SYNTHESIS AND CHARACTERIZATION OF SOME BIS-PYRAZOLONES AND SUBSTITUTED-2, 3, 8, 9-TETRA AZA DISPIRO-(4, 0, 4, 2)-DODECA 1-9-DIENES

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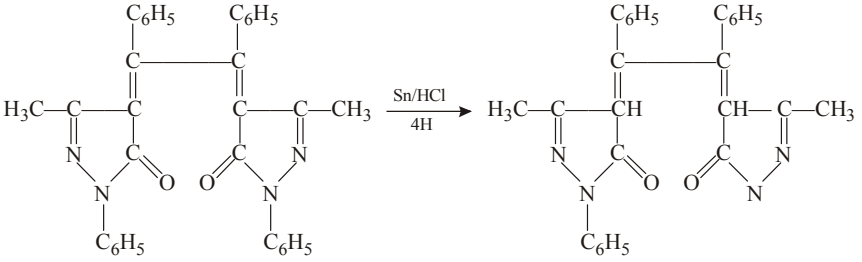
Some new components of 4, 4'-benzil/furil-bis-(1-phenyl/ hydrogen-3-methyl-2-pyrazolin-5-ones, their dihydro- and spiro-cyclobutane derivatives have been syntghesized. These are characterized by elemental analysis, n.m.r. and mass spectral studies. Fungicidal tests were done against the standard pathogens : *Pyricularia oryzac, Helminthosporium oryzae, Collectotrichum tabacum* and *Alternria solani*. Bactericidal tests were conducted against the bacteria *Salmonella typhosa* and *Staphylococcus Aurius*. The spirocyclobutane derivatives of bispyrazolones showed significant fungicial and bactericidal properties.

INTRODUCTION

Earlier work shows pyrazolones to possess remarkable fungicidal and bactericidal properties (Nanda, 1975, Dhal, 1975). In this communication,we report the synthesis, characterization of some 4,4'-benzil/furil-bis-[1-phenyl-hydrogen-3-methyl-2-pyrazolin-5-ones], their dihydro- and spiro-cyclobutane derivatives and their fungicidaland bactericidal studies. 1-Phyenyl-3-methyl-2-pyrazolone was prepared by following standard procedures (Vogel, 1972).

4, 4'-Benzil/furil-bis-pyrazolones and synthesized by reflux condensation of the above compound with benzyl or furil in presence of sodium acetatic and acetic acid involving Michael condensation.

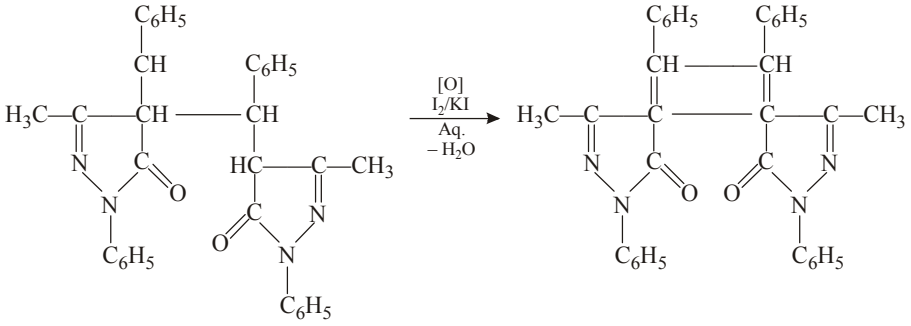
Dihydro derivatives of the above compound was formed by hydrogenation with tin-HCl.



4, 4'-dihydrobenzil-bis-[1-phenyl-3-methyl-2-pyrazolin-5-one]

The spirocyclobutane derivative of the above dihydro- compound was synthesized (Weston,1957) by adding I_2/KI(aq.) or passing chlorine through its aqueous solution in NaOH.The identity of the spiro-cyclobutanes obtained by both the methods was established from undepressed melting point, elemental analysis, n.m.r. and mass spectral studies.

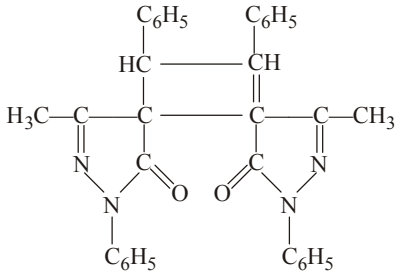
The pathway of the ring fusion of spirocyclobutane is illustrated below :



3, 8, 11, 12-Tetraphenyll, 1, 10-di-methyl-4, 7-dioxo-
2, 3, 8, 9-tetra-aza dispiro-(4, 0, 4, 2)-dedoca-1, 9-diene.

Spectral data :

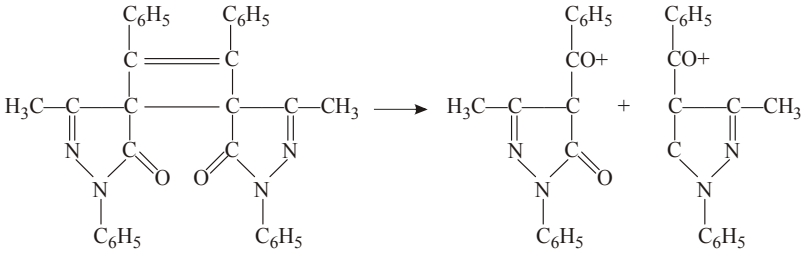
I.



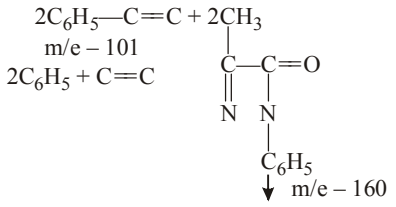
4,4'-Benzil-bis-[1-phenyl-3-methyl-2-pyrazolin-5-one]

The n.m.r. spectra shows signal at 2.03 (singlet) for the 6 protons of 2-CH_3 groups. Since this absorption occurs at same field strength, the molecule is considered symmetrical with respect to the pyrazolone nuclei. A multiplet centred at δ 7.9 is for the 20 protonsof the 4-phenyl nuclei.

In the atomic mass spectra, the molecular ion peak (m/e) was noticed at 522 which confirms to the molecular formula of the compound. The major peaks appeared at 261, 159, 101, 77, 42 and 41 basing upon which the fragmentation pattern was built as :



m/e – 522



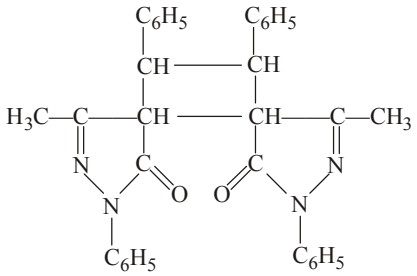
$2\ CH_3CN + C_6H_5 – N=C=0$

m/e – 41 m/e – 120

$C_6H_5 + N=C=0$

77 42

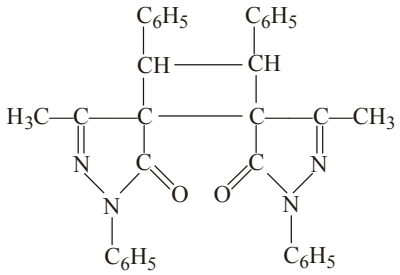
II. 4, 4'-Dihydrobenzil-bis-(1-phenyl-3-methyl-2-pyrazolin-54-one):



The n.m.r. signals seen at δ 7.9 (Multiplet, 20 protons of the $4C_6H_5$ groups) were similar to the parent compound. Additional signals were recorded at δ 1.9 (small doublet:methane bridge protons) and δ 6.17 (singlet: CH protons of the pyrazolone moiety). The splitting at δ = 1.9 is due to the spin-spin interaction between these protons. As the peak did not shift down field, the deshielding effect of the phenyl substituents is not mutually concelled by their trans disposition. This chemical shift at δ = 6.7 appeared as a low singlet down field due to the composite factors of deshielding effect of the pyrazolone ring, presence of C = 0 and benzene ring in the vicinity of the CH link.

In the atomic mass spectra, the molecular ion peak (m/e) appeared at 526. The major fragmentations were noticed at 263, 159, 103, 77, 42 and 41. A similar fragmentation pattern as the parent compound can be built.

III.



3, 8, 11, 12-tetraphenyl-1, 10-dimethyl-4, 7-dioxo-2, 3, 8, 9-tetra-aza-dispiro-(4, 0, 4, 2)-dodeca-1, 9-diene.

The n.m.r. signals for the above compounds were received at δ - 1.85 (singlet: 3-protons of one CH_3 group), δ - 2.0 (singlet: 3-protonsof the other CH_3 group), δ - 1.65 (singlet: 1-protonof one CH group), δ - 1.35 (singlet: 1-proton of the other C-group) and a multiplet at δ - 7 to 8.1. That the two methyl groups produce peaks at two different field strength points out to the unsymmetrical shape of the molecular (Fig.1).

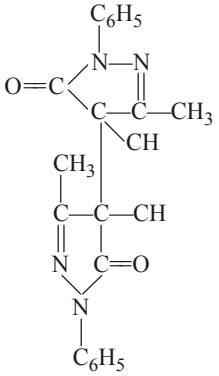
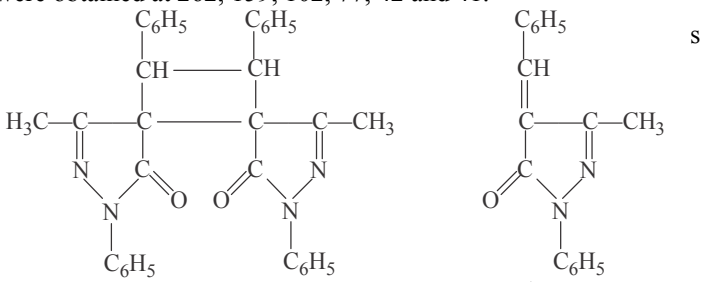


Fig. 1

The two small singlets appearing at δ 1.65 and δ 1.35 are due to the two protons in equatorial and axial conformations within the cyclo-butane ring system. It is interesting to note here that the multiplet for the dihydro derivative had two distinct doublets at δ 7.85 and 8.2. But these are merged into one quadruplet at δ - 7.85 to 7.82 in the spirocyclopropane derivative. This is explained by axial and equatorial disposition of the attached benzene rings. Absence of signal at δ - 6.7 confirms the ring closure of spirocyclobutane.

In the mass spectra, the molecular ion peaks (m/e) was noticed to 524. Major fragmentations were obtained at 262, 159, 102, 77, 42 and 41.



m/e = 524

m/e = 262

Rest of the fragmentations were similar to the corresponding dihydro compound (II).

Results and dicussions

1. Fungicidal Studies :

The fungicidal activity was determined by the method of Montgomery and Moore, 1938 with slight modifications. The fungi used were *Pyricularia oryzae, Helminthosporium oryzae, Collitotrichum tabacum* and *Alternala solani*. The fungicidal assay was based upon the percentage of non-germination at 62.5, 125, 250, 500 and 1000 ppm. concentrations. Time of

contact was 24 hours. Table-1 shows the fungicidal activity of these compounds at 1000 ppm. against all the pathogens. The activity was found to increase with concentrations.

Table I. Fungicidal and bactericidal results

Sl. No	Name of the Compound	% of spore germination inhibition at 1000 ppm				Bactericidal activity	
		P. Oryzae	H. oryzae	C. tabacum	Alt. solani	Salmonea Typhosa	S. aureus
1.	4, 4'-Benzil-bis-(1-phenyl-3-methyl-2-pyrazolin-5-one)	54	30	30	36	+	+
2.	4, 4'-Benzil-bis-(3-methyl-2-pyrazolin-5-one)	56	32	43	38	+	+
3.	4, 4'-Furil-bis-1-phenyl-3- methyl-2-pyrazolin-5-one)	55	52	45	43	+	+
4.	4, 4'-Furil-bis-(3-methyl-2-pyrazolin-5-one)	58	31	41	37	+	+
5.	4, 4'-Dihydrobenzil-bis-1-(1- phenyl-3-methyl-2-pyrazolin- 5-one)	28	32	22	32	+	+
6.	4, 4'-Dihydrobenzil-bis-(3-methyl-2-pyrazolin-5-one)	36	36	38	39	+	+
7.	4,4'-Dihydrofuril-bis-(1-phenyl-3-methyl-2-pyrazolin-5-one)	42	29	30	42	+	+
8.	4, 4'-Dihydrofuril-bis-(3- methyl-2-pyrazolin-5-one)	62	54	62	45	+	+
9.	Spirocyclobutane of (5)	76	81	62	45	-	-
10.	Spirocyclobutane of (6)	73	89	72	61	-	-
11.	Spirocyclobutane of (7)	85	82	42	48	-	-
12.	Spirocyclobutane of (8)	81	80	68	42	-	-

(+) Sign indicates bacterial growth.

(–) Sign indicates prevention of growth.

In general, the fungitoxicity was low for all the compounds of 4, 4'-benzil/furil-bis-(1-phenyl/hydrogen-3-methyl-2-pyrazolin-5-one and their dihydro-derivatives. However, one compound (No.8, Table-1) showed higher anti-fungal activity against all the pathogens. In contrast, spirocyclobutanes (No. 9-12) showed pronounced fungitoxicity (75%) against *Pyricularia oryzae* and *Helminthosporium oryzae*. The activity was reduced considerably when tested against *Collitotrichum tabacum* and *Alternaria solani*.

II. Bactericidal study :

The data on bactericidal studies are shown in table-1. 4, 4'-benzil/furil-bis-(1-phenyl/hydrogen-3-methyl-2-pyrozolin-5-ones) and their dihydro derivatives failed to inhibit the growth of the test bacteria, but the spirocyclobutanes (9-12) were found highly active against both *Salmonella typhosa* and *Staphylococcus aureus* at 1000 ppm. The

spirocyclobutanes of the dihydro benzyl analogues were found tobe more active and the potency extended upto 500 ppm.

Table II. Physical and analytical data of 4, 4'-benzil-bis-(1-phenyl-3-methyl-2-pyrazolin-5-one), their dihydro and spirocyclobutane derivatives

Sl. No.	Name of the Compound	Molecular formula	Colour	M.P.C	Yield %	% of C[1] Found	Carbon Calcd.	% of Hydrogen		% of Nitrogen	
								Found	Calcd.	Found	Calcd.
1.	4, 4'-Benzil-bis-(1-phenyl-3-methyl-2-pyrazolin-5-one)	$C_{30}H_8O_4O_2$	Red	168	80	75.98	76.0	4.32	4.99	10.71	10.72
2.	4, 4'-Benzil-bis-(3-methyl-2-pyrazolin-5-one)	$C_{22}H_8O_4O_2$	Yellow	213	82	71.21	71.19	4.32	4.34	12.49	12.50
3.	4, 4'-Furil-bis-1-phenyl-3-methyl-2-pyrazolin-5-one)	$C_{30}H_{82}O_4O_4$	Grey	110	85	71.39	71.42	4.36	4.36	11.12	11.11
4.	4, 4'-Furil-bis-(3-methyl-2-pyrazolin-5-one)	$C_{18}H_{14}O_4O_4$	Grey	73	84	62.04	62.06	3.42	3.44	16.03	16.09
5.	4, 4'-Dihydrobenzil-bis-1-(1-phenyl-3-methyl-2-pyrazolin- 5-one)	$C_{34}H_{30}O_4O_2$	Buff	163	50	77.53	77.56	5.69	5.67	10.63	10.64
6.	4, 4'-Dihydrobenzil-bis-(3-methyl-2-pyrazolin-5-one)	$C_{22}H_{22}O_4O_2$	Brown	161	52	70.92	70.96	5.35	5.37	15.1	15.05
7.	4, 4'-Dihydrofuril-bis-(1-phenyl-3-methyl-2-pyrazolin-5-one)	$C_{30}H_{26}O_4O_4$	White	226	56	70.85	70.86	5.04	5.11	11.6	11.20
8.	4, 4'-Dihydrofuril-bis-(3-methyl-2-pyrazolin-5-one)	$C_{18}H_{18}O_4O_4$	Grey	246	60	61.34	61.34	4.55	4.54	15.82	15.90
9.	Spirocyclobutane of (5)	$C_{34}H_{28}O_4O_2$	Orange	100	30	77.84	77.84	5.33	5.34	10.67	10.68
10.	Spirocyclobutane of (6)	$C_{22}H_{20}O_4O_2$	Brown	123	32	71.32	71.35	4.85	4.86	15.13	15.14
11.	Spirocyclobutane of (7)	$C_{30}H_{24}O_4O_4$	Grey	178	35	71.12	71.14	4.72	4.74	11.04	11.06
12.	Spirocyclobutane of (8)	$C_{18}H_{16}O_4O_4$	Grey	185	40	61.32	61.34	4.54	4.54	15.86	15.90

EXPERIMENTAL

All chemical used in the synthesis were of 'Anala R' grade. Melting points were taken taken in a 'Toshniwal Melting Point apparatus and were uncorrected. I.R. spectra were taken as a Perkin-Elmer-I.R.Spectrophotometer, n.m.r. spectrum Vurian-90D instrument with T.M.S. as internal structure and atomic mass spectra of J.M.C.-D-300 (Jeol Ltd., Tokyo) N.B. at E.I. mode at C.D.R.I., Lucknow.

A. Synthesis of 1-phenyl/hydrogen-3-methyl-2-pyrazolin-5-one :

These are synthesized following the standard method of condensation (Vogel, 1972).

B. Synthesis of 4, 4'-Benzil-bis-(1-phenyl-3-methyl-2- pyrazolin-5-ones) :

In the dry conical flask benzyl (1 mole) and 1-phenyl-3-methyl-2-pyrazolin-5-one (2 moles) were taken together with sodium acetate (2 moles) and glacial acetic acid (60ml.) and refluxed for 2 hours. It was cooled and kept overnight. The solid mass was filtered, drived and crystallized from ethyl alcohol. The furil analogous were prepared in similar manner.

C. Synthesis of 4, 4'-dihyrobenzil-bis-(1-phenyl-3-methy-2-pyrazolin-5-ones) :

4, 4'-Benzil-bis-(1-phenyl-3-methyl-2-pyrazolin-5-one (2 gms.) was taken in a conical flask and was made soluble in glacial acetic acid (4 ml). Metallic tin cut into pieces and 10ml of Conc. HCl was added to it. The contents were refluxed for 2 hours till there was distinct change or colour. The solution was filtered and neutral listed with conc. Ammonia and filtered. The residue was repeatedly boiled in rectified spirit and filtered hot to eliminate impurities. Lights coloured crystals appeared on cooling. It was filtered, crystallized from alcohol and dried.

D. Synthesis of 3, 8, 11, 12-tetra phenyl-1, 10-dimethyl-4, Z-dioxo-2, 3, 8, 9-tetra-aza dispiro-(4, 0, 4, 2)-dodeca-1, 9-diene :

4, 4'-Dihydro benzyl-bis-(1-phenyl-3-methyl-2-pyrazolin-5-one) (1 gm.) was taken in a conical flask and dissolved in rectified spirit (2ml). 10% solution of I_2/KI (aqueous) was added when a thick solid mass appeared immediately which was filtered and dried. Orange crystals appeared on crystallisation from hot alcohol.

References

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