

## NOTE

**Synthesis of Bis-Isoxazolines**

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Bis-isoxazolines (II) have been synthesised by the condensation of bis-chalcones (I) 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-isoxazolines have been characterised by a number of different activities. In the present work we report the reaction of bis-ketones with various substituted aromatic aldehydes to yield the corresponding bis-chalcones (Ia–h) which on treatment with hydroxylamine hydrochloride in pyridine medium give the corresponding bis-isoxazolines (IIa–h). Bis-isoxazolines were first synthesized as spiro bis-(isoxazoline) derivatives which serve as asymmetric ligands.<sup>1</sup> Isoxazolines are used as intermediates for the synthesis of anti-inflammatory agents<sup>2</sup>, analgesics<sup>2</sup> and antipyretics<sup>2</sup>. Synthesis of bi-hetero aromatic compounds is reported<sup>3</sup> *via* the 2-isoxazoline route. 3,5-Bis-(4-chlorophenyl) isoxazoline is used in sensitized photo reactions<sup>4</sup>. 2-(2,4-Dichlorophenyl methyl)-3-methyl isoxazolin-5-one is used as antiobesity agent<sup>5</sup>. Isoxazolines also serve as biologically active agents<sup>6</sup> and also exhibit antibacterial activity<sup>7</sup>. Literature survey reveals that the synthesized bis-isoxazolines from bis-chalcones have not been so far reported. It was therefore thought of interest to synthesize the title compounds.

Melting points were taken in open capillaries on 'precision melting point apparatus' and are uncorrected. IR spectra (KBr) were recorded on Perkin-Elmer 577 (4000–500 cm<sup>-1</sup>) and NMR (DMSO-d<sub>6</sub>) spectra were recorded on Bruker AC 300 NMR spectrometer at 300 MHz using TMS as an internal standard. Elemental analysis was carried out on Perkin-Elmer CHN 240A analyser and all compounds gave satisfactory C, H and N analysis. Purity of compounds was detected by TLC using CCl<sub>4</sub>-ethyl acetate (9 : 1) as a solvent.

**Preparation of 1,1-bis-{2-hydroxy-3-[5'-aryl-isoxazolin-3'-yl]-5-methyl phenyl} methane (IIa–h)**

1,1-Bis-{2-hydroxy-3-[3-phenyl-prop-2-en-1-one]-5-methyl phenyl} methane (Ia–h) (0.01 M) were refluxed with hydroxylamine hydrochloride (0.04 M) in pyridine (20 mL) for 5 h. The 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 mixture.

TABLE-1  
PHYSICAL CHARACTERISATION DATA OF BIS-CHALCONES (Ia-h)

Compound	R <sub>1</sub>	R <sub>2</sub>	Yield (%)	m.p. (°C)	m.f.
Ia	H	H	90	215–217	C <sub>33</sub> H <sub>28</sub> O <sub>4</sub>
Ib	H	OCH <sub>3</sub>	90	196–198	C <sub>35</sub> H <sub>32</sub> O <sub>6</sub>
Ic	OCH <sub>3</sub>	OH	95	156†	C <sub>35</sub> H <sub>32</sub> O <sub>8</sub>
Id	H	NO <sub>2</sub>	90	> 270	C <sub>33</sub> H <sub>26</sub> N <sub>2</sub> O <sub>8</sub>
Ie	OCH <sub>3</sub>	H	90	222–224	C <sub>35</sub> H <sub>32</sub> O <sub>6</sub>
If*	H	OH	85	139†	C <sub>33</sub> H <sub>28</sub> O <sub>6</sub>
Ig*	H	N(CH <sub>3</sub> ) <sub>2</sub>	80	128†	C <sub>37</sub> H <sub>38</sub> N <sub>2</sub> O <sub>4</sub>
Ih*	OCH <sub>3</sub>	OCH <sub>3</sub>	80	168†	C <sub>37</sub> H <sub>36</sub> O <sub>8</sub>

Melting points of a to e were tallied with authentic samples<sup>8</sup>.

\*New bis-chalcones. †Sharp melting points.

TABLE-2  
PHYSICAL CHARACTERISATION DATA OF BIS-ISOXAZOLINES (IIa-h)

Compound	R <sub>1</sub>	R <sub>2</sub>	Yield (%)	m.p. (°C)	m.f.	N % Found (Calcd.)
IIa	H	H	65	234–235	C <sub>33</sub> H <sub>30</sub> O <sub>4</sub> N <sub>2</sub>	5.23 (5.40)
IIb	H	OCH <sub>3</sub>	70	245–246	C <sub>35</sub> H <sub>34</sub> O <sub>6</sub> N <sub>2</sub>	4.40 (4.84)
IIc	OCH <sub>3</sub>	OH	70	274*	C <sub>35</sub> H <sub>34</sub> O <sub>8</sub> N <sub>2</sub>	8.89 (9.18)
IId	H	NO <sub>2</sub>	75	> 270	C <sub>33</sub> H <sub>28</sub> O <sub>8</sub> N <sub>4</sub>	8.93 (9.21)
IIe	OCH <sub>3</sub>	H	70	268*	C <sub>35</sub> H <sub>34</sub> O <sub>6</sub> N <sub>2</sub>	4.40 (4.84)
IIf	H	OH	80	276*	C <sub>33</sub> H <sub>30</sub> O <sub>6</sub> N <sub>2</sub>	4.94 (5.09)
IIg	H	N(CH <sub>3</sub> ) <sub>2</sub>	60	228–230	C <sub>37</sub> H <sub>40</sub> O <sub>4</sub> N <sub>4</sub>	9.01 (9.27)
IIh	OCH <sub>3</sub>	OCH <sub>3</sub>	75	229*	C <sub>37</sub> H <sub>38</sub> O <sub>8</sub> N <sub>2</sub>	4.10 (4.38)

\*Sharp melting points.

Structure of IIc was established from its spectra.

IR spectra:

IIc: 3396 cm<sup>-1</sup> ν(phenolic —OH); 1610 cm<sup>-1</sup> ν(C=N); 1250 cm<sup>-1</sup> ν(C—O); 1466 cm<sup>-1</sup> ν(Ar—H).

NMR spectra:

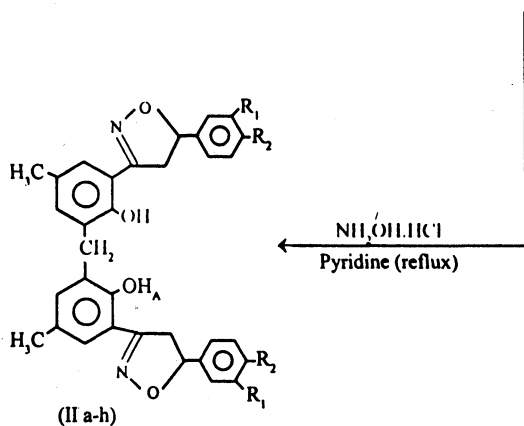
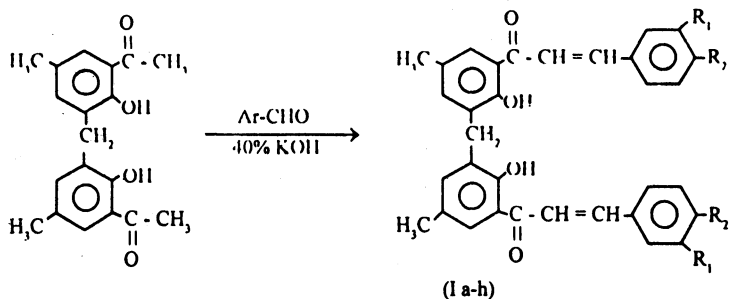
IIc: δ (DMSO-d<sub>6</sub>); δ 2.35 (6H, S, 2Ar—CH<sub>3</sub>); δ 2.9 (6H, S, 2Ar—OCH<sub>3</sub>);

δ 4.1 (2H, S, Ar—CH<sub>2</sub>—Ar); δ 6.9 (4H, S, 2—C(=O)—CH<sub>2</sub>— of isoxazoline);

δ 7.1 (2H, S, —CH—O— of isoxazoline); δ 7.5 (10 H, S, Ar—H);

δ 10.95 (2H, S, 2Ar—OH<sub>A</sub>); δ 11.91 [2H, S, 2Ar—OH<sub>B</sub> (R<sub>2</sub>=OH<sub>B</sub>)]

## SCHEME



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