Novel Production of 3-Benzoyl-2,1-benzisoxazoles from 2-Phenyl-quinolin-4(1*H*)-ones

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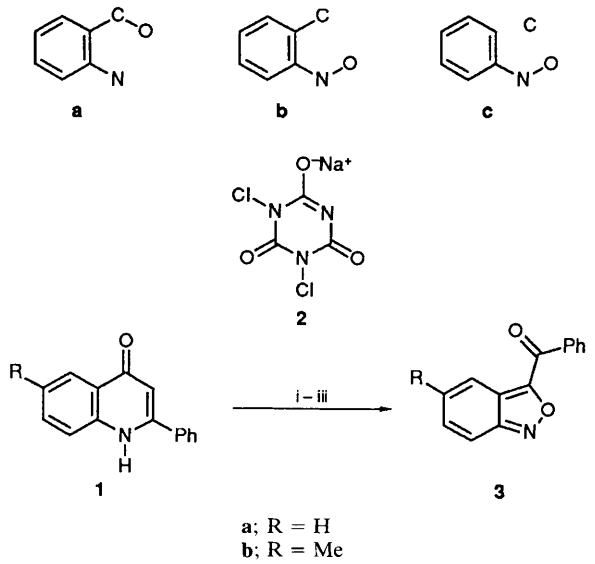
2-Phenylquinolin-4(1*H*)-ones **1a** and **1b** react with sodium dichloroisocyanurate **2** in methanolic aqueous sodium hydroxide, to afford, after acidification, 3-benzoyl-2,1-benzisoxazoles **3a** and **3b** (*ca.* 30%).

Two basic routes are available for the synthesis of 2,1-benzisoxazoles (anthranils), the subject of many investigations and two reviews:[1,2] (*i*) cyclization of types (*a*) and (*b*), in which the 1–2 and 2–3 bond, respectively, is formed, and (*ii*) introduction of C-3, forming bonds 2–3 and 3–3a (*c*).[2] There are also a number of less general and mostly multi-step synthetic methods.[1,2]

We report here a novel, mild and essentially one-pot synthesis of 3-benzoyl-2,1-benzisoxazole **3a** and its 5-methyl derivative **3b**, *via* a remarkable transformation of the corresponding 2-phenyl-quinolin-4(1*H*)-ones **1a** and **1b**. Thus, treatment of the readily available **1**,[3] in methanolic aqueous sodium hydroxide, with excess of sodium dichloroisocyanurate **2**,[4] and subsequent acidification of the reaction, afforded the aforementioned **3** (*ca.* 30%, not optimized). The constitution of product **3a**, $C_{14}H_9NO_2$, from **1a** was proved by direct comparison [IR (KBr), ^{1}H NMR ($CDCl_3$), mixed m.p.] with authentic 3-benzoyl-2,1-benzisoxazole **3a** prepared[5,6] from 2-phenylisatogen. The identity of the analogous product, m.p. 114–115 °C, from **1b** (previously[4] incorrectly formulated as 6-methyl-2-phenyl-4*H*-3,1-benzoxazin-4-one), was unequivocally established as the new 3-benzoyl-5-methyl-2,1-benzisoxazole **3b** from an X-ray crystal structure determination (Fig. 1).† The bond lengths and angles in **3b** are virtually the same as the corresponding ones in **3a**.[7]



Scheme 1 *Reagents and conditions*: i, **1** (4 mmol) in MeOH–2 mol dm^{-3} NaOH–H_2O (2 : 4 : 1) (90 ml), stir, sodium dichloroisocyanurate **2** (9 mmol) added in one portion, room temperature, 1 h; ii, chill, then conc. HCl (11 ml), continued stirring, 15 min; filter; iii, sparingly soluble **3** (plus other material) with MeOH–2 mol dm^{-3} NaOH–H_2O (1 : 1 : 1) (45 ml), stir, 15 min, filter, crystallization (Me_3OH–H_2O)

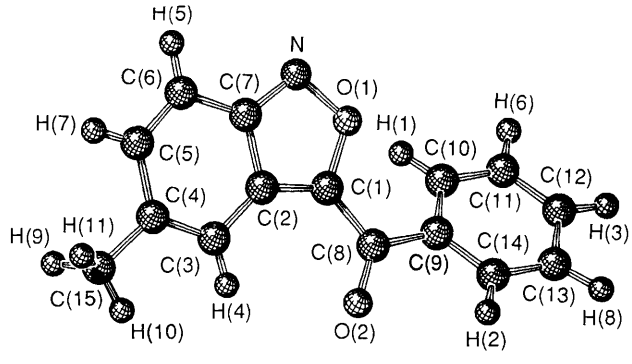


Fig. 1 The molecular structure and atomic numbering scheme for compound **3b**

† *Crystal data*: compound **3b**, $C_{15}H_{11}NO_2$, M_r = 237.26, monoclinic, space group *C2/c*, *a* = 24.415(4), *b* = 5.753(1), *c* = 17.143(2) Å, β = 94.483(7)°, *V* = 2400.9(7) Å^3, *Z* = 8, D_c = 1.313 g cm^{-3}, *F*(000) = 992, μ = 0.51 cm^{-1}, *R* = 0.063 for 2560 unique reflections with $F_o \geq 3\sigma(F_o)$, R_w = 0.059 where $w \propto 1/\sigma^2(F)$. Data were collected using an Enraf-Nonius CAD4 diffractometer with Mo-Kα radiation (λ = 0.71069 Å). The structure was solved by direct methods and refined by full-matrix least-squares analysis with anisotropic thermal parameters for all nonhydrogen atoms. Hydrogen atoms were refined isotropically. Lorentz–polarisation and empirical absorption corrections were applied to the data. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

The formation of **3** from **1** is the result of a series of reactions and intermediates that includes chlorination of **1** to a 3-chloroquinoline and subsequently to the corresponding, hitherto inaccessible, 3,3-dichloro-quinolin-4(3*H*)-one, and eventual loss of C-3 possibly *via* a decarboxylative elimination.[8] Studies are continuing to probe the scope and mechanistic aspects of this rapid and convenient method for accessing the 2,1-benzisoxazole ring system from a quinolinone derivative; to date only the reverse situation has been documented.[1,2]

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