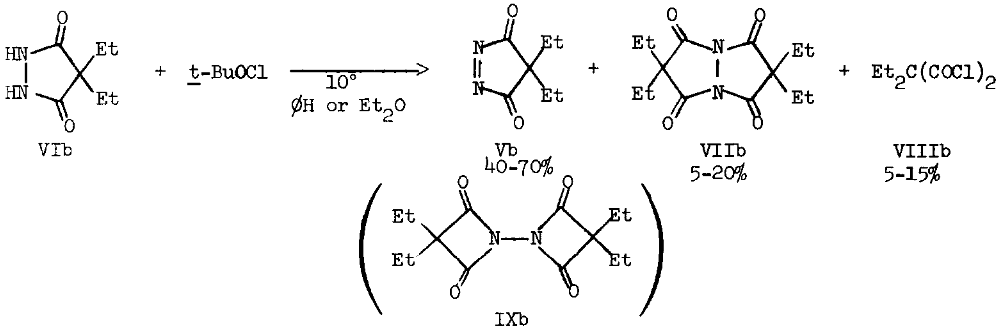


IV



V

4,4-Dimethyl- and 4,4-diethylpyrazoline-3,5-dione (Va,b) were prepared in two steps from the dialkyl malonate diesters.[6] Conversion of the diesters to the cyclic hydrazides VI (4,4-dialkylpyrazolidine-3,5-diones) was accomplished in > 60% yield by the method of Ruhkopf.[7] The hydrazides were oxidized with t-BuOCl to afford the pyrazoline-3,5-diones in satisfactory yield.[8]



VIb

Vb 40-70%

VIIb 5-20%

VIIIb 5-15%

IXb

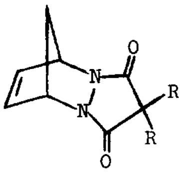
Both Va and Vb are deep blue, volatile (sublime by 25°/0.2 mm) compounds. The 4,4-diethylpyrazoline-3,5-dione is easily isolable: mp 35°; ir (CCl_4) 1795 cm^{-1}; uv max (CH_3CN) 629 mμ (ε 140); nmr (CCl_4) δ 0.82 (t, 6, *J*=7.2 Hz), 1.82 (q,4); mass spectrum (70 eV) m/e (rel. intensity) 154 (tr), 126 (0), 98 (23), 83 (20), 55 (66). 4,4-Dimethylpyrazoline-3,5-dione was difficult to purify: mp ~ 23°; ir (CCl_4) 1795; uv max (CH_3CN) 620 mμ (ε ~ 150); nmr (CCl_4) δ 1.30 (s). Both Va and Vb are thermally much more stable than II-IV. Solutions of Vb (~ 2 M) decolorized only after 2 hr at 80° or several weeks at 25°; crystalline samples had similar stability. Reaction with moist air is rapid, however, and Va,b should be handled under nitrogen.

Two minor products, diethylmalonyl dichloride and VIIb are formed during the oxidation of VIb (similar results are obtained with VIa). The data[13] indicate that VIIb is 2,2,-6,6-tetraethyl-1,3,5,7-tetraketopyrazolo[1,2-a]pyrazole: mp 205-6°; ir, 1775 and 1740 cm^{-1}; uv max (diox) 233 mμ (ε 1650), 260 (ε 1550) and 272 (ε 1400); nmr ($CDCl_3$) δ 1.0 (t, 6, *J*=7 Hz), 2.02 q (4); mass spectrum (70 eV) m/e 280 (32), 252 (26), 193 (11), 98 (100). This compound is also obtained by reaction of VIb and VIIIb at ~ 160°.[9] The isomeric structure IXb is also a possibility[10] but a less likely one; it can, however, only be excluded by independent synthesis or an x-ray analysis.

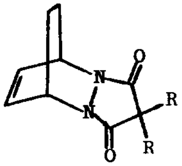
Control experiments indicate that VIIb is formed by attack of HCl on Vb[11] and not by reaction of VIb and VIIIb. The mechanism possibly involves the $ClCOC(Et)_2CO^-$ intermediate (X), which is formed by attack of Cl^- on Vb. Reaction of X with Vb affords VIIb while reaction with a positive chlorine donor such as *t*-BuOCl affords VIIIb. Only traces of VIIIb are formed from Vb in the absence of *t*-BuOCl.

Thermal decomposition of Vb was carried out in chlorobenzene at 100°; care was taken to remove acids and protic compounds. The only product observed (65% yield) was VIIb. Formation of VIIb here could involve adventitious acid catalysis, nucleophilic attack by a nitrogen of one molecule of Vb on the carbonyl of a second, or reaction of a $C_7H_{12}O_2$ specie (diethylcyclopropanedione?) with Vb. The first mechanism is the most likely, however, the last is intriguing and is being tested, as well.[12] X and diethylcyclopropanedione could afford similar cycloaddition products and attempts are under way to trap these species with suitable unsaturated systems.

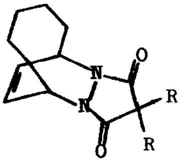
The 4,4-dialkylpyrazoline-3,5-diones have dienophilic reactivity comparable to I. Cyclopentadiene and cyclohexadiene react instantaneously at 25° and even less reactive dienes such as anthracene, 1,3-cyclooctadiene and the 4,4-dialkylisopyrazoles form 1,4-adducts within 1 hr; only cyclooctatetraene requires a longer time.[12] Isolated yields of the crystalline cycloadducts are 40-70%,[13] except for XV (10%).



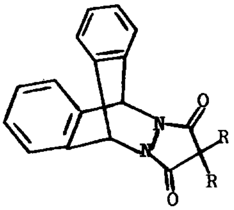
XIa $R=CH_3$
b $R=CH_3CH_2$



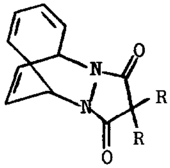
XII $R=CH_3CH_2$



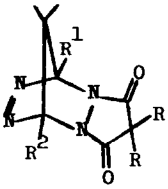
XIII $R=CH_3CH_2$



XIVa $R=CH_3$
b $R=CH_3CH_2$



XVa $R=CH_3$
b $R=CH_3CH_2$



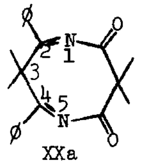
XVIa $R=R^1=R^2=CH_3$
b $R=CH_3CH_2$; $R^1=CH_3$
XVIIa $R=CH_3$; $R^1=\phi$; $R^2=CH_3$
b $R=CH_3CH_2$; $R^1=\phi$; $R^2=CH_3$
XVIIIa $R=CH_3$; $R^1=R^2=\phi$
b $R=CH_3CH_2$; $R^1=R^2=\phi$

The stereochemistry of the pyrazoline-3,5-dione cycloadducts was determined by variable temperature nmr studies; those with XIVa,b are illustrative. The spectra show magnetically equivalent dialkyl groups and an A_2B_2 pattern for the Ar$\underline{H}$ down to the lowest temperature examined (-40°). This indicates that the nitrogens are either planar, which is the preferred explanation, or are pyramidal but rapidly inverting with a low E_a.[14]

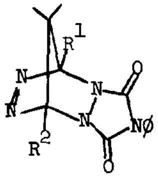
A partial examination of the chemistry of XI-XV has been made. The cycloadducts and their dihydroderivatives are surprisingly resistant to acidic or basic hydrolysis;[15] samples of XIa, its dihydroderivative and XV were recovered largely unchanged after treatment with KOH-$HOCH_2CH_2OH$ at 170° for 2 hr. Apparently attack of nucleophiles on the carbonyls is severely sterically hindered.

The adducts with isopyrazoles, XVI-XVIII, lose nitrogen when heated or irradiated as anticipated, however, the course of the decompositions is unexpectedly different than for the analogous compounds XXIa,b,c.[4a,b,c] Thermal decomposition of XVII or XVIII results in clean conversion to the corresponding 3,7-dihydro-1,5-diazocine-2,4-dione, XIX, XX. For example, XVIIIa affords a 70% yield of XXa: mp 172-4°; ir ($CHCl_3$) 1680 cm^{-1}, uv max (CH_3CN) 233 mμ (ε 9800); nmr ($CDCl_3$) δ 1.49 (s, 6), 1.58 (s, 6), 7.4 (m, 10);[16] absorbs two equivalents of H_2 at 25° over PtO_2. The solution photochemistry of XVI-XVIII is complex and as yet unresolved; matrix irradiation (77°K) affords no observable concentration of triplet species.

XVIIIa $\xrightarrow[\text{øH}]{80°}$



XXa



XXIa $R^1=R^2=CH_3$
b $R^1=CH_3$; $R^2=ø$
c $R^1=R^2=ø$

In contrast, no N-N bond breaking was observed during the thermal or photochemical decompositions of XXIa,b,c, and irradiation of matrices (-77°K) afforded triplet species. Apparently diradical intermediates are more destabilized and the N-N bond is stronger in XXI than in XVI-XVIII.[17] Studies of mechanistic details are in progress.

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(5) The anhydride $\underbrace{\mathrm{OCN{=}NCO}}_{\mathrm{O}}$ and thioanhydride $\underbrace{\mathrm{OCN{=}NCO}}_{\mathrm{S}}$ are expected to be extremely unstable. An attempt to prepare the hydrazine dicarboxylic anhydride $\underbrace{\mathrm{HNOCOCONH}}$ was unsuccessful: C. H. Hurd and F. F. Cesark, J. Am. Chem. Soc., 89, 1417 (1968).
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(7) H. Ruhkopf, Chem. Ber., 73, 820 (1940).
(8) Best yields were obtained by addition of pyridine during or immediately after oxidation.
(9) G. Zinner, R. Moll and B. Bohlke, Arch. Pharm., 299, 441 (1966).
(10) The possibility of this isomerism must be considered here since it has been observed in the homologous system: Tetraketopyridazopyridene → N,N'-bisuccinimide: E. Hedaya, R. L. Hinman, V. Schomaker, S. K. Theodoropulos and L. M. Kyle, J. Am. Chem. Soc., 89, 4875 (1967).
(11) Reactions of acids with dicarbonyl azo compounds have not been studied: E. Fahr and H. Lind, Angew. Chem. Int. Ed., 5, 372 (1966).
(12) Formation of a Diels-Alder adduct with COT has been previously observed only with I. Other dienophiles react only with [4.2.0] tautomer: A. B. Evnin, R. D. Miller and G. R. Evanega, Tetrahedron Letters, 56, 5863 (1968).
(13) Satisfactory elemental and spectral analyses were obtained for all compounds except the unstable adducts XVI-XVIII. These last were analyzed by mass spectrometry and other spectroscopic techniques, as well as by analysis of derivatives.
(14) Acyclic hydrazides are planar: R. Shintari, Acta Cryst., 13, 609 (1960). Pyramidal inversion around N in rigid molecules such as XIV is not expected to be fast at -40°: J. M. Lehn and J. Wagner, Tetrahedron, 25, 677 (1969).
(15) This precludes the use of the adducts XI-XV for synthesis of azo compounds by hydrolysis and oxidation.
(16) Unchanged down to -60°C.
(17) In XXI, diradical intermediates may be stabilized by 3e bonding and delocalization into the potentially aromatic triazoline ring. Amide resonance interaction is probably more extensive in XVI-XVIII making the lone pair less available. We observe that thermolysis of XVIIIa is faster than XXIc which raises the possibility that N-N bond breaking is concerted with loss of nitrogen.