Reaction of Oxazolines † with Phosphorus Oxychloride

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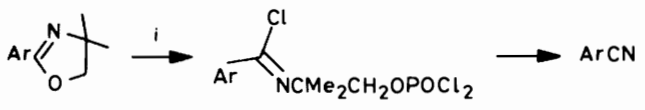
The reaction of simple aryloxazolines with phosphorus oxychloride in pyridine affords aryl nitriles. Alcohols, obtained by the reaction of *ortho*-lithiated oxazolines with ketones, under similar conditions, typically give substituted aryl nitriles. Exceptionally, further reaction can afford substituted indenone derivatives. Alcohols obtained by the reaction of *ortho*-lithiated oxazolines with aryl aldehydes react with phosphorus oxychloride in pyridine to give products by cleavage of the oxazoline ring.

The formation of carbon–carbon bonds *via ortho*-lithiation of substituted aromatic compounds is a recently developed technique now widely used in the synthesis of complex aromatic systems. Stabilisation of the intermediate organolithium compound has been achieved using a variety of *ortho*-substituents having a suitably positioned donor heteroatom. In particular, oxazolines [1,2] and proximate amide groups [2,3] have been successfully used. Although other *ortho*-substituents have been studied,[2] there is considerable interest in extending the range of possible *ortho*-substituents capable of facilitating *ortho*-lithiation procedures. *ortho*-Lithiation of nitriles has been relatively little investigated,[4] but a recent review [2] notes that 'the use of a nitrile as an *ortho* director is limited because of its highly electrophilic character'. An alternative strategy is the use of an oxazoline or amide group followed by transformation of this group into the nitrile after lithiation and introduction of the desired *ortho*-substituent. In the preceding paper [5] we have described the structure of the alcohols obtained by *ortho*-lithiation of aryloxazolines followed by reaction with aldehydes and ketones. In this paper we describe the reaction of these alcohols with phosphorus oxychloride in pyridine, conditions which in certain cases permit the transformation of oxazolines into nitriles.

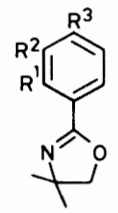
The reaction of phenyloxazoline (**1**) [5] with phosphorus oxychloride in pyridine affords benzonitrile (80% isolated yield). Similarly, the oxazoline (**2**) [5] gives *p*-methoxybenzonitrile (63% yield), but the presence of a strongly electron-withdrawing substituent prevents reaction; thus, the oxazoline (**3**) [5] is recovered unchanged from the attempted reaction with phosphorus oxychloride. The mechanism of the transformation of an oxazoline into a nitrile has not been investigated. However, it is probable that phosphorus oxychloride initially reacts with the oxazoline to afford an intermediate chloroimine which then, by fragmentation, affords the aryl nitrile (see Scheme).



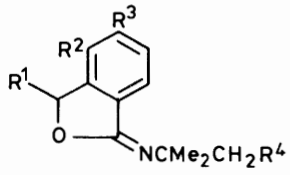
Scheme. *Reagents:* i, $POCl_3$

In the previous paper [5] we have shown that the reaction of *ortho*-lithiated oxazolines with aldehydes typically affords secondary alcohols with retention of the oxazoline moiety. The reaction of such secondary alcohols, however, does not lead to nitriles; instead the reaction of the oxazoline (**4**) with phosphorus oxychloride gives the primary chloride (**5**). The nature of the product is readily determined from microanalytical and spectroscopic data. In particular, it was distinguished from the alternative secondary chloride (**6**), retaining the oxazoline ring, by observation in the i.r. spectrum of $\nu_{max.}$(C=N) 1 685 cm^{-1}. In the mass spectrum of compound (**5**) a substantial fragmentation peak corresponding to ($M - CH_2Cl$) at *m/z* 250 accords with the proposed structure (**5**), but not that of the secondary chloride (**6**). A detailed comparison of the ^1H and ^{13}C n.m.r. spectra of (**5**) with the spectra of alcohols and oxazolines reported in the previous paper [5] support the assignment. Under similar reaction conditions the oxazolines (**7**)—(**9**) are transformed into the primary chlorides (**10**)—(**12**).

More than one possible route for the conversion of (**4**) and related oxazolines into the appropriate primary chlorides, such

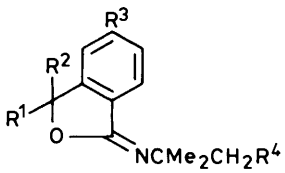


(**1**) $R^1 = R^2 = R^3 = H$
(**2**) $R^1 = R^2 = H$, $R^3 = OMe$
(**3**) $R^1 = R^2 = H$, $R^3 = NO_2$
(**4**) $R^1 = PhCHOH$, $R^2 = R^3 = H$
(**6**) $R^1 = PhCHCl$, $R^2 = R^3 = H$
(**7**) $R^1 = p\text{-}MeOC_6H_4CHOH$, $R^2 = R^3 = H$
(**8**) $R^1 = PhCHOH$, $R^2 = H$, $R^3 = OMe$
(**9**) $R^1 = PhCHOH$, $R^2 = OMe$, $R^3 = H$
(**14**) $R^1 = PhCHCl$, $R^2 = OMe$, $R^3 = H$

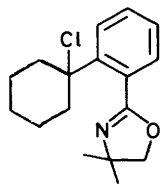


(**5**) $R^1 = Ph$, $R^2 = R^3 = H$, $R^4 = Cl$
(**10**) $R^1 = p\text{-}MeOC_6H_4$, $R^2 = R^3 = H$, $R^4 = Cl$
(**11**) $R^1 = Ph$, $R^2 = H$, $R^3 = OMe$, $R^4 = Cl$
(**12**) $R^1 = Ph$, $R^2 = OMe$, $R^3 = H$, $R^4 = Cl$
(**13**) $R^1 = Ph$, $R^2 = OMe$, $R^3 = H$, $R^4 = OH$

† The use of oxazoline, which refers to dihydro-1,3-oxazole, is not recommended by I.U.P.A.C., but is retained here for ease of comparison with the literature.



(15) $R^1, R^2 = [CH_2]_5, R^3 = H, R^4 = OH$
(16) $R^1, R^2 = [CH_2]_5, R^3 = H, R^4 = Cl$
(17) $R^1, R^2 = [CH_2]_5, R^3 = OMe, R^4 = OH$
(18) $R^1, R^2 = [CH_2]_4, R^3 = OMe, R^4 = OH$
(19) $R^1, R^2 = [CH_2]_6, R^3 = H, R^4 = OH$
(20) $R^1 = R^2 = Ph, R^3 = H, R^4 = OH$
(21) $R^1 = R^2 = Ph, R^3 = H, R^4 = Cl$
(22) $R^1, R^2 = [CH_2]_6, R^3 = H, R^4 = OTs$
(23) $R^1, R^2 = [CH_2]_6, R^3 = H, R^4 = Cl$



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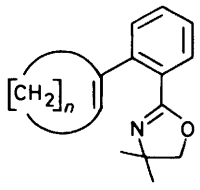
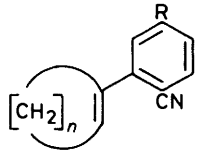
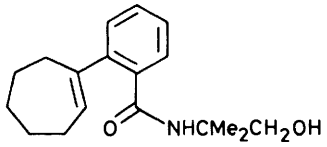


(25) $n = 4$
(26) $n = 5$



(27) $n = 4$, R = H
(28) $n = 4$, R = OMe
(29) $n = 3$, R = OMe
(30) $n = 5$, R = H



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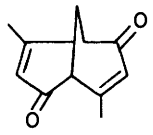

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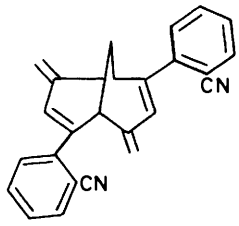

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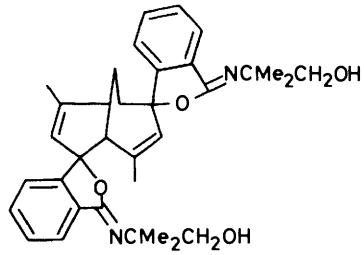

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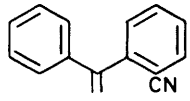

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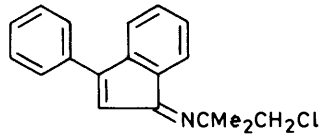

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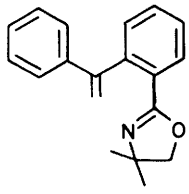

(38)

as (5), may be envisaged. We have already noted and explained [5] the ready interconversion of the isomeric alcohols (9) and (13). Such an equilibration prior to the reaction with phosphorus oxychloride might explain the preferential formation of the chloride (12) from the less hindered and more reactive primary alcohol (13). Alternatively, and more probably, the formation of a kinetically favoured chloride (14) by reaction at the reactive benzylic site might be followed by opening of the oxazoline ring with the resultant formation of the isomeric chloride (12). In such an effective equilibration of the isomeric chlorides (12) and (14), the return step of (12) ⟶ (14) is probably disfavoured on kinetic grounds. Our results do not permit a clear distinction between the possible routes to primary chlorides such as (5) and (12).

The formation of the primary alcohols by the reaction of *ortho*-lithiated oxazolines with ketones has been described in the previous paper.[5] The reaction of an alcohol such as (15) with phosphorus oxychloride can give either the primary chloride (16) or a tertiary chloride (24) with formation of an oxazoline ring. In addition, elimination from either compound (16) or (24) could lead to the oxazoline (25). We find that the reaction of primary alcohols such as (15) with phosphorus oxychloride leads directly to the formation of nitriles. Thus, compound (15) gives (27) in 65% yield, and similarly the primary alcohols (17)—(19) give the nitriles (28)—(30). Although the nature of the intermediates on the pathway between a primary alcohol such as (15) and the nitrile product (27) have not been clearly established, the initial conversion of the primary alcohol (15) into the primary chloride (16) is probable. We note that in the case of the alcohol (20), where elimination is prevented, the only product isolated from the reaction with phosphorus oxychloride is the primary chloride (21). The formation of the oxazoline (25) from (16) is readily envisaged, and support for the intermediacy of such oxazolines is found in the observation that the reaction of (19) with toluene-*p*-sulphonyl chloride gives the oxazoline (26) which, on further reaction with phosphorus oxychloride, gives the nitrile (30).

Further support for the proposed route from the primary alcohols to the nitriles is obtained by a study of the reaction of (19) with toluene-*p*-sulphonyl chloride. The reaction in pyridine at 60 °C affords the toluene-*p*-sulphonate (22) but at higher temperatures (75 °C) affords, after chromatography, the oxazoline (26) and the amide (31). These results suggest the initial formation of a toluene-*p*-sulphonate ester (22) which, at a higher temperature, can then give the oxazoline (26). In the case of the reaction with phosphorus oxychloride, the analogous conversion of the alcohol (19) into the oxazoline (26) is then followed by a more facile formation of the nitrile (30). In support of this scheme we find that the alcohol (19), on reaction with thionyl chloride, affords both the chloride and product (23) and again the oxazoline (26).

The utility of the conversion of an aryloxazoline into an *ortho*-substituted arylnitrile has been shown for a more complicated system. The reaction of the lithiated oxazoline (1)

with the diketone (**32**)[6] and treatment of the alcohol products with phosphorus oxychloride efficiently gives the crystalline dinitrile (**33**). In this case the complexity of the spectra of the poorly soluble intermediate diol makes the assignment of the structure tentative. However, the intermediacy of the diol (**34**) seems probable.

The above results indicate that in all alcohols capable of elimination to give substituted styrenes, treatment with phosphorus oxychloride affords nitriles. In contrast, where elimination to give styrenes is not possible then primary chlorides are formed, *i.e.* from those alcohols derived from the attack of metallated aryloxazolines on aryl aldehydes or on benzophenone. However, there is one interesting exception to this generalisation. The reaction of phosphorus oxychloride with the primary alcohol (**35**) affords, in addition to the expected nitrile (**36**), the chloride (**37**). We envisage that, following the formation of the oxazoline (**38**) by the route proposed above, there are subsequent competitive pathways. The nitrile (**36**) is formed by opening of the oxazoline ring and fragmentation as described above. Alternatively, electrophilic attack by the styrene moiety leads to formation of an indenone derivative (**37**).

The above results indicate that the combination of the reaction of a metallated aryloxazoline with a ketone or aldehyde followed by the reaction with phosphorus oxychloride to give an *ortho*-substituted aryl nitrile is only applicable to systems capable of formation of substituted styrenes. However, in those cases where this is not possible, access to unusual imino-2-benzofuran derivatives is achieved. In common with the few detailed studies[7] of the formation of this heterocyclic system, we have not assigned the stereochemistry about the carbon–nitrogen double bond. However, in this and the previous paper,[5] routes to stable imino-2-benzofurans containing a functionalised imine moiety are clearly established.

Experimental

General procedures are described in the previous paper.[5]

2-*Cyclohex*-1-*enylbenzonitrile* (**27**).—To a solution of 6-hydroxy-3-(2-hydroxy-1,1-dimethylethylimino)-1,3-dihydro-2-benzofuran-1-spirocyclohexane (**15**) (600 mg, 2.19 mmol) in dry pyridine (15 ml), phosphorus oxychloride (0.4 ml, 4.38 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). The aqueous solution was extracted with ether (2 × 50 ml) and the combined ether extracts were washed with dilute hydrochloric acid (2 × 25 ml), aqueous cupric sulphate solution (50 ml), and water (50 ml), dried ($MgSO_4$) and filtered. Removal of the solvent under reduced pressure afforded an oil (400 mg). Purification by column chromatography [eluant, ether–light petroleum (1:1)] afforded, as a yellow oil, 2-*cyclohex*-1-*enylbenzonitrile* (**27**) (260 mg, 65%) (Found M^+, 183.1041. $C_{13}H_{13}N$ requires M, 183.1048); $\nu_{max.}$($CHCl_3$) 2 935, 2 210, and 1 600 cm^{-1}; m/z 183 (M^+, 73%) and 182 (100); δ 1.6—2.6 (8 H, complex, CH_2), 5.9—6.1 (1 H, m, vinyl H), and 7.2—7.9 (4 H, complex, aromatic); δ_C(p.p.m.) 21.73, 22.82, 25.56, and 28.94 (CH_2), 110.65 (vinyl C), 118 (CN), and 126.84, 128.24, 130.08, 132.47, 133.36, 135.70, and 148.37 (aromatic and vinyl C).

2-*Cyclohex*-1-*enyl*-4-*methoxybenzonitrile* (**28**).—To a solution of 3-(2-hydroxy-1,1-dimethylethylimino)-6-methoxy-1,3-dihydro-2-benzofuran-1-spirocyclohexane (**17**) (2.0 g, 6.6 mmol) in dry pyridine (30 ml), phosphorus oxychloride (1.4 ml, 13.2 mmol) was added dropwise. The resulting solution was stirred at 85 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a yellow oil (1.76 g). Purification by flash chromatography [eluant, light petroleum–ether (1:1)] afforded as a yellow oil 2-*cyclohex*-1-*enyl*-4-*methoxybenzonitrile* (**28**) (1.0 g, 73%) (Found: M^+, 213.1094. $C_{14}H_{15}NO$ requires M, 213.1154); $\nu_{max.}$($CHCl_3$) 2 920, 2 210, and 1 603 cm^{-1}; m/z 213 (M^+, 81%) and 212 (100); δ 1.5—2.5 (8 H, complex CH_2), 3.85 (3 H, s, OMe), 5.8—6.0 (1 H, m, vinyl H), and 6.6—7.3 (3 H, complex, aromatic); δ_C (p.p.m.) 21.75, 22.84, 25.53, and 28.86 (CH_2), 55.50 (OCH_3), 102.42, 112.76, 113.75, 129.80, 135.02, 135.77, 150.38, and 162.66 (aromatic and vinyl C), and 119.32 (CN).

2-*Cyclopent*-1-*enyl*-4-*methoxybenzonitrile* (**29**).—To a solution of 3-(2-hydroxy-1,1-dimethylethylimino)-6-methoxy-1,3-dihydro-2-benzofuran-1-spirocyclopentane (**18**) (1.5 g, 5.2 mmol) in dry pyridine (20 ml), phosphorus oxychloride (1.1 ml, 10.4 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a red oil (1.0 g). Purification by flash chromatography [eluant, light petroleum–ether (1:1)] afforded as a yellow oil 2-*cyclopent*-1-*enyl*-4-*methoxybenzonitrile* (**29**) (0.48 g, 47%) (Found: M^+, 199.1035. $C_{13}H_{13}NO$ requires M, 199.0997); $\nu_{max.}$($CHCl_3$) 2 940, 2 210, and 1 600 cm^{-1}; m/z 199 (M^+, 68%) and 198 (100); δ 1.8—2.9 (6 H, complex CH_2), 3.84 (3 H, s, OCH_3, 6.46—6.58 (1 H, m, vinyl H), and 6.7—7.7 (3 H, complex, aromatic); δ_C(p.p.m.) 23.37, 34.00, and 34.80 (CH_2), 55.57 (OCH_3), 101.35, 112.44, 113.44, 133.31, 135.80, 139.78, 142.79, and 162.73 (aromatic and vinyl C), and 119.98 (CN).

2-*Cyclohept*-1-*enylbenzonitrile* (**30**).—To a solution of 3-(2-hydroxy-1,1-dimethylethylimino)-1,3-dihydro-2-benzofuran-1-spirocycloheptane (**19**) (1.0 g, 3.5 mmol) in dry pyridine (20 ml), phosphorus oxychloride (0.7 ml, 6.95 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a red oil (0.71 g). Purification by flash chromatography [eluant, light petroleum–ether (1:1)] afforded as a less polar fraction a yellow oil 2-*cyclohept*-1-*enylbenzonitrile* (**30**) (200 mg, 30%) (Found: M^+, 197.1106. $C_{14}H_{15}N$ requires M, 197.1201); $\nu_{max.}$($CHCl_3$) 2 920, 2 210, and 1 600 cm^{-1}; m/z 197 (100%) and 196 (59); δ 1.4—2.7 (10 H, complex, CH_2), 6.18 (1 H, m, vinyl H), and 7.2—7.7 (4 H, complex, aromatic); δ_C(p.p.m.) 26.57, 27.07, 29.15, 32.48, and 34.37 (CH_2), 110.37, 126.58, 128.42, 132.40, 133.18, 135.35, 142.58, and 150.33 (aromatic and vinyl C), and 119.11 (CN). An unidentified more polar fraction was also obtained.

Benzonitrile.—To a solution of 4,4-dimethyl-2-phenyl-2-oxazoline (**1**)[5] (0.85 g, 4.85 mmol) in dry pyridine (15 ml), phosphorus oxychloride (0.9 ml, 9.7 mmol) was added dropwise. The resulting solution was stirred at 85 °C (bath temperature under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded, as a colourless oil, benzonitrile (0.39 g, 80%).

p-*Methoxybenzonitrile*.—To a solution of 2-(4-methoxyphenyl)-4,4-dimethyl-2-oxazoline (**2**)[5] (1.0 g, 4.87 mmol) in dry pyridine (25 ml), phosphorus oxychloride (1.0 ml, 9.74 mmol) was added dropwise. The resulting solution was stirred at 85 °C (bath temperature) under nitrogen for 14 h and, after being

cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a yellow solid (0.96 g). Purification by flash chromatography afforded as white needles *p*-methoxybenzonitrile (0.41 g, 63%), m.p. 57—58 °C (lit.,[8] m.p. 59.5—60.5 °C).

3-(2-*Chloro*-1,1-*dimethylethylimino*)-1-*phenyl*-1,3-*dihydro*-2-*benzofuran* (**5**).—To a solution of 2-[2-hydroxy(phenyl)methylphenyl]-4,4-dimethyl-2-oxazoline (**4**) (4.1 g, 14.6 mmol) in dry pyridine (30 ml), phosphorus oxychloride (3 ml, 29.2 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a red oil. Crystallisation from ethyl acetate afforded as a white crystalline solid 3-(2-*chloro*-1,1-*dimethylethyl*(*imino*)-1-*phenyl*-1,3-*dihydro*-2-*benzofuran* (**5**) (1.32 g, 32%), m.p. 140—142 °C (Found: C, 72.1; H, 6.1; Cl, 12.1; N, 4.6. $C_{18}H_{18}ClNO$ requires C, 72.1; H, 6.0; Cl, 11.8; N, 4.6%); $\nu_{max.}$($CHCl_3$) 1 685 cm^{-1}, 299 (M^+, 1%), 250 ($M - CH_2Cl$, 56); δ 1.36 (3 H, s, CH_3), 1.58 (3 H, s, CH_3), 3.57 (1 H, d, *J* 11 Hz), 4.79 (1 H, d, *J* 11 Hz), 5.78 (1 H, s, ArCH), and 6.95—7.9 (9 H, complex, aromatic); δ_C(p.p.m.) 25.08 (CH_3), 51.28 (CH_2Cl), 58.74 ($NCMe_2$), 66.10 (Ar*C*O), 122.72, 123.26, 126.28, 128.03, 129.16, 131.16, 131.93, 140.60, and 146.89 (aromatic CH and C), and 170.23 (Ar*C*=N).

3-(2-*Chloro*-1,1-*dimethylethylimino*)-1-p-*methoxyphenyl*-1,3-*dihydro*-2-*benzofuran* (**10**).—To a solution of 2-[2-hydroxy(4-methoxyphenyl)methylphenyl]-4,4-dimethyl-2-oxazoline (**7**) (1.8 g, 5.78 mmol) in dry pyridine (30 ml), phosphorus oxychloride (1.2 ml, 11.5 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a red oil (800 mg). Crystallisation from ethyl acetate afforded as a white crystalline solid 3-(2-*chloro*-1,1-*dimethylethylimino*)-1-p-*methoxyphenyl*-1,3-*dihydro*-2-*benzofuran* (**10**) (0.66 g, 35%), m.p. 137—138 °C (Found: C, 69.0; H, 6.1; N, 4.1. $C_{19}H_{20}ClNO_2$ requires C, 69.2; H, 6.1; N, 4.2%); $\nu_{max.}$($CHCl_3$) 1 680 and 1 520 cm^{-1}; *m*/*z* 329 (M^+, 5%) and 280 ($M - CH_2Cl$, 100); δ 1.48 (3 H, s, CH_3), 1.56 (3 H, s, CH_3), 3.76 (3 H, s, OCH_3), 3.58 (1 H, d, *J* 11 Hz), 4.76 (1 H, d, *J* 11 Hz), 5.74 (1 H, s, ArCHO), and 6.8—7.9 (8 H, complex, aromatic); δ_C(p.p.m.) 25.07 (CH_3), 51.37 (CH_2Cl), 55.21 (OCH_3), 58.70 ($NCMe_2$), 65.56 (Ar*C*O), 114.51, 122.66, 123.17, 127.53, 127.94, 131.12, 131.91, 132.26, and 147.21 (aromatic CH and C), 159.35 ($COCH_3$), and 170.14 (Ar*C*=N).

3-(2-*Chloro*-1,1-*dimethylethylimino*)-6-*methoxy*-1-*phenyl*-1,3-*dihydro*-2-*benzofuran* (**11**).—To a solution of 2-[2-hydroxy-(phenyl)methyl-4-methoxyphenyl]-4,4-dimethyl-2-oxazoline (**8**) (4.0 g, 12.3 mmol) in dry pyridine (30 ml), phosphorus oxychloride (2.4 ml, 24.6 mmol) was added dropwise. The resulting solution was stirred at 85 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described for (**27**) afforded a red oil. Crystallisation from ethyl acetate–light petroleum afforded, as a white crystalline solid, 3-(2-*chloro*-1,1-*dimethylethylimino*)-6-*methoxy*-1-*phenyl*-1,3-*dihydro*-2-*benzofuran* (**11**) (1.35 g, 32%), m.p. 122—123 °C (Found: C, 69.1; H, 6.1; Cl, 10.8; N, 4.2. $C_{19}H_{20}ClNO_2$ requires C, 69.2; H, 6.1; Cl, 10.8; N, 4.2%); $\nu_{max.}$($CHCl_3$) 1 675 cm^{-1}; *m*/*z* 329 (M^+, 3%) and 260 ($M - CH_2Cl$, 100); δ 1.36 (3 H, s, CH_3), 1.58 (3 H, s, CH_3), 3.68 (3 H, s, OCH_3), 3.58 (1 H, d, *J* 10 Hz), 4.78 (1 H, d, *J* 10 Hz), 5.72 (1 H, s, ArCHO), and 6.4—7.75 (8 H, complex, aromatic); δ_C(p.p.m.) 25.11 (CH_3), 25.22 (CH_3), 51.46 (CH_2Cl), 55.46 (OCH_3), 58.64 ($NCMe_2$), 65.85 (ArCO), 107.34, 114.94, 123.90, 124.75, 126.30, 128.07, 129.21, 140.90, and 149.10 (aromatic CH and C), 163.12 ($COCH_3$), and 170.17 (Ar*C*=N).

3-(2-*Chloro*-1,1-*dimethylethylimino*)-7-*methoxy*-1-*phenyl*-1,3-*dihydro*-2-*benzofuran* (**12**).—To a solution of 2-(2-hydroxy-(phenyl)methyl-3-methoxyphenyl)-4,4-dimethyl-2-oxazoline (**9**) (4.0 g, 12.9 mmol) in dry pyridine (35 ml), phosphorus oxychloride (2.9 ml, 25.8 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a red oil. Crystallisation from ethyl acetate afforded as a white crystalline solid 3-(2-*chloro*-1,1-*dimethylethylimino*)-7-*methoxy*-1-*phenyl*-1,3-*dihydro*-2-*benzofuran* (**12**) (1.4 g, 33%), m.p. 188—189 °C (Found: C, 69.2; H, 6.0; Cl, 10.9; N, 4.1. $C_{19}H_{20}ClNO_2$ requires C, 69.2; H, 6.1; Cl, 10.8; N, 4.2%); $\nu_{max.}$($CHCl_3$) 1 675 cm^{-1}; *m*/*z* 329 (M^+, 6%) and 280 ($M - CH_2Cl$, 100); δ 1.36 (3 H, s, CH_3), 1.52 (3 H, s, CH_3), 3.52 (1 H, d, *J* 11 Hz), 3.60 (3 H, s, OCH_3), 4.75 (1 H, d, *J* 11 Hz), 5.78 (1 H, s, ArCHO), and 6.75—7.5 (8 H, complex, aromatic); δ_C(p.p.m.) 24.70 (CH_3), 24.80 (CH_3), 51.24 (CH_2Cl), 55.36 (OCH_3), 58.70 ($NCMe_2$), 64.12 (ArCO), 113.77, 115.31, 127.44, 127.59, 128.28, 129.92, 133.15, 134.67, and 139.07 (aromatic CH and C), 153.93 ($COCH_3$), and 170.17 (Ar*C*=N).

3-(2-*Chloro*-1,1-*dimethylethylimino*)-1,1-*diphenyl*-1,3-*dihydro*-2-*benzofuran* (**21**).—To a solution of 3-(2-hydroxy-1,1-dimethylethylimino)-1,1-diphenyl-1,3-dihydro-2-benzofuran (**20**) (1.05 g, 3.2 mmol) in dry pyridine (20 ml), phosphorus oxychloride (0.7 ml, 6.4 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described for (**27**) afforded a red oil (0.85 g). Crystallisation from ethyl acetate–light petroleum afforded, as a white crystalline solid, 3-(2-*chloro*-1,1-*dimethylethylimino*)-1,1-*diphenyl*-1,3-*dihydro*-2-*benzofuran* (**21**) (0.41 g, 34%), m.p. 138—140 °C (Found: M^+, 377.1263. $C_{24}H_{22}ClNO$ requires *M*, 377.1361) (C.I. using NH_3); $\nu_{max.}$($CHCl_3$) 1 690 cm^{-1}; δ 1.54 (6 H, s, CH_3), 3.79 (2 H, s, CH_2), and 7.1—8.0 (14 H, complex, aromatic); *m*/*z* 377 (M^+) [not observed without chemical ionisation (C.I.)] and 326 ($M - CH_2Cl$, 100); δ_C(p.p.m.) 25.14 (CH_3), 55.26 (CH_2Cl), 56.95 ($NCMe_2$), 94.03 (Ar_2CO), and 123.66, 124.10, 127.01, 128.08, 128.32, 128.73, 131.26, 142,40, 147.52, and 155.61 (aromatic CH and C). The signal attributable to (Ar*C*=N) was not observed in this weak spectrum.

Reaction of 3-(2-*Hydroxy*-1,1-*dimethylethylimino*)1,3-*dihydro*-2-*benzofuran*-1-*spirocycloheptane* (**19**) *with* p-*Tosyl Chloride at* 60 °C.—To a solution of compound (**19**) (1.0 g, 3.58 mmol) in dry pyridine (50 ml), toluene-*p*-sulphonyl chloride was added. The resulting solution was stirred at 60 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). The aqueous solution was extracted with ether (3 × 50 ml). The combined ether extracts were washed with dilute hydrochloric acid (2 × 50 ml) and water (50 ml), dried ($MgSO_4$), and filtered. Removal of the solvent under reduced pressure afforded a yellow solid (260 mg, 17%). Recrystallisation from ethyl acetate–pentane afforded, as a white crystalline solid, the tosylate (**22**,) m.p. 110—112 °C; *m*/*z* 270 (M − OTs, 8%), 269 (M − TsOH, 37), 256 ($M - CH_2OTs$, 19), and 226 (100); *m*/*z* [C.I. using NH_3] 442 (95%) and 270 (100); $\nu_{max.}$($CHCl_3$) 1 690 cm^{-1}; δ(60 MHz) 1.39 (6 H, s, CH_3), 1.6—2.1 (12 H, complex CH_2), 2.43 (3 H, s, CH_3), 4.08 (2 H, s, CH_2O), and 7.2—7.95 (8 H, complex, aromatic).

Reaction of the Spiroheptane (**19**) *with* p-*Tosyl Chloride at* 75 °C.—To a solution of compound (**19**) (0.5 g, 1.74 mmol) in dry pyridine (25 ml), toluene-*p*-sulphonyl chloride (0.66 g, 3.48 mmol) was added. The resulting solution was stirred at 75 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a red oil (300 mg). Flash chromatography (eluant, ether) afforded, as the less polar fraction, a yellow oil, 2-cyclohept-2-enylphenyl-4,4-dimethyl-2-oxazoline (**26**) (104 mg, 22%) (Found: M^+, 269.1830. $C_{18}H_{23}NO$ requires M, 269.1779); $\nu_{max.}$($CHCl_3$) 2 920 and 1 650 cm^{-1}; *m/z* 269 (M^+, 15%) and 226 (100); δ 1.38 (6 H, s, CH_3), 1.5—2.6 (10 H, complex, CH_2), 4.06 (2 H, s, CH_2), 5.84 (1 H, m, vinyl H), 7.1—7.9 (4 H, complex, aromatic), 26.75 and 26.93 (CH_2), 28.30 (CH_3), 29.00, 32.46, and 34.89 (CH_2), 67.47 ($NCMe_2$), 79.49 (CH_2O), 126.15, 129.03, 129.88, 130.22, 130.54, 145.62, 146.18, and 149.50 (aromatic and vinyl C), and 162 (Ar*C*=N); the more polar fraction was recrystallised from ethyl acetate to afford as a white crystalline solid, the amide 2-*cyclohept*-1-*enyl*-N-(2-*hydroxy*-1,1-*dimethylethyl*)*benzamide* (**31**) (103 mg, 21%), m.p. 105—107 °C (Found: M^+, 287.1890. $C_{18}H_{25}NO_2$ requires M, 287.1895); $\nu_{max.}$($CHCl_3$) 3 440—3 260, 2 910, and 1 635 cm^{-1}; δ 1.36 (6 H, s, CH_3), 1.45—2.6 (10 H, complex, CH_2), 3.63 (2 H, s, CH_2), 4.9—5.1 (1 H, m, OH), 5.95 (1 H, m, vinyl H), 6.2—6.35 (1 H, br, NH), and 7.1—7.7 (4 H, complex, aromatic); δ_C(p.p.m.) 24.53 (CH_3), 26.55, 26.67, 28.92, 32.41, and 35.49 (CH_2), 56.52 ($NCMe_2$), 70.86 (CH_2OH), 126.93, 128.66, 129.34, 130.38, 132.46, 133.61, 144.08, and 145.80 (aromatic and vinyl CH and C), and 170.33 (Ar*C*=O).

Reaction of the Spiroheptane (**19**) *with Thionyl Chloride.*—To a solution of compound (**19**) (1.0 g, 3.5 mmol) in dry pyridine (20 ml), thionyl chloride (0.52 ml, 0.70 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded an oil (1.0 g). Flash chromatography [eluant, light petroleum–ether (1:1)] afforded, as the less polar fraction, a yellow oil, 3-(2-*chloro*-1,1-*dimethylethylimino*)-1,3-*dihydro*-2-*benzofuran*-1-*spirocycloheptane* (**23**) (260 mg, 26%); δ 1.46 (3 H, s, CH_3), 1.64 (3 H, s, CH_3), 1.55—2.0 (12 H, complex, CH_2), 3.75 (2 H, s, CH_2Cl), and 7.2—7.8 (4 H, complex, aromatic); the unsaturated oxazoline (**26**) (410 mg, 44%) was isolated as a colourless liquid from the more polar fraction.

2-(2-*Cyclohept*-1-*enylphenyl*)-4,4-*dimethyl*-2-*oxazoline* (**26**) *with Phosphorus Oxychloride.*—To a solution of 2-(2-cyclohept-1-enylphenyl)-4,4-dimethyl-2-oxazoline (**26**) (0.40 g, 1.48 mmol) in dry pyridine (20 ml), phosphorus oxychloride (0.3 ml) was added dropwise. The resulting solution was stirred at 85 °C (bath temperature) for 14 h under nitrogen, cooled to room temperature, and poured into a cold saturated solution of sodium carbonate. Work-up as described above for (**27**) afforded a tan oil (300 mg). Purification by preparative t.l.c. [light petroleum–ether (1:1)] afforded, as a pale yellow oil, 2-cyclohept-1-enylbenzonitrile (**30**) (170 mg, 58%).

4,8-*Bis*-(2-*cyanophenyl*)-2,6-*dimethylenebicyclo*[3.3.1]*nona*-3,7-*diene* (**33**).—To a stirred solution of 4,4-dimethyl-2-phenyl-2-oxazoline (**1**) (1.09 g, 6.25 mmol) in dry tetrahydrofuran (30 ml), butyl-lithium (4.5 ml; 1.4M-solution in hexane) was added slowly under nitrogen at −78 °C. The solution was stirred at −78 °C for 1 h, and then the temperature was allowed to rise to −20 °C. At this temperature, the ketone (**32**) (500 mg, 2.84 mmol) in tetrahydrofuran (15 ml) was added during 20 min. The solution was stirred for 1 h at −20 °C and then allowed to warm to room temperature. The solvent was removed under reduced pressure and the residue partitioned between ether (100 ml) and water (100 ml) containing ammonium chloride. Work-up afforded a crude yellow oil (1.68 g). Purification by flash chromatography [chloroform–methanol (99:1)] afforded the alcohol (**34**) as a yellow oil (0.60 g, 39%).

To a solution of the alcohol (**34**) (600 mg, 1.14 mmol) in dry pyridine (15 ml), phosphorus oxychloride (0.4 ml, 4.56 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described above for (**27**) afforded a yellow oil (300 mg). Crystallisation from ethyl acetate–ether (1:1) afforded, as a pale yellow crystalline solid, 4,8-*bis*(2-*cyanophenyl*)-2,6-*dimethylenebicyclo*-[3.3.1]*nona*-3,7-*diene* (**33**) (260 mg, 66%), m.p. 152—154 °C (Found: M^+, 346.1179. $C_{25}H_{18}N_2$ requires M, 346.1469); $\nu_{max.}$($CHCl_3$) 2 210 cm^{-1}; δ 2.32 (2 H, t, *J* 3 Hz, CH_2), 3.56 (2 H, t, *J* 3 Hz, CH), 4.52 (2 H, s) and 4.82 (2 H, s) (vinyl CH_2), 6.12 (2 H, s, vinyl CH), and 7.2—7.7 (8 H, complex, aromatic).

Reaction of 3-(2-*Hydroxy*-1,1-*dimethylethylimino*)-1-*methyl*-1-*phenyl*-1,3-*dihydro*-2-*benzofuran* (**35**) *with Phosphorus Oxychloride.*—To a solution of the dihydrobenzofuran (**35**) (1.15 g, 3.9 mmol) in dry pyridine (25 ml), phosphorus oxychloride (0.8 ml, 7.8 mmol) was added dropwise. The resulting solution was stirred at 80 °C (bath temperature) under nitrogen for 14 h and, after being cooled to room temperature, was poured into a cold saturated solution of sodium carbonate (100 ml). Work-up as described for (**27**) afforded a dark oil (1.10 g). The oil was fractionated by h.p.l.c. [solvent, 10% ethyl acetate–n-hexane, then 20% ethyl acetate–n-hexane] into four fractions, in increasing order of polarity. (i) 1-(2-*Hydroxy*-1,1-*dimethylethylimino*)-3-*phenylindene* (**37**) (140 mg), m.p. 67—68 °C (Found: M^+, 295.1106. $C_{19}H_{18}ClN$ requires M, 295.1128); $\nu_{max.}$($CHCl_3$) 1 640 cm^{-1}; *m/z* 295 (M^+, 4%), 246 ($M - CH_2Cl$, 100); δ 1.47 (6 H, s, CH_3), 3.75 (2 H, s, CH_2Cl), 6.42 (1 H, s, vinyl H), and 7.2—7.8 (9 H, complex, aromatic); δ_C(p.p.m.) 26.66 (CH_3), 56.57 (CH_2Cl), 60.56 ($NCMe_2$), 117.37, 120.55, 121.50, 127.51, 127.85, 128.80, 129.43, and 129.75 (aromatic and vinyl CH), 134.27, 138.25, 140.88, and 155.34 (aromatic and vinyl C), and 164.83 (Ar*C*=N). (ii) α-(2-*Cyanophenyl*)*styrene* (**36**) (80 mg) as an oil (Found: M^+, 205.0838. $C_{15}H_{11}N$ requires M, 205.0298); *m/z* 205 (M^+, 100%); δ(60 MHz) 5.45 (1 H, s, vinyl H), 5.85 (1 H, s, vinyl H), and 7.2—7.8 (9 H, complex, aromatic). (iii) An unidentified fraction (280 mg) (unstable). (iv) A further unidentified fraction (280 mg).

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