Friedel-Crafts Acylation of 2(3H)-Benzoxazolone: Investigation of the Role of the Catalyst and Microwave Activation

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Summary. To study the scope and limitations of the use of complexed species of AlCl₃ in Friedel-Crafts reactions, we investigated the acetylation and benzoylation of 2(3H)-benzoxazolone and 3-methyl-2(3H)-benzoxazolone varying the amide complexing agent. We replaced dimethylformamide by N-methylformamide, dimethylacetamide, pyrrolidone, N-methylpyrrolidone, tetramethylurea, and dimethylsulfoxide. However, there was no particular advantage of substituting dimethylformamide by another amide ligand. This can probably be ascribed to the fact that the complex formed between AlCl₃ and the complexing agent becomes too stable. Alternatively, a route using polyphosphoric acid and microwave activation was explored. The major advantage of running the reaction in a microwave oven was that a good yield was reached in a rather short period of time.

Keywords. 2(3H)-Benzoxazolone; Friedel-Crafts reaction; AlCl₃-DMF complex; Microwave irradiation.


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Introduction

In a series of recent papers, we have reported on the AlCl$_3$-DMF complex as a useful catalyst in the Friedel-Crafts (FC) reaction [1–4]. This catalyst displays a rather unique behaviour in the acylation of electron-rich compounds which are quite basic substrates. Using classical Lewis acid catalysts (AlCl$_3$, BF$_3$, ZnCl$_2$, TiCl$_4$, etc.), these substrates are strongly complexed; they become therefore heavily deactivated in electrophilic substitution reactions such as the FC reaction, and yields are low. When AlCl$_3$-DMF is used as a catalyst, acylation products are obtained in good yields. The use of the AlCl$_3$-DMF catalyst has been exemplified in several publications concerning the acylation of 2(3$H$)-benzoxazolone and 2(3$H$)-benzothiazolone using activated forms of carboxylic acids (acid halides or anhydrides) [5–12].

The initial paper of the series [1] was seminal in that several other groups were prompted to investigate the same or similar Lewis acid-base complexes such as AlCl$_3$-DMSO, AlCl$_3$-dimethylsulfone, or AlCl$_3$-nitromethane [13–15]. The FeCl$_3$-graphite complex can be regarded as another example of a Lewis salt used as FC catalyst [16].

An alternative route employs polyphosphoric acid (PPA) as catalyst [17]. In all cases, regioselectivity for position 6 of the heterocycle was observed. However, in the case of $\omega$-halogenoaocids or dicarboxylic acids, PPA was not found as satisfactory as the AlCl$_3$-DMF complex, since either the expected acylation product was not formed or low yields were obtained. The problem of $\omega$-halogenoaocids has been addressed in a previous paper [3]. In an effort to further study the scope and limitations of the use of complexed species of AlCl$_3$ in the Friedel-Crafts reaction, we investigated the acetylation and benzoylation of 2(3$H$)-benzoxazolone (1) and 3-methyl-2(3$H$)-benzoxazolone (2) as pilot reactions varying the amide complexing agent (Fig. 1). In a second part, we also briefly report on the use of PPA taking advantage of the well-known potentialities offered nowadays by the use of microwave ovens. Microwave irradiation has been shown to be a very useful alternative to conventional heating for chemical reactions [18].

![Fig. 1. Regioselectivity in the FC acylation of 2(3$H$)-benzoxazolone (1, $R^1$ = H) and 3-methyl-2(3$H$)-benzoxazolone (2, $R^1$ = CH$_3$); $R^2$ = CH$_3$ or C$_6$H$_5$; methods: (a) $R^2$COCl, AlCl$_3$-X (X = complexing agent), 85°C; (b) $R^2$COOH, PPA, 80–125°C.](image-url)