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Studies on 5-Bromodehydroacetic Acid : Synthesis of 1,5-Diphenyl-3-(5-bromo-4-hydroxy-6-methyl-2H-pyran-2-one-3-yl)-2-pyrazolines

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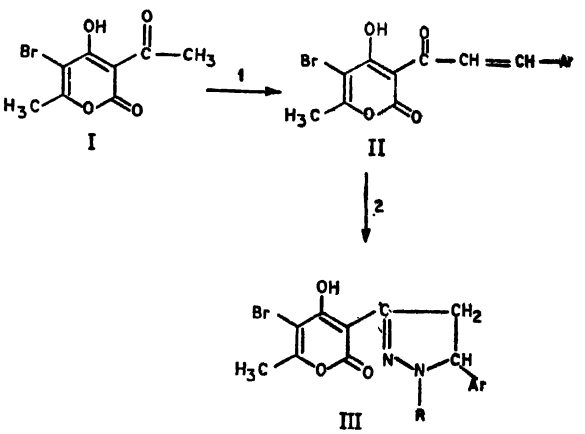
5-Bromodehydroacetic acid(I), on condensation with aromatic aldehydes in the presence of piperidine gave chalcone type compounds(II). Reaction of II with phenylhydrazines in ethanol-acetic acid afforded 1,5-diphenyl-3-(5-bromo-4-hydroxy-6-methyl-2H-pyran-2-one-3-yl)-2-pyrazolines(III).

IN view of physiological importance of pyrones and pyrazolines it was considered worthwhile to synthesise certain compounds having mixed features. In the present study, the synthesis of pyrazoline derivatives having an α-pyrone ring system at position 3 has been carried out by the condensation of 5-bromodehydroacetic acid(I) with different aromatic aldehydes followed by treatment of the resulting chalcone derivatives(II) with phenylhydrazines.

5-Bromodehydroacetic acid (3-acetyl-5-bromo-4-hydroxy-6-methyl-2H-pyran-2-one), (I), exists as a completely enolized species[1] in solution. The condensation of I with aromatic aldehydes in the presence of piperidine[2] gave 3-cinnamoyl-5-bromo-4-hydroxy-6-methyl-2H-pyran-2-ones(II) (Table 1). All of these compounds show characteristic absorption at 1700 (lactone); 1600(C=C) and 1000 (C-O-C) cm^{-1}. In case of hydroxy cinnamoyl derivatives(II_2 and II_3) absorption in the range of 3360-3300 cm^{-1} is clearly indicative of the phenolic hydroxyl group. Synthesis of pyrazolines(III) has been effected by the action of phenylhydrazines on



Scheme 1

Reagents : 1 – ArCHO/Piperidine-Chloroform
2 – $RNHNH_2$/Ethanol-acetic acid.

cinnamoyl derivatives(II) in ethanol-acetic acid[3] (10 : 1) at reflux temperature (Table 2). The NMR spectra of 1,5-diphenyl-3-(5-bromo-4-hydroxy-6-methyl-2H-pyran-2-one-3-yl)-2-pyrazoline(III_1) in

TABLE 1—3-CINNAMOYL-5-BROMO-4-HYDROXY-6-METHYL-2H-PYRAN-2-ONES(II)

Compound No.	Ar	Yield %	M. P. °C	Molecular Formula	Analysis Found / Calcd. C	Analysis Found / Calcd. H
1	Phenyl	55	130	$C_{15}H_{11}BrO_4$	53.64 53.73	3.15 3.28
2	4-Hydroxy-3-methoxyphenyl	50	232	$C_{16}H_{13}BrO_6$	50.46 50.39	3.44 3.41
3	2-Hydroxyphenyl	50	208	$C_{15}H_{11}BrO_5$	51.18 51.28	3.10 3.13

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TABLE 2—1,5-DIARYL-3-(5-BROMO-4-HYDROXY-6-METHYL-2H-PYRAN-2-ONE-3-YL)-2-PYRAZOLINES(III)

Compound No.	Ar.	R	Yield %	M.P. °C	Molecular Formula	Analysis* Calcd. / Found Nitrogen	
1.	Phenyl	Phenyl	30	150d	$C_{21}H_{17}BrN_2O_3$	6.58	6.48
2.	Phenyl	4-Nitrophenyl	32	138-9	$C_{21}H_{16}BrN_3O_5$	8.93	8.84
3.	Phenyl	2,4-Dinitrophenyl	35	215	$C_{21}H_{15}BrN_4O_7$	10.87	10.88
4.	Phenyl	Thiosemicarbazido	30	168	$C_{16}H_{14}BrN_3O_2S$	10.29	10.36
5.	Phenyl	Semicarbazido	30	157	$C_{16}H_{14}BrN_3O_4$	10.71	10.60
6.	4-Hydroxy-3-methoxyphenyl	Phenyl	25	120	$C_{22}H_{19}BrN_2O_5$	5.94	5.80
7.	4-Hydroxy-3-methoxyphenyl	4-Nitrophenyl	25	184	$C_{22}H_{18}BrN_3O_7$	8.13	8.22
8.	4-Hydroxy-3-methoxyphenyl	2,4-Dinitrophenyl	30	177	$C_{22}H_{17}BrN_4O_9$	9.98	9.85
9.	4-Hydroxy-3-methoxyphenyl	Thiosemicarbazido	30	230	$C_{17}H_{16}BrN_3O_5S$	9.25	9.18
10.	4-Hydroxy-3-methoxyphenyl	Semicarbazido	25	195	$C_{17}H_{16}BrN_3O_6$	9.58	9.52
11.	2-Hydroxyphenyl	Phenyl	30	242	$C_{21}H_{17}BrN_2O_4$	6.35	6.22
12.	2-Hydroxyphenyl	4-Nitrophenyl	35	174	$C_{21}H_{16}BrN_3O_6$	8.64	8.58
13.	2-Hydroxyphenyl	2,4-Dinitrophenyl	35	220	$C_{21}H_{15}BrN_4O_8$	10.54	10.40
14.	2-Hydroxyphenyl	Thiosemicarbazido	25	182	$C_{16}H_{14}BrN_3O_4S$	9.90	9.98
15.	2-Hydroxyphenyl	Semicarbazido	25	190	$C_{16}H_{14}BrN_3O_5$	10.29	10.18

* The carbon and hydrogen analysis of III are also found to be within ±0.4% of theoretical values.

DMSO-d_6 exhibited signals at τ 2.70(s, 5, C_5-ArH), 3.14(m, 5, N_1-ArH) and 7.36(s, 3, CH_3). The most convincing proof of pyrazoline structure is the absorption due to one proton at C_5 (suppose H_a) and two at C_4(H_b and H_c). The peaks due to these protons appear as an ABX system as in styrene oxide[4] wherein each proton shows a quartet due to coupling with each other and signals due to them are centered at 4.70 (H_a), J_{ab}=7 cps, 6.75 (H_b), J_{ac}=12 cps and 5.90 (H_c), J_{bc}=19 cps. A broad signal at 1.60 can safely be assigned to hydroxyl proton of pyran ring.

Experimental

All melting points reported are uncorrected. IR spectra were taken on a Beckman IR-20 instrument. The NMR were run on a Varian A-60 spectrometer using tetramethylsilane as the internal standard, chemical shifts are expressed in τ.

5-Bromodehydroacetic acid was prepared by treating anhydrous dehydroacetic acid in chloroform with 2.5 equiv. of bromine containing 1 mole % iodine[5].

3-Cinnamoyl-5-bromo-4-hydroxy-6-methyl-2H-pyran-2-one(II_1) :

A mixture of I (5.0g, 0.02 mole), benzaldehyde (2.2 g, 0.02 mole), chloroform (40 ml) and piperidine (2 ml) was refluxed for 4 hr, concentrated under *vacuuo* and the residue is crystallized from ethanol to give II_1. (Yield : 2.6 g, 54%) ; m.p. 130° ; IR (KBr) : 1700 (lactone), 1600(C=C) and 1000(C–O–C) cm^{-1} ; Anal. Found : C, 53.64 ; H, 3.15 ; $C_{15}H_{11}BrO_4$ requires C, 53.73 ; H, 3.23%.

1,5-Diphenyl-3-(5-bromo-4-hydroxy-6-methyl-2H-pyran-2-one-3-yl)-2-pyrazoline(III_1) :

II_1, (4.70 g, 0.02 mole), phenylhydrazine (2.2 g, 0.02 mole) were refluxed in ethanol (40 ml) and acetic acid (4 ml) for 2 hr, cooled and the product which separated out was filtered and crystallised from ethanol. (Yield : 2.0 g, 30%) ; m.p.150°d ; IR(KBr) : 1700 (lactone) ; 1600(C=C) ; and 1000 (C–O–C) cm^{-1}. NMR(DMSO d_6) : 2.70(s,5, C_5–ArH) ; 3.14(m, 5,N_1–ArH) ; 7.36(s, 3,CH_3) ; 4.70(dd, 1,H_a, J_{ab}=7 cps) ; 6.75(dd, 7, H_6, J_{ac}=12 cps) 5.90 (dd, 1, H_c, J_{bc}=19 cps) and 1.60 (s, 1, OH). Anal. Found : N, 6.48 ; $C_{21}H_{17}BrN_2O_3$ requires N, 6.58%.

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