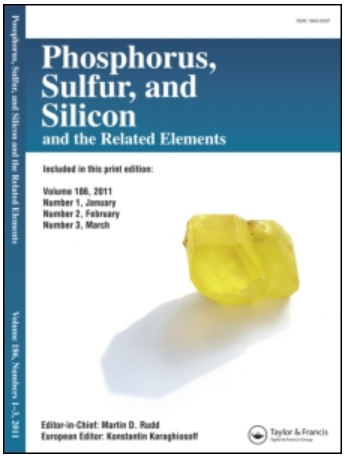

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FACILE SYNTHESIS OF 4-SUBSTITUTED 2-PYRAZOLIN-5-ONES UNDER PHASE TRANSFER CATALYSIS

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FACILE SYNTHESIS OF 4-SUBSTITUTED 2-PYRAZOLIN-5-ONES UNDER PHASE TRANSFER CATALYSIS

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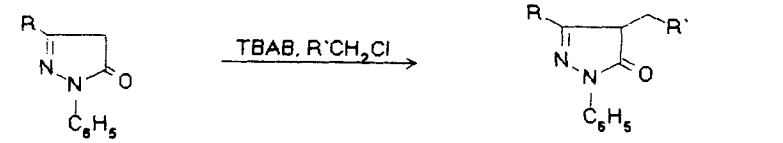
Nucleophilic displacement of organohalogen compounds by 2-pyrazolin-5-ones (**1**) in absence/or presence of carbon disulphide or phenyl isothiocyanate under phase transfer catalysis conditions have been studied to give 4-substituted-2-pyrazolin-5-ones (**2–8**).

As an extension of our work[1,2] we report here the facile synthesis of 4-substituted 2-pyrazolin-5-ones via phase transfer catalysis (PTC) conditions as one of the most important techniques in organic synthesis,[3–5] the method is highly versatile with wide universal applications.[6]

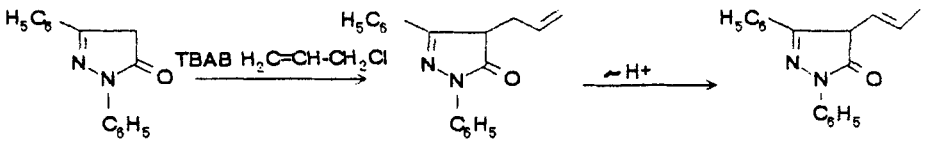
In our present PTC investigation, we have used solid-liquid phases[7,8] the solid phase being anhydrous potassium carbonate and the liquid phase benzene or toluene, while tetrabutyl ammonium bromide[9,10] is used as a catalyst in the nucleophilic displacement of some aliphatic halo compounds by 2-pyrazolin-5-ones (**1**) in the absence or presence of carbon disulphide[11] or phenyl isothiocyanate. Treatment of 3-methyl-1-phenyl and/or 1,3-diphenyl-2-pyrazolin-5-ones (**1a, b**) with chloro acetonitrile and/or benzyl chloride under our PTC conditions, afforded 4-cyanomethyl and/or 4-benzyl-2-pyrazolin-5-one derivatives (**2a–d**).



1
a)R=CH_3, b)R=C_6H_5

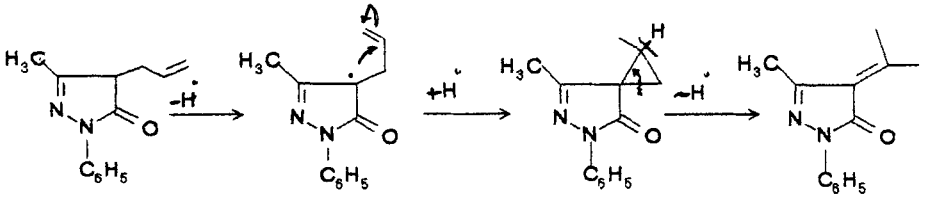
2
a)R=CH_3, R'=CN b)R=C_6H_5, R'=CN
c)R=CH_3, R'=C_6H_5 d)R=R'=C_6H_5

In the PTC reaction of 2-pyrazolin-5-one (**1b**) with allyl chloride at 60°C for 15 h. the 4-allyl pyrazolinone (**A**) is formed by nucleophilic attack of the pyrazolinone anione, then rearranged (by 1,3-proton shift) under the reaction conditions to give 4-(1-propenyl)-1,3-diphenyl-2-pyrazolin-5-one (**3**).



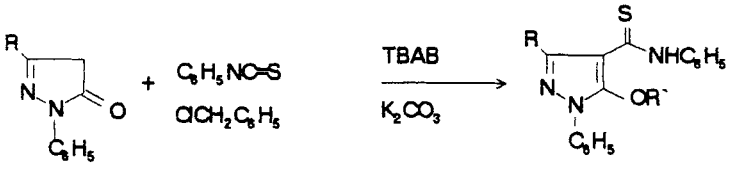
1 b (A) 3

On the other hand, the reaction of (**1a**) with allyl chloride at 80°C for 24 h afforded the 4-isopropylidene-3-methyl-1-phenyl-2-pyrazolin-5-one (**4**) via a homo allylic free radical mechanism[12,13] of the intermediate (**A**) as shown below.



(A) 4

PTC reaction of pyrazolinones (**1a**, **b**) with phenyl isothiocyanate afforded 3-methyl-1-phenyl and/or 1,3-diphenyl-5-hydroxy-1H-pyrazol-4-thio carbanilides (**5a**, **b**) respectively. On the other hand, a one pot reaction of pyrazolinones (**1a**, **b**) with phenyl isothiocyanate in the presence of benzyl chloride produced 5-benzyloxy-3-methyl-1-phenyl and/or 1,3-diphenyl-1H-pyrazol-4-thio carbanilides (**5c**, **d**) respectively.



1

a) R=CH_3

b) R=C_6H_5

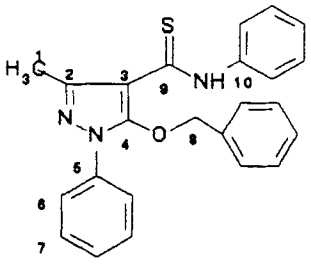
5

a)R=CH_3,R`=H b)R=$C_6H_5$,R`=H

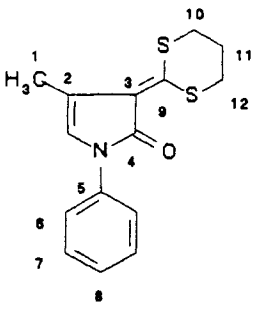
c)R=CH_3, R`= -$CH_2C_6H_5$

d)R=C_6H_5, R`= -$CH_2C_6H_5$

^{13}C-chemical shifts (δ ppm) and off resonance data[14–17] of (**5c**); 1, 18.3 q-2, 165-4s-3, 105.8s-4, 148.6s-5, 130.5s-6, 119.0d-7, 128.7d-8, 38.6t-9, 206.ls-10, 140.2s, and (**7a**); 1, 18.7 q-2, 161.9s-3, 146.1s-4, 172.9s-5, 138.6s-6, 118.7d-7, 128.7d-8, 124.3d-9, 168.5s-10, 28.9t-11, 23.6t-12, 29.9t are shown on the structure below.

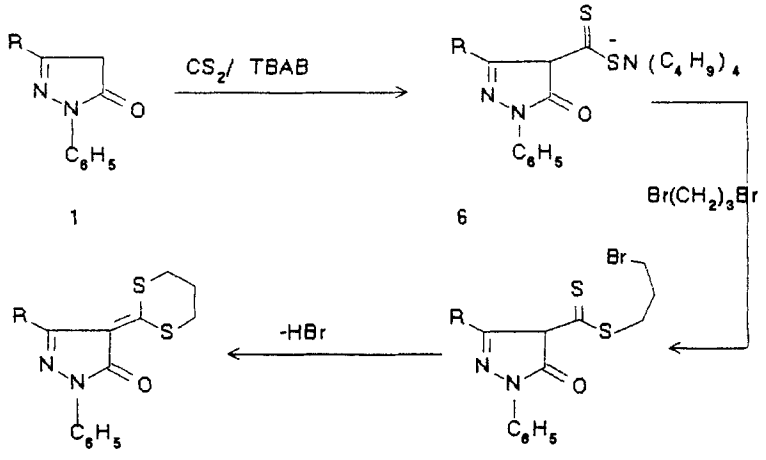


5c



7a

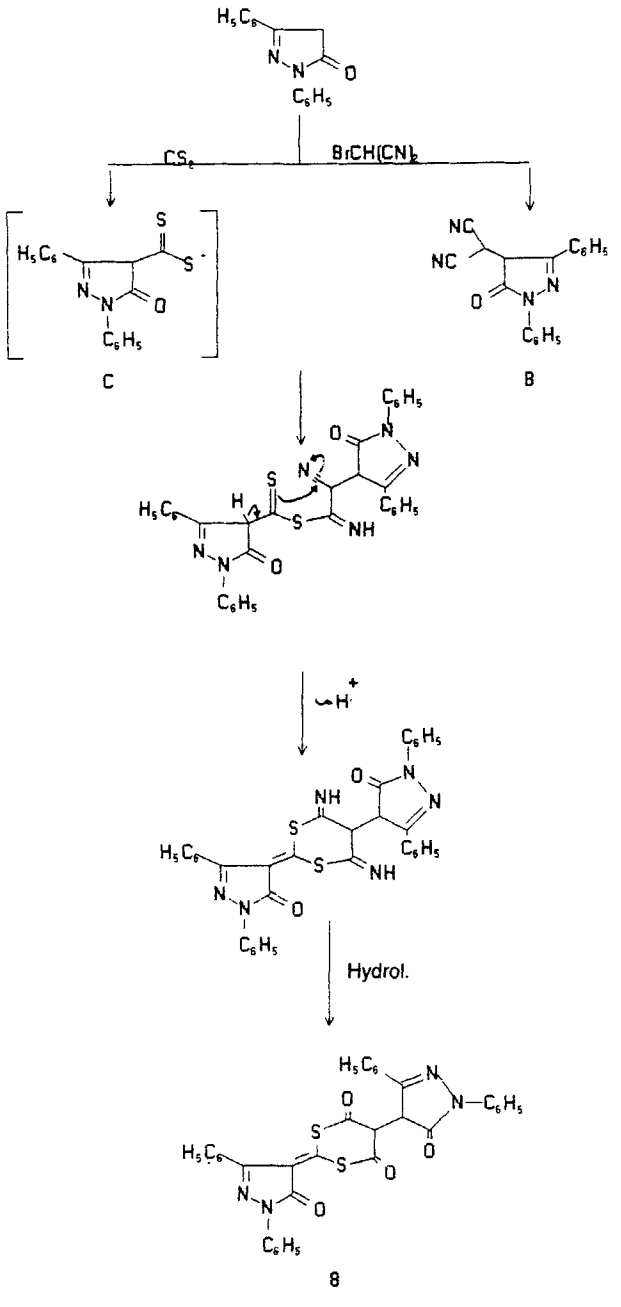
Treatment of pyrazolinones (**1a, b**) with 1,3-dibromo propan in the presence of carbon disulphide[11] under PTC conditions afforded 2-(1,5-dihydro-3-methyl-1-phenyl and/or 1,3-diphenyl-5-oxo-1H-pyrazol-4-ylidene)-1,3-dithiones (**7a, b**). The reaction proceeds by addition of the intermediate C_4-active anion to carbon disulphide to give in the presence of TBAB the ammonium salt of dithiolate anion (**6**) (isolated in the reaction with **1a**). The intermediate dithiolate anion reacted with 1,3-dibromo propane to give dithiones (**7a, b**) as shown below.



1 6 7

a) R=CH_3 b) R=C_6H_5

PTC one pot reaction of pyrazolinone (**1b**) with bromo malononitrile in the presence of carbon disulphide afforded 2-(1,5-dihydro-1,3-diphenyl-5-oxo-1H-pyrazol-4-ylidene)-5-(4,5-dihydro-1,3-diphenyl-5-oxo-1H-pyrazol-4-yl)-1,3-dithian-4,6-dione (**8**). The reaction probably proceeds via nucleophilic attack of the C_4-anion to bromo malononitrile to give intermediate (**B**), while a second C_4-anion was added to carbon of carbon disulphide to give the thiolate anion (**C**), followed by addition of (**C**) to (**B**) with subsequent cyclization and hydrolysis of the imino group during the working up of the reaction to give adduct (**8**) as shown below.



EXPERIMENTAL

Melting points reported are uncorrected. Physical data and reaction conditions are listed in Table I. Ir spectra were recorded in KBr on Pye Unicam SP 200G spectrometer. The ^{1}H-nmr spectra were determined on a Varian FT-90 and Brucker AC-200 spectrometer. The ^{13}C-nmr spectra were measured on a Brucker-300 AX, with Dept Experiment. In all nmr experiments the internal standard was TMS and the solvent was $CDCl_3$ except of 8 was DMSO-d_6. All chemical shifts are in ppm down field from TMS.

General procedure: To a solution (0.01 mol) of 3-methyl-1-phenyl and/or 1,3-diphenyl-2-pyrazolin-5-one (**1a**, **b**) (1.74 g and/or 2.36 g) in dry benzene or toluene (50 ml), potassium carbonate anhydrous (2.7 g, 0.02 mol) and halogen compounds such as chloro acetonitrile (0.7 ml, 0.01 mol), benzyl chloride (1.3 ml, 0.01 mol), allyl chloride (0.8 ml, 0.01 mol), 1,3-dibromopropane (2.0 ml, 0.01 mol) and/or bromo malononitrile (1.4 g, 0.01 mol) were added in absence or presence of phenyl isothiocyanate (1.35 g, 0.01 mol) or carbon disulphide (7.6 ml, 0.1 mol) then tetrabutyl ammonium bromide (TBAB) (0.09 g, 0.003 mol) was added to the reaction mixture at 25°C. The reaction mixture was stirred over a period of time (Table I) and 50–70°C. At the end of the reaction (TLC), the organic layer was

TABLE I

Physical data of compounds **2–8**

compd	react time	M.P.°C	Mol. formula	Analysis%	Ir Spectra (cm^{-1})
	yield %	solvent	Mol. weight	Calc/Found	
2a	8	164	$C_{12}H_{11}N_3O$	C,67.58- H,5.20- N,19.17	3450 (OH - enol)
	(35)	B	(213.23)	66.80 4.80 19.90	2250 (C=N)
2b	8	234	$C_{17}H_{13}N_3O$	C,74.17- H,4.76- N,15.20	3470 (OH- enol)
	(70)	B	(275.29)	74.31 4.90 15.53	2230 (C=N)
2c	18	112	$C_{17}H_{16}N_2O$	C,77.25- H,6.10- N,10.59	3560 (OH - enol)
	(20)	P	(264.31)	77.33 5.92 10.80	1650 (C=O)
2d	15	149	$C_{22}H_{18}N_2O$	C,80.90- H,5.56- N,8.58	3500 (OH - enol)
	(30)	E	(326.38)	80.80 5.41 8.32	1720 (C=O)
3	15	168	$C_{18}H_{16}N_2O$	C,78.23- H,5.84- N,10.14	3390 (OH - enol)
	(25)	P	(276.32)	78.40 5.73 9.92	
4	24	95	$C_{13}H_{14}N_2O$	C,72.87- H,6.59- N,13.07	1650 (C=O)
	(23)	P	(214.25)	72.60 6.41 13.30	
5a	3	146	$C_{17}H_{15}N_3OS$	C,66.01- H,4.89- N.13.59	3500(NH),3180(OH),
	(45)	P	(309.33)	66.31 5.00 13.49	1200 (C=S)
5b	4	165	$C_{22}H_{17}N_3OS$	C,71.14- H,4.61- N,11.31	3450(NH),3375(OH),
	(60)	B	(371.39)	70.98 4.40 11.62	1200 (C=S)
5c	12	192	$C_{24}H_{21}N_3OS$	C,72.16- H,5.30- N,10.52	3350 (NH)
	(80)	B	(399.45)	72.04 5.55 10.41	1220 (C=S)
5d	12	197	$C_{29}H_{23}N_3OS$	C,75.47- H,5.02- N,9.10	3450 (*NH*)
	(65)	B	(461.51)	75.71 4.91 8.85	1230 (C=S)
6	6	215	$C_{27}H_{45}N_3OS_2$	C,65.95- H,9.23- N,8.55	3400 (OH- enol),
	(10)	E	(491.69)	65.62 9.01 8.60	1650(C=O),1195(C=S)
7a	6	166	$C_{14}H_{14}N_2OS_2$	C,57.92- H,4.86- N.9.65	1650 (C=O)
	(73)	B	(290.30)	57.98 4.61 9.50	
7b	5	204	$C_{19}H_{16}N_2OS_2$	C,64.76- H,4.58-N,7.95	1675 (C=O)
	(80)	B	(352.37)	64.44 4.30 8.01	
8	48	185	$C_{34}H_{22}N_4O_4S_2$	C,66.44- H,3.61- N,9.12	3450(OH- enol),1710
	(25)	P	(614.58)	66.31 3.70 9.30	(C=O),1705&1650(C=O)

B=benzene, P=pet.ether 60-80°C and E=ethanol

TABLE II

^{1}H-NMR data of prepared compounds

Compound No	^{1}H-NMR signals-δ
2a	2.15 (s, 3H, CH3), 2.60 (s, 2H, CH2) and 7.42 (m, 6H, Ar-H + OH-enol)
2d	1.72 (s, 2H, CH2) and 7.72 (m, 11H, Ar-H + OH- enol)
3	2.21 (d, 3H, CH3), 2.83 (d, 1H, C4-H), 5.0 (m, 1H, CH=CH-CH3), 5.9 (d,1H, CH=CH) and 7.62 (m, 10H, Ar-H)
4	2.31 (s, 3H, CH3), 2.40 (s, 3H, CH3), 2.61 (s, 3H, CH3) and 7.55 (m, 5H, Ar-H)
5c	2.55 (s, 3H, CH3), 3.75 (s, 2H, OCH2), 7.45 (m, 15H, Ar-H) and 12.88(s, 1H, NH)
6	0.94(t, 12H, 4xCH3), 1.44(m, 16H, 8xCH2), 2.70(s, 3H, CH3), 3.14(t, 8H, 4xCH2-N) and 7.52 (m, 5H, Ar-H)
7a	2.32(q, 2H, C5H2), 2.48 (s, 3H, CH3), 3.09(t, 4H, 2xCH2-S) and 7.56 (m, 5H, Ar-H)
7b	2.28(q, 2H, C5H2), 2.93 (t, 2H, CH2-S), 3.09 (t, 2H, CH2-S), and 7.62(m, 10H, Ar-H)
8	1.50 (d,1H, CH), 1.95(d, 1H, CH) and 7.12(m, 20H, Ar-H)

separated and the solvent was removed under reduced pressure, then the residue obtained was crystallized from the proper solvent (Table I) to give the products; (**2**, **3**, **5a**, **5d** and **6–8**) as yellow crystals and products; (**4**, **5a**, and **5b**) as colourless crystals.

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