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Synthesis of 2,4,5-Trisubstituted Oxazoles and a Study of their Fluorescent Properties

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ABSTRACT

The synthesis of 2,4,5-trisubstituted oxazoles was achieved by condensation of arylcyanohydrins (prepared in situ*) with arylcarboxylic acid chlorides, treatment of cyanohydrincarboxylic acid esters thus formed with araldehyde in one pot using phase-transfer catalysis and cyclization of the resulting α-aroylarmethyl-α-arylketones with ammonium acetate or urea in boiling acetic acid. The fluorescent properties of 2,4,5-trisubstituted oxazoles were studied. Some of these compounds when applied on polyester fibres as fluorescent brighteners gave excellent results.*

1 INTRODUCTION

The oxazole heterocycle has been extensively used in the synthesis of fluorescent brighteners applicable to polyester fibres.[1–6] In the present paper, we report the synthesis of a variety of 2,4,5-trisubstituted oxazoles by a method involving application of phase-transfer catalysis.

2 RESULTS AND DISCUSSION

Greene[7] had reported the synthesis of benzoylfuroin in two steps, involving the condensation of furfuraldehyde, benzoyl chloride and potassium

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cyanide with the formation of an intermediate benzoylfurfuraldehyde-cyanohydrin which was further condensed with a second mole of furfuraldehyde in boiling ethanolic sodium ethoxide.

The application of phase-transfer catalysts in the formation of cyanohydrincarboxylic acid esters from aldehyde, sodium cyanide and carboxylic acid chloride has been reported.[8]

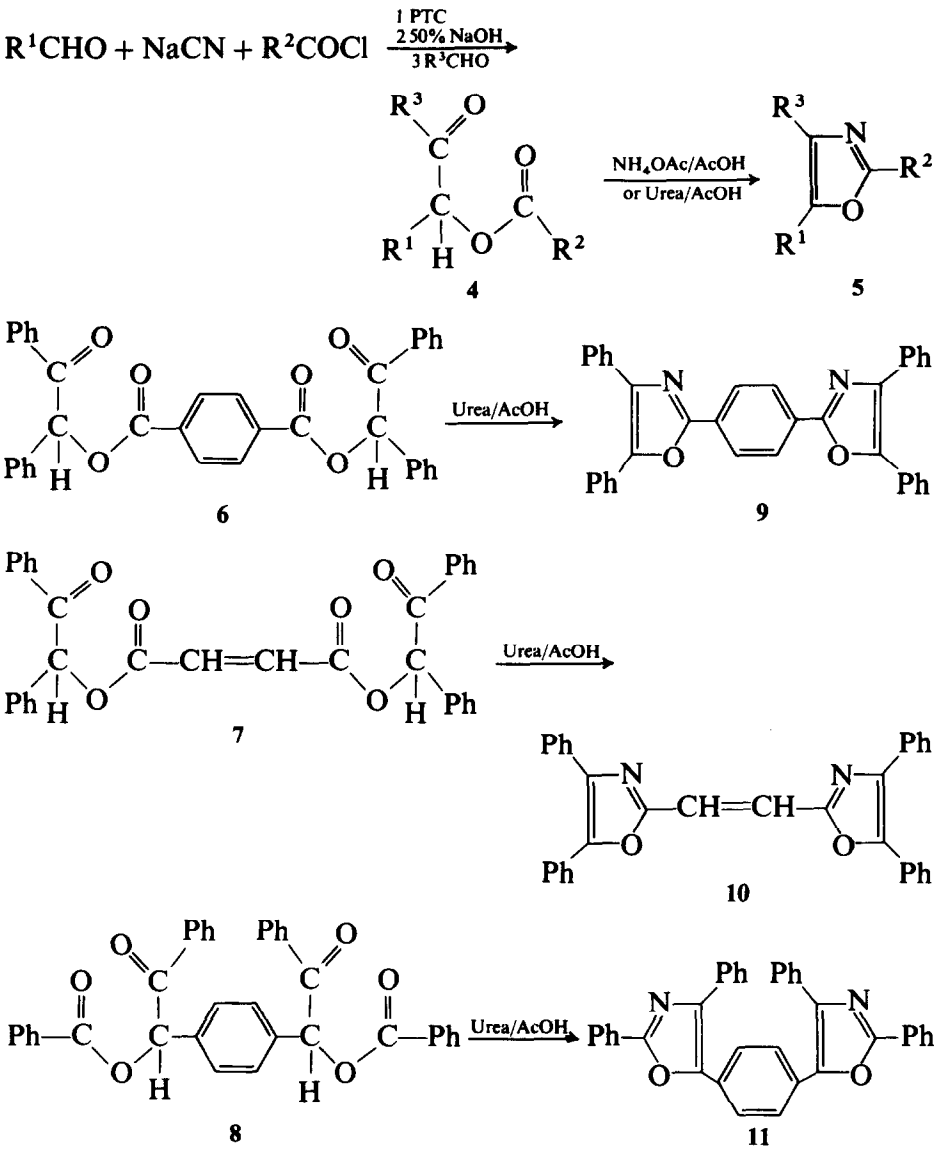
With a view to developing 2,4,5-trisubstituted oxazoles, we investigated the synthesis of α-aroylarmethyl-α-arylketones by the application of phase-transfer catalysis. A one-pot method involving phase-transfer catalysis was developed and was used to synthesize a variety of these compounds by condensation of araldehyde, sodium cyanide and arylcarboxylic acid chloride, followed by the treatment of the same or different araldehyde without isolation of the intermediate cyanohydrins and cyanohydrin-carboxylic acid esters. The method finds general application to the synthesis of α-aroylarmethyl-α-arylketones and has advantages in that it is a simple technique, resulting in good yields of the products in a one-pot synthesis at convenient temperatures. It also avoids the requirement for completely anhydrous conditions during the synthesis. Amongst various phase-transfer catalysts examined, triethylbenzylammonium chloride (TEBA) was found to be most suitable.

The various α-aroylarmethyl-α-arylketones (**4a–4e**, **6**, **7** and **8**) were obtained in good yields (53–70%) (Scheme 1). In the isolation of the compounds, the products obtained after neutralizing the reaction mixture were oily because of the presence of residual traces of araldehyde. The products were purified by column chromatography on neutral silica using *n*-hexane as eluant and this yielded solid materials which were further purified by recrystallization.

The substituted α-aroylarmethyl-α-arylketones thus prepared were cyclized to 2,4,5-trisubstituted oxazoles following Davidson's method,[9] involving treatment with ammonium acetate in boiling glacial acetic acid, or following Backeberg's method),[10] involving treatment with urea in boiling glacial acetic acid.

The 2,4,5-trisubstituted oxazoles (**5a–5e**, **9**, **10** and **11**) were obtained in good yields (60–85%) and were purified by column chromatography and recrystallization of the resulting solids from DMF.

The 2,4,5-trisubstituted oxazoles were pale yellow compounds and exhibited fluorescence properties in daylight in DMF solution. Compounds **5c** and **5e** showed violet fluorescence, **5a**, **5b**, **5d** and **11** showed blue fluorescence whereas **9** and **10** showed greenish-blue fluorescence in daylight. The absorption maxima and fluorescence emission maxima are given in Table 1. Absorption maxima varied from 293 to 345 nm and fluorescence maxima from 414 to 458 nm.



		R^1	R^2	R^3
4a	**5a**	Ph	Ph	Ph
4b	**5b**	Ph	Ph	—CH=CH—Ph
4c	**5c**	—CH=CH—Ph	Ph	Ph
4d	**5d**	Ph	—CH=CH—Ph	Ph
4e	**5e**	—C_6H_4Cl	Ph	Ph

Scheme 1.

TABLE 1
Absorption and Fluorescence Emission Spectra (in DMF) of 2,4,5-Trisubstituted Oxazoles

Compound	*Absorption maximum (nm)*	*Fluorescence emission maximum (nm)*	*log E*	*Quantum yield (mg)*
5a	340	433	4·40	0·76
5b	293	430	3·58	11·11
5c	337	435	4·41	0·71
5d	334	416	4·42	0·85
5e	316	414	4·53	2·70
9	345	442	4·41	0·78
10	315	449	3·89	4·06
11	313	440	4·30	3·36
Standard[a]	376	458	4·40	1·68

[a] 7-*N*,*N*-Diethylamino-4-methylcoumarin was used as standard fluorescent compound.

The 2,4,5-trisubstituted oxazoles were applied on polyester fibres and the whitening effects of compounds **5a**, **5c** and **5d** were found to be excellent (grade 3), compounds **5e** and **9** gave moderate whitening effects (grade 1), whereas compounds **5b**, **10** and **11** showed no whitening effect, but a yellowing of the polyester fibre. It was of interest to note that of the isomeric 2,4,5-(monostyryldiphenyl)oxazoles (**5b**, **5c** and **5d**), 2-styryl-4,5-diphenyloxazole (**5c**) and 2,4-diphenyl-5-styryloxazole (**5d**) gave excellent whitening effects, whereas 2,5-diphenyl-4-styryloxazole (**5b**) did not give any whitening effect on polyester fibres.

3 EXPERIMENTAL

All the melting points are uncorrected and are in °C. Visible and emission spectra in DMF solution were recorded on a Beckman Model 25 spectrophotometer and Aminco Bowman spectrophotofluorimeter, respectively. Infrared spectra (IR) were recorded on a Perkin–Elmer Model 397 spectrometer.

3.1 Preparation of starting materials

Cinnamic acid chloride,[11] fumaric acid chloride[12] and terephthaloyl chloride[13] were prepared by reported methods.

3.2 α-Benzoylbenzyl-α-phenyl ketone (desyl benzoate) (4a)

To a mixture of benzoyl chloride (1·41 g, 0·01 mol), TEBA (2·23 g, 0·012 mol), sodium cyanide (0·49 g, 0·01 mol), water (2 ml) and methylene chloride (10 ml) was added, with good stirring, over 30 min, benzaldehyde (1·06 g, 0·01 mol) in methylene chloride (10 ml). Stirring was continued at 40°C until reaction was complete (3 h, monitored by TLC). Aqueous sodium hydroxide solution (50%, 8 ml) was then added and the mixture was stirred for 0·5 h. Benzaldehyde (1·06 g, 0·01 mol) in methylene chloride (20 ml) was slowly added to the above mixture with efficient stirring at 40°C. The reaction mixture was then gently refluxed for 3 h until the reaction was complete. The resulting mixture was carefully acidified with dilute acetic acid (10%) and the organic layer was separated from the aqueous layer and washed with water. The organic layer was dried over anhydrous sodium acetate, methylene chloride was removed under vacuum and the resulting oil was passed over a column packed with neutral silica using *n*-hexane as eluant. The resultant solid product was recrystallized from methanol to give 2·2 g (70%) **4a** as colourless needles, m.p. 122–123°C (Lit.[14] m.p. 122·5°C). Calculated for $C_{21}H_{16}O_3$: C, 79·75, H, 5·1. Found: C, 79·7; H, 5·1%.

3.3 α-Benzoylbenzyl-α-(2-styryl)ketone (4b)

This compound was synthesized as described above for 4*a* except that in place of the benzaldehyde used for the second condensation stage, cinnamaldehyde (1·32 g, 0·01 mol) in methylene chloride (20 ml) was used (5 h for the completion of the reaction. The product was isolated as for **4a** and was recrystallized from methanol in colourless needles (65%), m.p. 115–116°C. Calculated for: $C_{23}H_{18}O_3$: C, 80·7; H, 5·3. Found: C, 80·7; H, 5·2%.

3.4 α-Benzoylcinnamyl-α-phenylketone (4c)

The procedure for **4a** was followed, but using, instead of benzaldehyde in the first condensation stage, cinnamaldehyde (1·32 g, 0·01 mol) in methylene chloride (20 ml). The completion of reactions at the first and second stages required 5 h and 4 h, respectively. The product after isolation as described for **4a** was recrystallized from methanol as colourless needles (58%), m.p. 129–130°C. Calculated for $C_{23}H_{18}O_3$: C, 80·7; H, 5·3. Found: C, 80·7; H, 5·2%.

3.5 α-Cinnamoylbenzyl-α-phenylketone (4d)

The procedure for **4a** was used, except that in place of benzoyl chloride, cinnamoyl chloride (1·67 g, 0·01 mol) was used. Completion of the reactions

for the two stages required 3 h and 4 h respectively. The product was isolated in the manner described for **4a** and was recrystallized for methanol as colourless needles (73%), m.p. 98–99°C. Calculated for $C_{23}H_{18}O_3$: C, 80·7; H, 5·3. Found: C, 80·8; H, 5·2%.

3.6 α-Benzoyl(4-chlorobenzyl)-α-phenylketone (4e)

The procedure described above for **4a** was followed except that in place of benzaldehyde in the first condensation stage, 4-chlorobenzaldehyde (1·41 g, 0·01 mol) in methylene chloride (10 ml) was used. Completion of the reactions required 4 h at each stage. The product isolated in the usual manner was recrystallized from methanol as colourless needles (57%), m.p. 97–98°C. Calculated for $C_{21}H_{15}ClO_3$: C, 71·9; H, 4·3; Cl, 10·1. Found: C, 72·1; H, 4·2; Cl, 10·0%.

3.7 α,α′-Terephthaloyl bis(benzyl-α-phenylketone) (6)

The procedure described for **4a** was followed except that in place of benzoyl chloride, terephthaloyl chloride (1·02 g, 0·005 mol) was used. Completion of reaction required 5 h for each stage. After isolation of the product, it was recrystallized from methanol as colourless crystals (70%), m.p. 125–126°C. Calculated for $C_{36}H_{26}O_6$: C, 78·0; H, 4·7. Found: C, 78·15; H, 4·7%.

3.8 α,α′Fumaroyl bis(benzyl-α-phenylketone) (7)

The procedure described for **4a** was followed except that fumaric acid chloride (0·77 g, 0·005 mol) in place of benzoyl chloride was used. Completion of the reaction for the two stages required 5 h and 4 h respectively. The product was recrystallized from methanol as colourless crystals (53%), m.p. 109–110°C. Calculated for $C_{32}H_{24}O_6$: C, 76·2; H, 4·8. Found: C, 76·2; H, 4·7%.

3.9 α,α′-Dibenzoyl(4-xylyl)-α,α′-bis(phenylketone) (8)

The procedure described for **4a** was followed except that in place of benzaldehyde in the first condensation stage, terephthalaldehyde (0·67 g, 0·005 mol) in methylene chloride (20 ml) was used. Completion of the reactions required 5 h and 4 h respectively. The product was recrystallized from methanol as colourless crystals (62%), m.p. 99–100°C. Calculated for $C_{36}H_{26}O_6$: C, 78·0; H, 4·7. Found: C, 78·3; H, 4·7%.

3.10 2,4,5-Triphenyloxazole (5a)

A mixture of α-benzoylbenzyl-α-phenylketone (desylbenzoate (**4a**) (1·58 g, 0·005 mol) and ammonium acetate (2·31 g, 0·03 mol) in glacial acetic acid (10 ml) was refluxed for 4 h. The reaction mixture was cooled, poured onto crushed ice (about 100 g) and the separated solid was filtered, washed with water and dried. The crude 2,4,5-triphenyloxazole was passed over a column of neutral silica using *n*-hexane as eluant and the resultant solid product was recrystallized from DMF to yield pale yellow crystals, 1·26 g (85%), m.p. 114–115°C (lit.[15] m.p. 114°C). Calculated for $C_{21}H_{15}NO$: C, 84·8; H, 5·05; N, 4·7. Found: C, 84·75; H, 5·1; N, 4·65%.

3.11 2,5-Diphenyl-4-(2-styryl)oxazole (5b)

This was synthesized from **4b** as described for **5a** and was recrystallized from DMF as pale yellow crystals (60%), m.p. 118–119°C (lit.[16] m.p. 119°C). Calculated for $C_{23}H_{17}NO$: C, 85·45; H, 5·3; N, 4·3. Found: C, 85·4; H, 5·2; N, 4·25%.

3.12 2,4-Diphenyl-5-(2-styryl)oxazole (5c)

α-Benzoylcinnamoyl-α-phenylketone (**4c**) (1·71 g, 0·005 mol) and urea (3·0 g, 0·05 mol) were fused at 170–180°C for 1 h. The reaction mixture was cooled, glacial acetic acid (10 ml) was added and the mixture was refluxed for 1 h. The hot solution was filtered, cooled to room temperature and poured onto crushed ice (about 100 g). The solid was filtered, washed with water, dried and purified by column chromatography on neutral silica using *n*-hexane as eluant. The product was recrystallized from DMF as pale yellow crystals, 1·15 g (71%), m.p. 115–116°C. Calculated for $C_{23}H_{17}NO$: C, 85·45; H, 5·3; N, 4·3. Found: C, 85·4; H, 5·2; N, 4·3%.

The other 2,4,5-trisubstituted oxazoles (**5d**, **5e**, **9**, **10** and **11**) were synthesized in the manner described for **5c**.

3.13 4,5-Diphenyl-2-(2-styryl)oxazole (5d)

Recrystallized from DMF to give pale yellow crystals (69%), m.p. 124–126°C (lit.[17,18] m.p. 118°C). Calculated for $C_{23}H_{17}NO$: C, 85·45; H, 5·3; N, 4·3. Found: C, 85·4; H, 5·1; N, 4·1%.

3.14 2,4-Diphenyl-5-(4-chlorophenyl)oxazole (5e)

Recrystallized from DMF as pale yellow crystals (65%), m.p. 111–112°C. Calculated for $C_{21}H_{14}ClNO$: C, 76·0; H, 4·2; N, 4·2; Cl, 10·7. Found: C, 76·1; H, 4·1; N, 4·2; Cl, 10·7%.

3.15 1,4-Bis(4,5-diphenyloxazol-2-yl)benzene (9)

Recrystallized from DMF as pale yellow crystals (7·1%), m.p. 260–261°C (lit.[17,18] m.p. 260°C). Calculated for $C_{36}H_{24}N_2O_2$: C, 83·7; H, 4·65; N, 5·4. Found: C, 83·5; H, 4·5; N, 5·3%.

3.16 1,2-Bis(4,5-diphenyloxazol-2-yl)ethylene (10)

Recrystallized from DMF as pale yellow crystals (63%), m.p. 288–290°C. Calculated for $C_{23}H_{22}N_2O_2$: C, 82·4, H, 4·7; N, 6·0. Found: C, 82·5; H, 4·4; N, 5·9%.

3.17 1,4-Bis(2,4-diphenyloxazol-2-yl)benzene (11)

Recrystallized from DMF as pale yellow crystals (68·5%), m.p. 132–135°C. Calculated for $C_{36}H_{24}N_2O_2$: C, 83·7; H, 4·65; N, 5·4. Found: C, 83·7; H, 4·4; N, 5·5%.

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