# A General Synthesis of 2,5-Diaryl-4-chloro (or Bromo)oxazoles

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Reaction between acylcyanides (ArCOCN) and aldehydes (ArCHO) in the presence of ether and hydrogen chloride (or hydrogen bromide) gives good yields of 2,5-diaryl-4-chloro (or bromo)oxazoles **(2)**.

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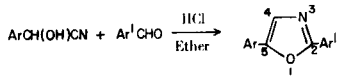
2,5-Diaryloxazoles **(1)**, especially 2,5-diphenyloxazole (PPO), are widely used as organic scintillators for measurement of soft beta activity. The Fischer synthesis (1) from the reaction between aromatic aldehyde cyanohydrins and aromatic aldehydes has been used to obtain 2,5-diaryloxazoles,



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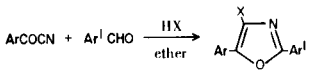
but it suffers from two defects: formation of 2,5-diaryl-4-oxazolidones as by-products, and a certain ambiguity in that the starting materials may exchange hydrogen cyanide, thus causing "scrambling" of Ar and $Ar^1$ in the product (2).

We have been interested in the preparation of substituted 2,5-diaryloxazoles as potential new scintillators, and we now report (3) that a modification of the Fischer synthesis, using an acyl cyanide instead of a cyanohydrin, affords 2,5-diaryl-4-chloro (or bromo)oxazoles **(2)**.



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X = Cl, Br

The Table gives a list of compounds **(2)** prepared by this method. The yields are generally good, except for 4-bromo-2-*p*-methoxyphenyl-5-phenyloxazole; the reaction fails completely when *p*-methoxybenzoyl cyanide is used.

The mechanism of the reaction may involve iminohalide intermediates **(3)** and **(4)** similar to those suggested by Cornforth (4) in his comments on the Fischer synthesis:

$$ArCOCN \xrightarrow{HX} ArCOC(X)=NH \quad \textbf{(3)}$$

$$\xrightarrow{Ar^1CHO} ArCOC(X)=NCH(OH)Ar^1 \quad \textbf{(4)}$$

$$\longrightarrow \textbf{(2)}$$

## EXPERIMENTAL

Benzoyl cyanide (5), *p*-nitrobenzoyl cyanide (6) and *p*-methoxybenzoyl cyanide (7) were prepared from the corresponding acyl chloride by heating with cuprous cyanide (5).

The acyl cyanide (0.1 mole), the aldehyde (0.11 mole) and dry ether (100 ml.) were mixed, cooled in an icebath and saturated with hydrogen chloride (or hydrogen bromide). The mixture was kept at 0° overnight, then poured onto crushed ice (300 g.) and extracted with more ether (200 ml.). The ether extract was washed with water, saturated sodium bisulphite solution, and water again, then dried and evaporated. The residue was recrystallised from acetone or an acetone/methanol mixture to give the final crystalline product indicated in the Table.

## REFERENCES AND NOTES

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(6) B. Flürscheim and E. L. Holmes, *J. Chem. Soc.*, 478 (1928).

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Table

Preparation of 4-Halogeno-2,5-diaryloxazoles (**2**) from Acyl Cyanides (ArCOCN) and Aldehydes ($Ar^1CHO$)

| X | Ar | $Ar^1$ | Yield % | m.p. °C | Formula | Found / Calcd. | C | H | N | Br |
|---|---|---|---|---|---|---|---|---|---|---|
| Cl | Ph | Ph | 60 | 71-72 (a) | | | | | | |
| Cl | Ph | *p*-MeOPh | 65 | 142-143 | $C_{16}H_{12}ClNO_2$ | Found | 67.43 | 4.26 | 4.70 | |
| | | | | | | Calcd. | 67.26 | 4.23 | 4.90 | |
| Cl | Ph | *p*-MePh | 66 | 97-98 | $C_{16}H_{12}ClNO$ | Found | 71.59 | 4.69 | 4.87 | |
| | | | | | | Calcd. | 71.25 | 4.48 | 5.19 | |
| Cl | Ph | *p*-$O_2$NPh | 75 | 193-195 | $C_{15}H_9ClN_2O_3$ | Found | 59.86 | 3.08 | 9.26 | |
| | | | | | | Calcd. | 59.92 | 3.02 | 9.32 | |
| Cl | Ph | *p*-HOPh | 60 | 113-114 | $C_{15}H_{10}ClNO_2$ | Found | 65.91 | 3.69 | 5.28 | |
| | | | | | | Calcd. | 66.31 | 3.71 | 5.16 | |
| Cl | Ph | *p*-EtPh | 78 | 70-71 | $C_{17}H_{14}ClNO$ | Found | 72.21 | 5.16 | 4.88 | |
| | | | | | | Calcd. | 71.96 | 4.97 | 4.93 | |
| Cl | *p*-$O_2$NPh | Ph | 50 | 178-180 | $C_{15}H_9ClN_2O_3$ | Found | 60.24 | 3.36 | 9.51 | |
| | | | | | | Calcd. | 59.92 | 3.02 | 9.32 | |
| Br | Ph | Ph | 67 | 74-75 (b) | $C_{15}H_{10}BrNO$ | Found | 60.11 | 3.48 | 4.88 | 26.80 |
| | | | | | | Calcd. | 60.02 | 3.36 | 4.67 | 26.62 |
| Br | Ph | *p*-MeOPh | 3 | 122-123 (c) | $C_{16}H_{12}BrNO_2$ | Found | 58.43 | 3.67 | 4.24 | 24.30 |
| | | | | | | Calcd. | 58.20 | 3.66 | 4.24 | 24.20 |
| Br | Ph | *p*-$O_2$NPh | 75 | 168-170 | $C_{15}H_9BrN_2O_3$ | Found | 52.50 | 3.10 | 8.06 | 23.00 |
| | | | | | | Calcd. | 52.20 | 2.63 | 8.12 | 23.15 |
| Br | *p*-$O_2$NPh | Ph | 68 | 195-196 | $C_{15}H_9BrN_2O_3$ | Found | 52.37 | 2.51 | 8.05 | |
| | | | | | | Calcd. | 52.20 | 2.63 | 8.12 | |

(a) Lit. (8) m.p. 71°. (b) Lit. (9) m.p. 66°. (c) Reaction mixture contained much unreacted starting materials; solid product separated and recrystallized from methanol.