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I.P. Beletskaya on Her Jubilee

## Unexpected Products from Carbonylation of Lithiated Quinazolin-4(3*H*)-one Derivatives\*

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**Abstract**—Doubly lithiated 3-pivaloylaminoquinazolin-4(3*H*)-one reacts with carbon(II) oxide at 0°C to give 77% of a mixture of azetidinone and indole derivatives, each incorporating a diisopropylamide unit from lithium diisopropylamide used for lithiation. No analogous reaction occurs with doubly lithiated 3-acetyl-aminoquinazolin-4(3*H*)-one and 3-acyl-2-alkylquinazolin-4(3*H*)-one. Carbonylation of doubly lithiated 2-alkyl-3-aminoquinazolin-4(3*H*)-ones at 0°C results in deamination to give 2-alkylquinazolin-4(3*H*)-ones in good yields.

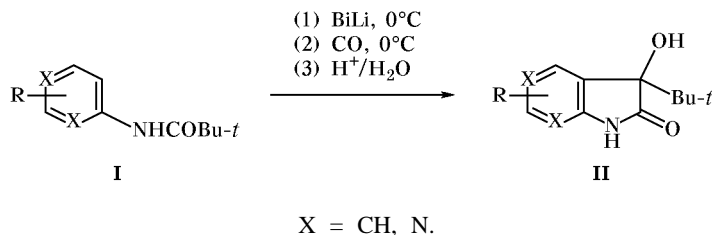
Reactions of organolithium compounds with carbon monoxide are rarely used in synthetic chemistry, presumably because of the instability and high reactivity of acyllithium intermediates which can lead to a variety of products [1]. To circumvent this problem, organic chemists have devised a number of acyl carbanion equivalents which are effective in nucleophilic acylation reactions [2]. Seyferth *et al.* [3] have shown that it is possible to trap acyllithium intermediates formed by carbonylation of alkylolithium reagents provided that the temperature is kept very low and that the trapping electrophile can be used *in situ*. However, the conditions are rather restrictive, and the method has rarely been used with aryllithium derivatives [4].

Better results are obtained when the incipient aryllithium is trapped intramolecularly [5]. For example,

we have previously shown that doubly lithiated *N*-pivaloylanilines and *N*-pivaloylaminopyridines **I** smoothly react with carbon monoxide at 0°C under atmospheric pressure to give 3-*tert*-butyldioxindoles and 3-*tert*-butylazadioxindoles **II** in good yields as a result of intramolecular trapping [6] (Scheme 1). Carbon(II) oxide reacts in a similar way with doubly lithiated *N'*-aryl-*N,N*-dimethylthiureas to give indogutins [7] and with lithiated *N'*-aryl-*N,N*-dimethylureas to give isatins [8].

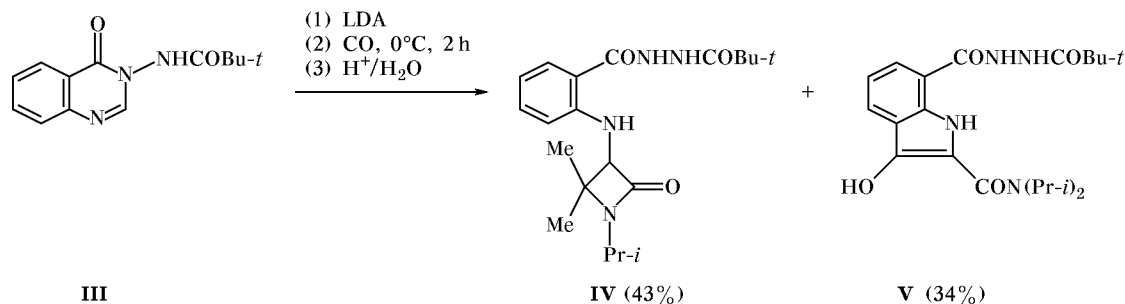
We have also shown that doubly lithiated 3-(acylamino)quinazolin-4(3*H*)-ones can be successfully trapped with a variety of electrophiles [9–11]. Compounds possessing this ring system exhibit versatile biological activity [12]. Therefore, it was reasonable to extend the range of electrophiles to include carbon monoxide with a view to obtain some interesting

Scheme 1.



\* The original article was submitted in English.

Scheme 2.



fused quinazolinone derivatives by analogy with Scheme 1. The present article reports on our attempts at such reactions, which gave unexpected results.

3-Pivaloylaminoquinazolin-4(3H)-one (**III**) was doubly lithiated with LDA and was then brought into reaction with carbon(II) oxide at 0°C under atmospheric pressure. The subsequent protonation gave two new products. They were purified by column chromatography and were identified as azetidinone derivative **IV** and substituted indole **V** (Scheme 2).

The <sup>1</sup>H NMR spectrum of compound **IV** showed three exchangeable doublets resonating in the δ 7.92–9.24 ppm region. Two of these signals were coupled

to each other ( $J \approx 5$  Hz), and the third was coupled to a CH doublet resonating at δ 4.19 ppm ( $J \approx 7$  Hz). The spectrum clearly showed an isopropyl group and two separate methyl groups in addition to the *tert*-butyl group, as well as four aromatic protons of an *ortho*-substituted benzene ring. The IR spectrum showed two carbonyl groups, and the accurate mass of the molecular ion in the mass spectrum indicated a formula of C<sub>20</sub>H<sub>30</sub>N<sub>4</sub>O<sub>3</sub>. The <sup>13</sup>C NMR spectrum of **IV** contained 18 different signals, only the three methyl groups of the *tert*-butyl group being degenerate. These data are consistent with the proposed structure.

Scheme 3.

