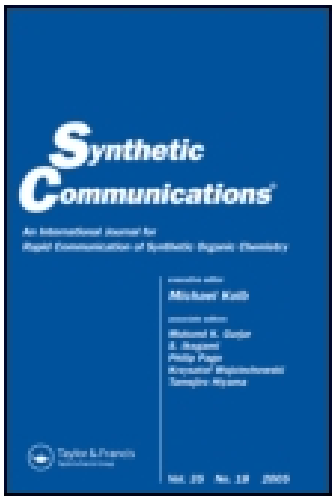

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A CONVENIENT SYNTHESIS OF 1,3-DISUBSTITUTED-4-(1′,3′-DITHIOLANE/ DITHIANE-2′-YLIDENE)-2-PYRAZOLIN-5-ONES

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ABSTRACT

1,3-Disubstituted-4-(1′,3′-dithiolane/dithiane-2′-ylidene)-2-pyrazolin-5-one derivatives like (**1a–c**), (**2a–c**), (**3a–c**) have been obtained by condensation of 2-pyrazolin-5-ones (**1**), (**2**) and (**3**) with carbon disulfide in presence of triethylamine followed by the reaction with 1,2-dibromoethane (**4a**), 1,3-dibromopropane (**4b**) and 1,3-dibromobutane (**4c**) respectively.

The formation of ketene dithioacetals by the condensation of compounds containing active methylene groups with carbon disulfide and alkyl halides is very well documented.[1] Various types of physiological activities, viz., fungicidal and pesticidal have been associated with 2-pyrazolin-5-

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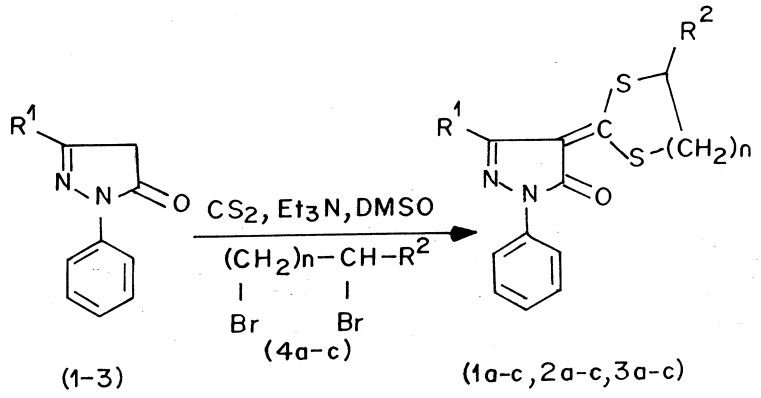
ones[2,3] as well as 1,3-dithiane/1,3-dithiolane derivatives.[4-6] These in combination are also reported to exhibit fungicidal activity.[7]

Earlier methods for the synthesis of the title compounds required strong bases like methanolic potassium hydroxide[7] or n-butyllithium[8] and these required longer time and inert atmosphere. Recently the synthesis of 5-(1,3-dithiolan-2-ylidene)-barbiturate has been reported[9a] by using modification of method of Huang and Cheng[9b] under similar experimental conditions.

In this paper, we report the synthesis of title compounds by one pot method involving reaction of 2-pyrazolin-5-ones with carbon disulfide in presence of triethylamine and dimethyl sulfoxide (DMSO) followed by the reaction of the formed salts of dithioacids with dihalides, viz., 1,2-dibromoethane (**4a**), 1,3-dibromopropane (**4b**) and 1,3-dibromobutane (**4c**) (Scheme 1).

This method has the advantage over earlier methods in manipulative convenience and milder basic conditions, the reaction completing in much



	R^1
1	CH_3
2	Ph
3	n-Pr

4	n	R^2
a	1	H
b	2	H
c	2	CH_3

	n	R^2
1a,2a,3a	1	H
1b,2b,3b	2	H
1c,2c,3c	2	CH_3

Scheme 1.

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shorter time with improved yields. Use of the dipolar aprotic solvents like DMSO has the additional advantage to carry out the polar reaction by stabilizing and increasing the neucleophillic ability of the salt of bis-hydrodithioylidene derivatives. Thus, the reaction of 3-methyl-1-phenyl-2-pyrazolin-5-one (**1**) with carbon disulfide in presence of triethylamine as the base and using DMSO as the solvent followed by the reaction with 1, 2-dibromoethane (**4a**) resulted in 3-methyl-1-phenyl-4-(1′,3′-di-thiane-2′-ylidene)-2-pyrazolin-5-one (**1a**) with good yields of 89%. Use of 1,3-diphenyl-2-pyrazolin-5-one (**2**) or 1-phenyl-3-propyl-2-pyrazolin-5-one (**3**) afforded the corresponding 4-(1′,3′-dithiane-2′-ylidene)-2-pyrazolin-5-ones (**1b**), (**2b**), (**3b**) and 4-(4′-methyl-1′, 3′-dithiane-2′-ylidene)-2-pyrazolin-5-one (**1c**), (**2c**), (**3c**), respectively, with higher yields as much as 79–89%.

The structures of all these compounds (**1a–c**), (**2a–c**) and (**3a–c**) were assigned on the basis of the microanalysis, ^{1}H NMR, IR, UV and Mass spectral data. The starting compounds 2-pyrazolin-5-ones (**1–3**) were obtained by the Knorr's condensation[10, 11] of β-ketoester viz., ethyl acetoacetate, ethyl benzoylacetate and ethyl butylacetate with phenylhydrazine. The Knorr's condensation under microwave irradiation gave 90% yield compared to 75–80% yield in the earlier methods.[7,8,10] This method has an additional advantage of carrying out the reaction in 8–10 minutes compared to 2 h in the conventional methods.[10] One of the pyrazolones (**1**) has been prepared earlier by the microwave irradiation method.[12]

EXPERIMENTAL

Melting points are uncorrected. IR spectra were recorded on a Shimadzu infrared spectrophotometer IR-435 (ν_{max} in cm^{-1}). ^{1}H NMR spectra were recorded in $CDCl_3$ and $CDCl_3$ + TFA on a Perkin Elmer R-32 (90 MHz) spectrometer using TMS as internal standard (Chemical shifts in δ, ppm). UV spectra were recorded on a Beckman DU-64 spectrophotometer.

3-Methyl-1-phenyl-2-pyrazolin-5-one (1): It has been prepared as reported earlier.[12]

1,3-Diphenyl-2-pyrazolin-5-one (2): Ethyl benzoylacetate (3.8 g, 19 mmol) and phenylhydrazine (2.15 g, 19 mmol) were mixed in a conical flask (50 ml). The mixture was irradiated in a microwave oven for 9 min. After cooling it, 10-ml ether was added to a yellowish brown viscous mass. After scratching it vigorously, a white solid separated out. The white solid was recrytallised in ethanol. A yield of 4.4 g, (94%), m.p.: 137–138°C (lit.[13] m.p: 137–137.5°C) was obtained.

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Table 1. Spectral Data of Compounds (**1a–c**)

Compd.	R^1	R^2	n	UV(λ_{max}) [nm]	IR(Nujol) cm^{-1}	^{1}H NMR [$CDCl_3$/TMS] [δ/ppm]
1a	CH_3	H	1	256, 288 (Sh.) 327, 400 (Sh.)	1680[C = O] 1600[C = N] 1540[C = C] 1420, 1405, 1270, 1230, 1145[C-H]	2.4 [s, 3H, C**H**$_3$] 3.5 [s, 4H, 2x-S-C**H**$_2$-] 6.9–8.3 [m, 5H, Ar-**H**]
1b	CH_3	H	2	251, 288 (Sh.) 346, 411 (Sh.)	1680[C = O] 1600[C = N] 1540[C = C] 1420, 1425, 1405, 1230, 1145[C-H]	1.91–2.28 [m, 2H,-CH_2-C**H**$_2$-CH_2], 2.45 [s, 3H, C(3)-C**H**$_3$], 3.00 [t, 4H,-S-C**H**$_2$-CH_2-C**H**$_2$-S] 7.00–8.20 [m, 5H, Ar-**H**]
1c	CH_3	H	2	255, 294 (Sh.) 344, 421 (Sh.)	1680[C = O] 1600[C = N] 1540[C = C] 1470, 1425, 1405, 1230, 1145[C-H]	1.40 [d, 3H,-S-CH(C**H**$_3$)-CH_2-CH_2-S], 1.61 [q, 2H,-S-CH(CH_3)-C**H**$_2$-CH_2-S], 2.36 [s, 3H, C(3)-C**H**$_3$], 3.61–3.82 [m, 3H, -S-C**H**(CH_3)-CH_2-C**H**$_2$-S-], 6.61–8.21 [m, 5H, Ar-**H**]

Table 2. Spectral Data of Compounds (**2a–c**)

Compd.	R^1	R^2	n	UV(λ_{max}) [nm]	IR(Nujol) cm^{-1}	^{1}H NMR [$CDCl_3$/TMS] [δ/ppm]
2a	C_6H_5	H	1	263, 309 (Sh.) 335, 425 (Sh.)	1685[C = O] 1600[C = N] 1540[C = C] 1425, 1405, 1285, 1145[C-H]	3.53 [s, 4H, 2x-S-C**H**$_2$-] 7.1–8.2 [m, 10H, Ar-**H**]
2b	C_6H_5	H	2	262, 305 (Sh.) 355, 427 (Sh.)	1685[C = O] 1600[C = N] 1540[C = C] 1425, 1405, 1290, 1145[C-H]	2.20 [m, 2H, -S-CH_2 -C**H**$_2$-CH_2-S-] 2.95 [t, 4H, -S-C**H**$_2$ -CH_2-C**H**$_2$-S] 7.00–8.35 [m, 10H, Ar-**H**]
2c	C_6H_5	CH_3	2	265, 310 (Sh.) 356, 429 (Sh.)	1685[C = O] 1600[C = N] 1540[C = C] 1425, 1470, 1290, 1155[C-H]	1.40 [d, 3H, -S-CH(C**H**$_3$) -CH_2-CH_2-S-], 1.61–2.1 [q, 2H-S-CH(CH_3) -C**H**$_2$-CH_2-S], 2.7–3.2 [m, 3H, -S-C**H**(CH_3) -CH_2-C**H**$_2$-S-], 7.0–8.2 [m,10H, Ar-**H**]

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Table 3. Spectral Data of Compounds (**3a–c**)

Compd.	R^1	R^2	n	UV(λ_{max}) [nm]	IR(Nujol) cm^{-1}	^{1}H NMR[$CDCl_3$/TMS] [δ/ppm]
3a	C_3H_7	H	1	254, 237 (Sh.) 328, 400(Sh.)	3050, 2850, 2950[C-H] 1660[C = O] 1600[C = N] 1540[C = C] 1475, 1425, 1410, 1270, 1145[C-H]	1.01[t, 3H, -CH_2-CH_2-C**H**$_3$] 1.63[m, 2H, -CH_2-C**H**$_2$-CH_3] 3.0[t, 2H, -C**H**$_2$-CH_2-CH_3] 3.88[s, 4H, 2x-S-C**H**$_2$] 7.55[m, 5H, Ar-H]
3b	C_3H_7	H	2	251, 286(Sh.) 324, 411(Sh.)	3050, 2850, 2950[C-H] 1660[C = O] 1600[C = N] 1540[C = C] 1470, 1420, 1415, 1270, 1145[C-H]	1.01*[t,3H,-CH_2-CH_2-C**H**$_3$] 1.45–1.98[m, 4H, -CH_2-C**H**$_2$-CH_3 and S-CH_2-C**H**$_2$-CH_2-S] 2.91–3.33[t, 4H, -S-CH_2-CH_2C**H**$_2$-S] 7.10–8.21[m, 5H, Ar-H]
3c	C_3H_7	CH_3	2	256, 290(Sh.) 342, 417(Sh.)	3050, 2850, 2950[C-H] 1660[C = O] 1600[C = N] 1540[C = C] 1470,1420, 1410, 1270, 1145[C-H]	1.01[t, 3H, -CH_2-CH_2-C**H**$_3$] 1.40[d, 3H, -S-CH(C**H**$_3$) -CH_2-CH_2-S-], 2.15–2.55[m, 4H, -S-CH (CH_3)-C**H**$_2$-CH_2-S- and–CH_2-C**H**$_2$-CH_3], 2.77[t, 2H, -C**H**$_2$-CH_2-CH_3] 2.94–3.65[m, 3H, -S-C**H** (CH_3)-CH_2-C**H**$_2$-S-], 6.85–8.15[m, 5H, Ar-**H**]

*$CDCl_3$/TFA/TMS.

1-Phenyl-3-propyl-2-pyrazolin-5-one (3): Ethyl butyrylacetate (5.1 g, 32 mmol) and phenylhydrazine (3.5 g, 32 mmol) were mixed in a conical flask (50 ml). The mixture was placed in a microwave oven. After 8 min, reaction was complete as checked by TLC. After cooling it, 20-ml ether was added to a viscous mass. The white solid separated out after scratching it vigorously. This white solid recrystallised by ethanol to obtain **3** as a white crystalline compound. A yield of 5.9 g, (90.5%), m.p.: 110–111°C (lit[14] m.p.: 110–110.5°C) was obtained.

General Procedure: 1,3-Disubstituted-4-(1′,3′-dithiane-2′ylidene)-2-pyrazolin-5-ones (1a), (2a) and (3a): 3-Methyl-1-phenyl-2-pyrazolin-5-one (**1**, 0.174 g, 1 mmol) was stirred in DMSO (4 ml) for 3–4 min. To this were added a well stirred solution of triethylamine (0.2 g, 2 mmol) and carbon disulfide (0.76 g, 1 mmol) in succession with the gap of 3 min. The mixture

was stirred for another 30 min at room temp. With a colour change in the solution, 1,2-dibromoethane (4a, 0.18 g, 1 mmol) was added. The stirring was continued for another 2 h at room temperature and completion of the reaction was checked by TLC. The reaction mixture was poured into ice water (20 ml) and kept for 1 h. The solid product was collected by filtration, washed several times with water and dried. It was crystallized by ethanol as yellow crystals of **1a**. A yield of 0.245 g (89.7%), m.p.: 152–153°C (lit.[8] m.p.: 162–163°C) was obtained. Similarly **2a** and **3a** were prepared by using appropriate 2-pyrazolin-5-ones (**2** and **3**). The characterization data of the compounds prepared are given in Table 1.

General Procedure: 1,3-Disubstituted-4-(1′,3′-dithiane-2′-ylidene)-2-pyrazolin-5-ones (1b), (2b) and (3b): Compound **1b** was obtained under similar conditions as in the preparation of **1a** by condensation of **1** with 1,3-dibromopropane (0.2 g, 1 mmol) in the presence of triethylamine and DMSO. The yield obtained was 0.260 g (89.6%), m.p. 164–165°C (lit.[8] m.p. 164–165°C). Similarly **2b** and **3b** were obtained by using appropriate 2-pyrazolin-5-ones (**2** and **3**). The characterization data of the compounds prepared are given in Table 2.

General Procedure: 1,3-Disubstituted-4-(4′-methyl-1′,3′-dithiane-2′-ylidene)-2-pyrazolin-5-ones (1c), (2c) and (3c): Condensation of **1** (0.174 g, 1 mmol) with carbon disulfide in presence of triethylamine was followed by treatment with 1,3-dibromobutane (0.21 g, 1 mmol) in a similar manner as in **1a** gave **1c** as a yellow solid. The yield obtained was 0.265 g (87.2%)

Table 4. Physical and Analytical Data of Compounds (**1a**–c), (2**a**–c) and (3**a**–c)

Compd.#		R^1	R^2	n	Yield (%)	Time (hrs)	m.p. (°C)	Molecular formula[(a)] (Mol. Wt.)
1.	a	CH_3	H	1	89.7	3.5	152–153	$C_{13}H_{12}N_2OS_2$ (276)
	b	CH_3	H	2	89.6	3.0	164–165	$C_{14}H_{14}N_2OS_2$ (290)
	c	CH_3	CH_3	2	87.2	3.0	173–174	$C_{15}H_{16}N_2OS_2$ (304)
2.	a*	C_6H_5	H	1	88.7	2.0	205–206	$C_{18}H_{14}N_2OS_2$ (338)
	b	C_6H_5	H	2	86.6	2.0	241–242	$C_{19}H_{16}N_2OS_2$ (352)
	c	C_6H_5	CH_3	2	81.9	2.5	275–276	$C_{20}H_{18}N_2OS_2$ (366)
3.	a	C_3H_7	H	1	80.5	2.5	128–129	$C_{15}H_{16}N_2OS_2$ (304)
	b**	C_3H_7	H	2	81.7	2.5	133-134	$C_{16}H_{18}N_2OS_2$ (318)
	c	C_3H_7	CH_3	2	79.8	3.0	141–142	$C_{17}H_{20}N_2OS_2$ (332)

(a) Microanalysis was found to be in agreement with expected values.
*MS (m/z) : 338 (M), **:MS (m/z) : 318 (M^+).
#: Crystallized from 1a, 1b: ethanol; 1c: Ethanol-chloroform; 2a, 2b: benzene; 2c: benzene-petroleum ether; 3a: t-butyl alcohol; 3b: t-butanol-chloroform; 3c: Petroleum ether-chloroform.

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m.p. 173–174°C. Similarly **2c** and **3c** were obtained by using appropriate 2-pyrazolin-5-ones (**2** and **3**). The characterization data of the compounds prepared are given in Table 3. Physical and analytical data of all compounds prepared are given in Table 4.

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