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NOTE

Synthesis of Bis-Isoxazoles

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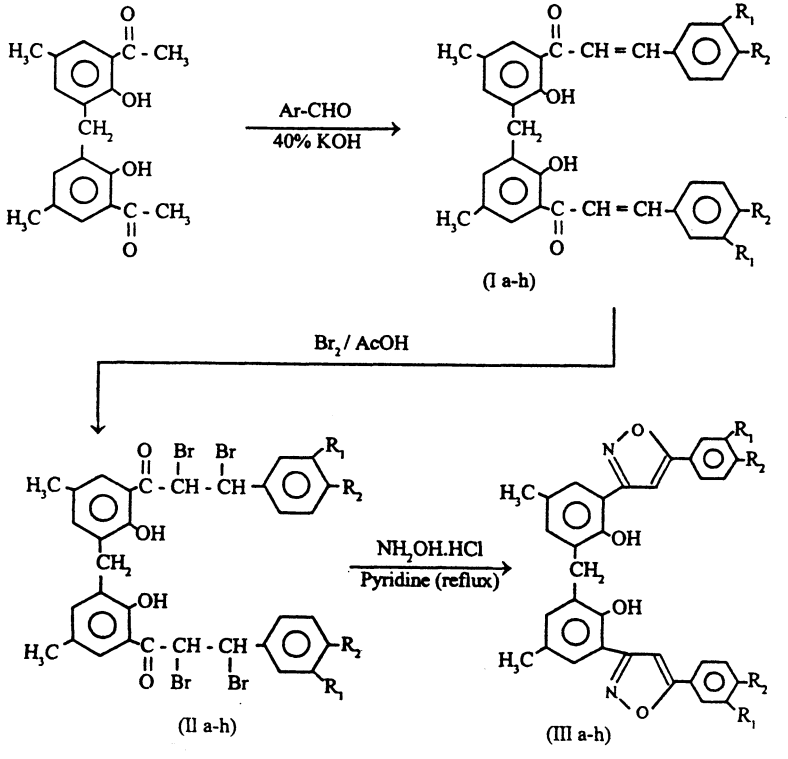
Bis-isoxazoles **(III)** have been synthesised by the reaction of bis-chalcone dibromides **(II)** with hydroxylamine hydrochloride in pyridine medium. Structures of these compounds have been established by chemical properties, elemental analysis and spectral analysis (*viz.*, IR and NMR).

Bis-isoxazoles are used in the synthesis of insecticides[1] and acaracides[1]. They are also being used in the synthesis of pharmaceuticals[2] and herbicides[3]. Bis-isoxazoles act as lipooxygenase inhibitors[4], anti-inflammatory agents[5], analgesics[5] and antipyretics[5]. Bis-isoxazoles are widely used as potential antifeedants[6] and whitening agents[7]. They are also used as oral anti-diabetics[8]. Literature survey shows that the synthesis of bis-isoxazoles from bis-chalcone dibromides has not so far been reported. It was therefore thought of interest to synthesise bis-isoxazoles.

SCHEME-I



The present work deals with the synthesis of 1,1-bis-{2-hydroxy-3-[5′-aryl-isoxazol-3-yl]-5-methyl phenyl} methane **(IIIa–h)** from 1,1-bis-{2-hydroxy-3-[2,3-dibromo-3-phenyl propan-1-one]-5-methyl phenyl} methane**(IIa–h)** using pyridine as a medium.

Melting points are uncorrected. IR spectra were recorded on Perkin-Elmer 577 (4000–500 cm^{-1}). NMR spectra were recorded on Brucker AC300 NMR spectrometer at 300 MHz in DMSO. Purity of compounds was checked by TLC.

Preparation of 1,1-Bis-{2-hydroxy-3-[5′-aryl-isoxazol-3-yl]-5-methyl phenyl} methane(III a-h)

1,1-Bis-{2 - hydroxy - 3 - [2,3 - dibromo - 3 - phenyl propan-1-one] - 5 - methyl phenyl} methane**(IIa–h)** (0.01 M) was refluxed with hydroxylamine hydrochloride (0.04 M) in pyridine medium (20 mL) for about 5 h. Reaction mixture was cooled, diluted with water and acidified with dilute HCl. The solid product obtained was filtered and crystallised from ethanol and acetic acid (Scheme-I).

TABLE-1
PHYSICAL CHARACTERIZATION DATA OF BIS-CHALCONES (I a–h)

Compound	R_1	R_2	Yield (%)	m.p. (°C)	m.f.
Ia	H	H	90	215	$C_{33}H_{28}O_4$
Ib	H	OCH_3	90	196	$C_{35}H_{32}O_6$
Ic	OCH_3	OH	95	156	$C_{35}H_{32}O_8$
Id	H	NO_2	90	> 270	$C_{33}H_{26}N_2O_8$
Ie	OCH_3	H	90	222	$C_{35}H_{32}O_6$
If*	H	OH	85	139	$C_{33}H_{28}O_6$
Ig*	H	$N(CH_3)_2$	80	128	$C_{37}H_{38}N_2O_4$
Ih*	OCH_3	OCH_3	80	168	$C_{37}H_{36}O_8$

Melting Points of **a** to **e** were tallied with authentic samples[9].

*New bis-chalcones.

TABLE-2
PHYSICAL CHARACTERIZATION DATA OF BIS-CHALCONE DIBROMIDES (II a–h)

Compound	R_1	R_2	Yield (%)	m.p. (°C)	m.f.
IIa	H	H	90	197	$C_{33}H_{28}O_4Br_4$
IIb	H	OCH_3	90	232	$C_{35}H_{32}O_6Br_4$
IIc	OCH_3	OH	95	180	$C_{35}H_{32}O_8Br_4$
IId	H	NO_2	90	>270	$C_{33}H_{26}N_2O_8Br_4$
IIe	OCH_3	H	90	236	$C_{35}H_{32}O_6Br_4$
IIf*	H	OH	85	194	$C_{33}H_{28}O_6Br_4$
IIg*	H	$N(CH_3)_2$	80	166	$C_{37}H_{38}N_2O_4Br_4$
IIh*	OCH_3	OCH_3	85	220	$C_{37}H_{36}O_8Br_4$

Melting Points of **a** to **e** were tallied with authentic samples[9].

*New bis-chalcone dibromides.

TABLE-3
PHYSICAL CHARACTERIZATION DATA OF BIS-ISOXAZOLES (**III a–h**)

Compound	R_1	R_2	Yield (%)	m.p. (°C)	m.f.	N% Found (Calcd.)
IIIa	H	H	60	268	$C_{33}H_{28}N_2O_4$	5.39 (5.42)
IIIb	H	OCH_3	75	242	$C_{35}H_{32}N_2O_6$	4.72 (4.86)
IIIc	OCH_3	OH	80	270	$C_{35}H_{32}N_2O_8$	4.53 (4.60)
IIId	H	NO_2	85	> 270	$C_{33}H_{26}N_4O_8$	9.19 (9.24)
IIIe	OCH_3	H	70	249	$C_{35}H_{32}N_2O_6$	4.72 (4.86)
IIIf	H	OH	70	257	$C_{33}H_{28}N_2O_6$	4.98 (5.10)
IIIg	H	$N(CH_3)_2$	60	251	$C_{37}H_{38}N_4O_4$	8.87 (9.30)
IIIh	OCH_3	OCH_3	75	253	$C_{37}H_{36}N_2O_8$	4.31 (4.40)

Spectral interpretation ν of IIIa–h

IR (ν_{max}): 3396 cm^{-1} ν(—OH); 1610 cm^{-1} ν(C=N); 1250 cm^{-1} ν(C—O); 1800–1500 cm^{-1} ν(C=C); 1467 cm^{-1} ν(Ar—H).

NMR: δ 2.2 (S, 6H, 2-CH_3); δ 2.6 (S, 6H, 2-OCH_3); δ 3.4 (S, 2H, -CH_2) δ 5.4 (S, 4H, 4-OH); δ 3.9 (S, 2H, 2-CH); δ 6.7–7.7 (m, 10H, Ar—H).

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