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Synthesis of Quinazolin-4-(3h)-ones from O-Amidobenzonitriles Using Ureahydrogen Peroxide¹

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SYNTHESIS OF QUINAZOLIN-4-(3H)-ONES FROM o-AMIDOBENZONITRILES USING UREA-HYDROGEN PEROXIDE¹

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ABSTRACT: Synthesis of quinazolin-4-(3H)-ones from o-amidobenzonitriles has been carried out by using urea-hydrogen peroxide as a mild, stable and non-hazardous reagent.

The peracids are relatively unstable and potentially explosive. Hydrogen peroxide is quite weak oxidising agent which often requires specific activation towards the functional group to be transformed.² Another important disadvantage is that concentrated hydrogen peroxide is not readily available and is furthermore, very dangerous to handle.³ Hence these reagents are now replaced by more stable and safe reagents. Urea-hydrogen peroxide (UHP)⁴ is a safe alternative to anhydrous hydrogen peroxide, relatively stable

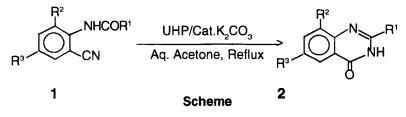
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and commercially available.Recently UHP has been used for selective, mild oxidation of N-heteroatomic compounds, tertiary amines⁵ and conversion of nitriles to amides.⁶

Quinazolin-4-(3H)-one systems are versatile and may be further modified in the construction of new pharmaceutical entities. Author now reports herein the use of UHP in the Radziszewski reaction⁷⁻⁸ as a mild, safe and non-hazardous oxidising agent for the synthesis of quinazolin-4-(3H)-ones from suitably functionalised o-amidobenzonitriles (scheme).



In summary mild method of oxidative hydration of o-amidobenzonitriles using UHP followed by cyclisation has been shown to allow access to a variety of fuctionalised quinazolin-4-(3H)ones in one pot procedure. Excellent yields and short reaction time are important advantages of this methodology.

Experimental

Solvents were distilled before use. Urea-hydrogen peroxide (Aldrich) was used as obtained and suitably functionalised oamidobenzonitriles were prepared by using standard synthetic methods.

General Procedure

To a mixture of o-amidobenzonitrile (3 mmol) in acetone: water, 1:1 (20 mL) and anhydrous potassium carbonate (50 mg), UHP (6 mmol) was added and the resulting mixture was refluxed for 2 h. Reaction was monitored by TLC. After cooling the reaction

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QUINAZOLIN-4-(3H)-ONES

Entry	Substrate	Product	Yield (%)
1		N CH ₃	97
2 Br		Br NH	95
3 Bi		Br NHCH3	94
4		NH Ph	96
5 Bi		Br NH	86
6 B	Br NHCOPh Br CN	Br N Ph	98
7 O ₂ N-	O NHCOPh CN	O ₂ N NH	88

Table : Synthesis of quinazolin-4-(3H)-ones using UHP

mixture, acetone was removed under reduced pressure and the product crystallised out from the reaction mixture. The product was washed with water, air dried and then washed with cold ether to give a white solid in excellent yield. Product was characterised by their IR, ¹H NMR and by comparison with literature data.

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Reference and footnotes

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