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SYNTHESIS OF 3-BENZYLIDENE-1-METHYLPYRROLIDIN-2-ONE THROUGH 3-CHLOROMETHYLENE-1-METHYLPYRROLIDIN-2-ONE

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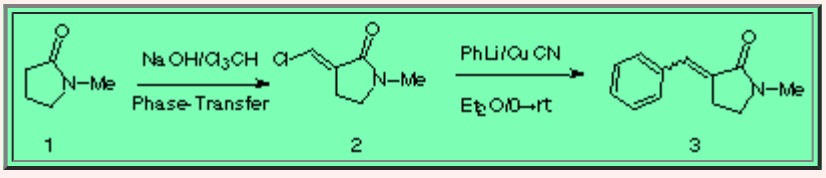
Introduction of a carbon chain in the α-position of amides is a common step to many organic synthesis. Here we describe an improvement in a simple way to achieve 3-chloromethylene-1-methylpyrrolidin-2-one **2**, and its reaction with phenyllithium/CuCN to afford 3-arylidene-1-methylpirrolidin-2-one **(3)**, this would represent an approach to a kind of carbon skeleton present in a wide variety of pharmacologically active compounds[1]. The preparation of **2** was previously reported[2] by addition of dichlorocarbene to N-methyl-2-pyrrolidone **(1)** under phase transfer catalysis (PTC), but the yield reported , using Bu_4NCl, was too low (30%) to make it a practical way to achieve **2** in a preparative scale.

As we became interested in compounds like **3**, through **2,** we did some attempts to get a yield that was useful for a preparative scale. The procedure was described as a phase transfer addition of dichlorocarbene followed of a ß-elimination, as both steps were phase-transfer catalyzed, we thought that we should focus our efforts in the nature of the catalyst. When Bu_4NBr, instead of the chloride, was used we achieved only a slight improvement in the yield (39%), a change towards more lipophylic catalysts showed a noteworthy improvement, with adogen ($(CH_3(CH_2)_7)_3NCl$) a 60% of addition elimination product was obtained, and with cetyltrimetilammonium bromide ($CH_3(CH_2)_7NMe_3Br$) the yield was similar (62%)



As an application of this product to the synthesis of 3-arylidenepyrrolidin-2-ones. Compound **2** was treated with PhLi/CuCN in ethyl ether at 0ºC and left overnight at r. t., as expected the phenyl ring gave a conjugated addition to the C=C, followed by chloride elimination regenerating the C=C, thus **3** was obtained in 78% yield.

We think that with this report it is opened an easy access to **2** which could be used as a versatile synthon whose

position α to carbonyl shows a functionality that can be interconverted with another groups, allowing to use this procedure as an intermediate step in the design of synthetic strategies. On the other hand the addtion-elimination of PhLi to **2**, opens a new route to the 3-arylidene-1-methylpirrolidin-2-ones, in fact actually we are investigating the application of this strategy to a variety of substitution in the aromatic ring and in the pyrrolinone nucleus.

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