

## REACTION OF OXAZOLINES WITH PHOSPHORUS OXYCHLORIDE

Isabelle M. Dordor and John M. Mellor\*

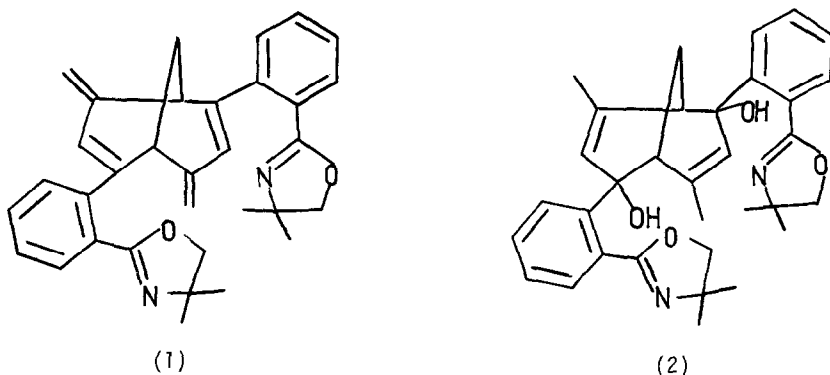
Department of Chemistry, The University, Southampton, SO9 5NH, U.K.

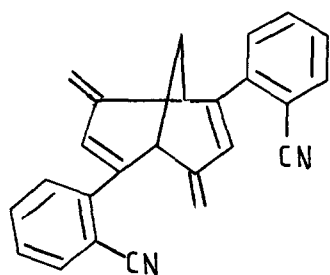
and Peter D. Kennewell,

Roussel Laboratories, Kingfisher Drive, Covingham, Swindon SN3 5BZ, U.K.

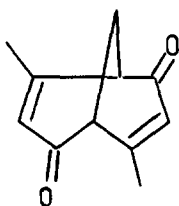
Reaction of Oxazolines with phosphorus oxychloride in pyridine gives nitriles and the value of the procedure is shown for substituted oxazolines obtained *via* addition of *ortho*-lithiated oxazolines to aldehydes and ketones.

The versatility of oxazolines<sup>1</sup> as intermediates in the synthesis of both carbocyclic and heterocyclic aromatics is well known. Formation of carbanions *ortho* to the oxazoline group proceeds readily and can be used in processes of carbon-carbon bond formation, as in the recent syntheses of milbemycin.<sup>2</sup> Stabilisation of related carbanions may alternatively be achieved by a neighbouring amide functionality,<sup>3</sup> as in the synthesis of acridones.<sup>4</sup> However, 'the use of a nitrile as an *ortho* director is limited because of its highly electrophilic character'.<sup>5</sup> We now report the direct transformation of oxazolines to nitriles by reaction with phosphorus oxychloride. The consequent possibility of formation of a carbon-carbon bond *ortho* to the nitrile function in an aromatic nitrile *via* lithiation of an oxazoline followed by subsequent transformation of the oxazoline group to a nitrile is demonstrated.

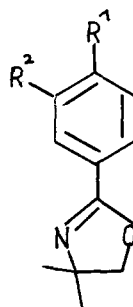




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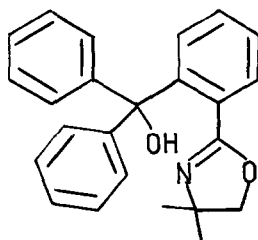


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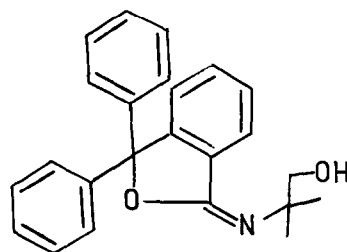
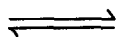
(5)  $R_1 = R_2 = H$ (6)  $R_1 = OMe; R_2 = H$ (7)  $R_1 = NO_2; R_2 = H$ 

In attempted preparation of the polyene (1) the diol (2) was reacted with phosphorus oxychloride. In addition to facile dehydration, conversion of the oxazoline functionality to a nitrile group occurred. Thus under optimum conditions (pyridine at 80°C for 14 h) the crystalline dinitrile (3) was obtained in 66% yield from the diol (2), which is easily prepared from the diketone (4)<sup>6</sup> via the lithiation procedure of an oxazoline established by Meyers.<sup>7</sup>

Although the transformation of oxazolines by ring opening to give amides<sup>8</sup> is known, the potential of a general procedure for conversion of oxazolines to nitriles has not been established. We find that reaction of (5) with phosphorus oxychloride gave benzonitrile smoothly in 80% yield and reaction was possible with other electron donating substituents present. Thus (6) gave p-methoxybenzonitrile in 63% yield. However, strongly electron withdrawing substituents prevented reaction. Thus (7) was recovered unchanged.



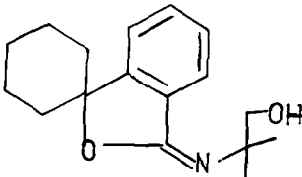
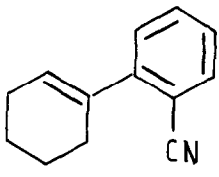
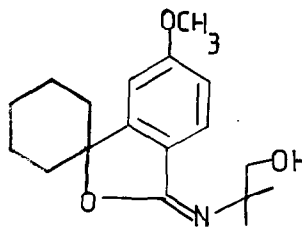
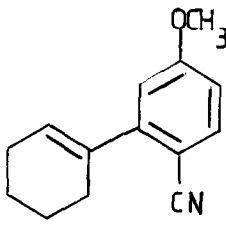
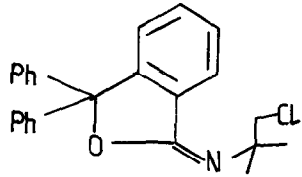
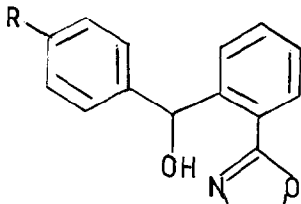
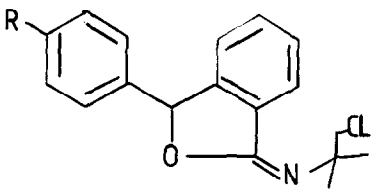
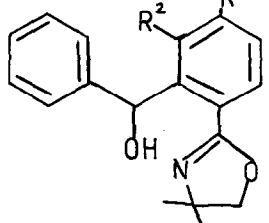
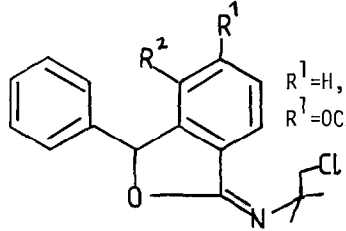
(8a)



(8b)

The utility of a procedure based on lithiation of an oxazoline and function of a carbon-carbon bond at the *ortho* site, followed by conversion of the oxazoline to a nitrile group was examined using a series of intermediates generated by reaction of the appropriate aryl lithiums with ketones and aldehydes. Synthesis of the alcohols shown in the Table by the method of Meyers<sup>9</sup> and Gschwend<sup>10</sup> via the lithiated oxazolines proceeded in ~50% yield. Each reaction can lead to a mixture of isomeric alcohols. We find that addition to benzophenone leads to both alcohols (8a) and (8b) but in all other cases the single alcohol

TABLE  
Products from Reaction with Phosphorus Oxichloride<sup>a</sup>

Reactant	Product <sup>b</sup>	Yield <sup>c</sup> %
		65 (oil)
		73 (oil)
(8a) $\rightleftharpoons$ (8b)		40
		R=H 32 R=OCH <sub>3</sub> 35
		R <sup>1</sup> =H, R <sup>2</sup> =OCH <sub>3</sub> 33 R <sup>1</sup> =OCH <sub>3</sub> , R <sup>2</sup> =H 32

a Reaction at 80°C in pyridine

b All products had satisfactory spectral and microanalytical data

c Isolated yields of crystalline products

isolated has the structure shown in the Table (established by  $^1\text{H}$  and  $^{13}\text{C}$ -n.m.r. and m.s.). However, in the subsequent reaction conditions (pyridine phosphorus oxychloride) ready equilibration of the isomeric alcohols [for example (8a) and (8b)] is to be expected.

Products of reaction of the alcohols with phosphorus oxychloride are shown in the Table. Two series of products are observed. Where dehydration of a secondary or tertiary alcohol is possible then nitriles are obtained. However, in those cases where such dehydration is not possible only cyclic ethers are obtained. Hence the synthetic strategy of use of oxazolines to afford indirectly *ortho*-substituted aryl nitriles is limited by the complication of possible ring-opening of the oxazoline. Where this is not important the strategy is effective. Further illustrative results will be published in a subsequent full paper.

#### References

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