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The Activating Effect of $CoCl_2$ in Reactions of 1,2-di-*t*-butyl-diaziridinone with Alcohols and Amines

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Na presença de quantidades catalíticas de cloreto de cobalto, a reatividade da 1,2-di-*t*-butyldiaziridinona frente a nucleófilos é aumentada. Devido ao efeito ativante provocado pelo metal de transição, que aumenta a susceptibilidade do carbono carbonílico do heterociclo ao ataque nucleofílico, as reações com álcoois e aminas, formando carbazatos e uréias com rendimentos elevados, ocorrem sob condições suaves em apenas algumas horas.

The reactivity of 1,2-di-*t*-butyldiaziridinone with nucleophiles increases in the presence of catalytic amounts of cobalt dichloride. Owing to the activating effect of the transition metal, which increases the susceptibility of the carbonyl carbon to nucleophilic attack, the reactions with alcohols and amines, forming carbazates and ureas in high yields, occur under mild conditions in a few hours.

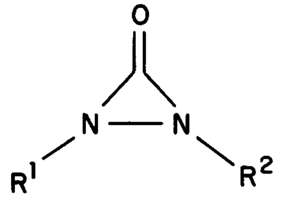
Keywords: *diaziridinone, cobalt dichloride activation, nucleophilic attack*

Introduction

The chemistry of strained small-ring compounds, which began more than 100 years ago with the synthesis of cyclopropane[1], has become synthetically important only in the last 20 years[2]. During this time it has been shown that these compounds are not only reaction intermediates but are also stable and well-characterized molecules which can be used as synthons in organic synthesis. Among these strained rings, nitrogenated three-membered heterocycles appear to be versatile as starting reagents in the synthesis of heterocyclic compounds.

Diaziridinones *1*, first described in the literature almost 30 years ago[3], show a number of interesting properties and considerable potencial as synthetic intermediates. Among the unusual properties of 1,2-di-*t*-butyldiaziridinone, *1a*, are high thermal stability (only slight decomposition after 2 h at 175 °C), and poor reactivity towards nucleophiles: for example, only 50% conversion to the corresponding carbazate in reaction with potassium *t*-butoxide in *t*-butyl alcohol for 16 h under reflux and no reaction of *1a* with aniline in ether after 6 days at 25 °C[3].

Diaziridinones are reactive with acids such as hydrogen chloride, picric acid, benzoic acid and formic acid, with resultant ring opening of diaziridinone and the formation of substituted carbazates[4]. Diaziridinones are only moderately reactive towards a range of nucleophiles, and function as a mild oxidizing agent towards thiols, phenols, enols and some hydrazines[4].



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1a: $R^1 = R^2 = t\text{-}C_4H_9$

Structure 1.

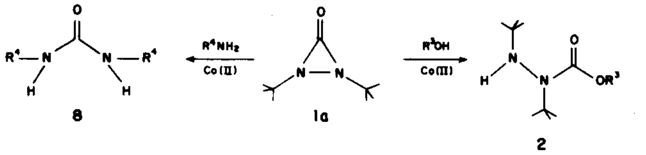
Among the reactions studied, only the reaction of di-*t*-butyldiaziridinone with methanol at reflux, affording the corresponding methyl 2,3-di-*t*-butylcarbazate in 67% yield, is catalyzed by the addition of concentrated sulfuric acid[4]. However, nothing is known about the behavior of diaziridinones in the presence of transition metal compounds and other Lewis acids. This, due to our interest in the chemistry of small ring compounds[5], prompted the present study.

Results and Discussion

Reactions with alcohols

In the reaction of stoichiometric amounts of ***1a*** and cobalt dichloride in ethanol at room temperature, the formation of a colorless oil occurs. Based on elemental analysis, and IR and ^{1}H-NMR spectra this product was identified as di-*t*-butylcarbazate ***2a***, which results from the incorporation of an ethanol molecule into the diaziridinone ring system (Scheme 1). At the end of the reaction the cobalt dichloride was recovered unchanged. Similarly, after 3 h in ethanol at room temperature, in the presence of 1 mol% of cobalt dichloride, the diaziridinone was catalytically converted to the corresponding carbazate ***2a***, in a quantitative yield. This product can also be obtained in 60% yield, in the absence of cobalt dichloride after 36 h under reflux in ethanol.

This reaction was extended to methyl and *i*-propyl alcohols, resulting in the formation of the corresponding di-*t*-butylcarbazates ***2b, c*** in good yields. These results show that the transition metal activates the heterocycle, facilitating its reaction under mild conditions

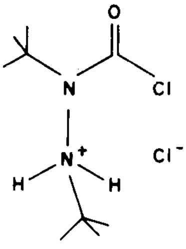


8	R^4	Yield (%)
a	$(CH_3)_3C$	85
b	$(CH_3)_2CH$	90
c	$C_6H_5CH_2CH_2$	90

2	R^3	Yield (%)
a	CH_3CH_2	100
b	CH_3	80
c	$(CH_3)_2CH$	75

Scheme 1.

In the reaction of 1,2-di-*t*-butyldiaziridinone with dry hydrogen chloride in pentane, the protonation occurs at the nitrogen atom with the formation of the salt ***3***, rather than a protonated diaziridinone ***4***[4]. This indicates that the nitrogen atom is more basic than oxygen in the diaziridinone ring system.



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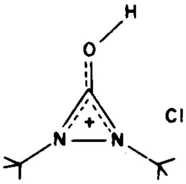

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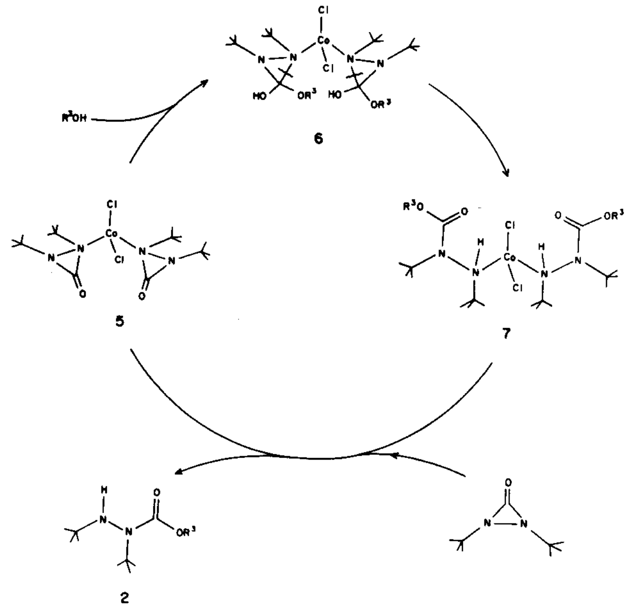
This is in accordance with our assumption that coordination to cobalt occurs through the nitrogen atom, forming intermediate ***5*** (Mechanism 1) in which two molecules of the diaziridinone are bound to the metal. After the coordination an electronic de-shielding on the heterocycle occurs, which diminishes the basicity of the non-coordinated nitrogen atom, inhibiting the formation of a polymeric complex, in the same way as is observed in the reactions with diaziridines[5]. After the incorporation of the alcohol molecule into the heterocycle, ring-opening occurs at one of the carbon-nitrogen bonds of ***6***, forming the corresponding intermediate ***7***. From this intermediate, the carbazate ***2*** can be displaced by other diaziridinone molecules forming ***5***, which re-starts the catalytic cycle.



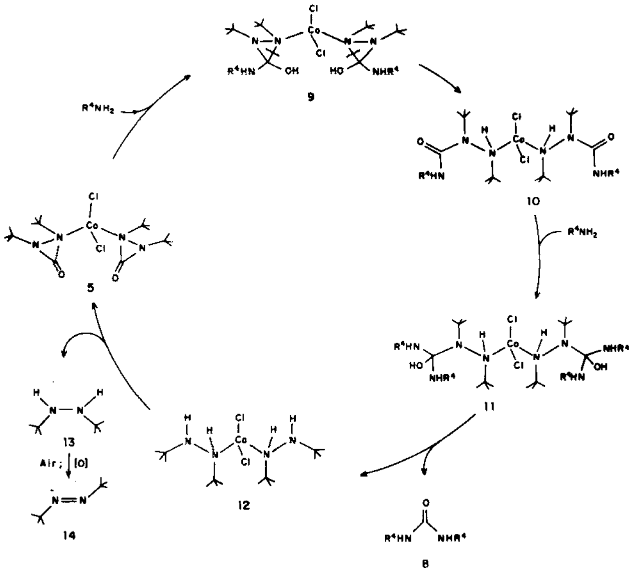
Mechanism 1.

Using methanol as a nucleophile, in the absence of cobalt dichloride, a reaction time of 43 h is necessary to quantitatively convert the diaziridinone to the corresponding carbazate[4]. These results indicate that the nucleophilic attack at the carbonyl carbon of the diaziridinone is easy for the coordinated heterocycle, but difficult when it is in its free form. This difficulty can be interpreted with the aid of structural data which provide a strong indication that diaziridinones have a *trans* stereochemistry in which the *trans*-oriented *t*-alkyl groups provide considerable steric hindrance to the carbonyl group[4]. On the other hand, a nucleophilic attack at the carbonyl carbon is much faster for *trans*-2,3-di-*t*-butylcyclopropanone[6] than for di-*t*-butyldiaziridinone. Thus, delocalization of the nitrogen lone pair electrons contributes to the low reactivity towards nucleophilic attack at the carbonyl carbon of the diaziridinones. Another factor that contributes to the reduced reactivity of the diaziridinones may be the repulsion between a nitrogen lone pair of electrons and the nucleophile as it approaches the carbonyl carbon. In this way, coordination to the transition metal lowers the electronic delocalization of the nitrogen lone pair electrons at the same time as it diminishes the repulsion with the nucleophile, enhancing reactivity at the carbonyl carbon.

Reactions with amines

Nucleophilic attack at the carbonyl carbon of 1,2-di-*t*-butyldiaziridinone is also very slow. In the reaction with stoichiometric amounts of *i*-propylamine, after stirring for 96 h at room temperature, the formation of a mixture of 1,2-di-*t*-butyl-4-isopropylsemicarbazide (35%), 1,3-diisopropylurea (43%) and 1,2-di-*t*-butylhydrazine (11%) is observed[4]. On the other hand, 1,2-di-*t*-butyldiaziridinone reacts with amines in the presence of catalytic amounts of cobalt dichloride, at room temperature for 4 h, forming the corresponding ureas ***8*** in yields up to 92% (Scheme 1).

Again, after the coordination of two molecules of the diaziridinone to cobalt dichloride, forming intermediate ***5*** (Mechanism 2), it easily reacts with two molecules of the amine, forming ***9***, which undergoes ring opening at the carbon-nitrogen bond. The intermediate ***10*** reacts with two more molecules of the amine forming ***11***, from which the elimination of the corresponding urea ***8*** occurs. From intermediate ***12***, the displacement of the hydrazine ***13*** by another diaziridinone molecule occurs, forming ***5***, which re-starts the catalytic cycle. It is important to note that all the cobalt is recovered as aminecobalt(III) chloride complexes, which are the products of air oxidation of the corresponding aminecobalt(II) chloride complexes. This indicates that intermediate ***12***, even in the absence of diaziridinone, eliminates the hydrazine ***13*** which is further air oxidized to the corresponding azo compound ***14***.



Mechanism 2.

Based on these results, we can observe that when cobalt dichloride is used to activate the heterocycle the formerly difficult nucleophilic attack at the carbonyl carbon of diaziridinones can be performed under mild conditions in few hours. It is still important to note that these reactions present high selectivity, leading to the formation of carbazates and ureas without any by-products. This clearly shows the activating effect of cobalt dichloride on the reactivity of the heterocycle. Unfortunately, it was not possible to isolate any complex in which the ring system of the diaziridinone is preserved, which would allow study of the electronic effects on the heterocycle, due to coordination to a transition metal.

It is important to note that the use of other salts, including $NiCl_2$, $PdCl_2$ or $RhCl_3$, leads to the stoichiometric formation of insoluble complexes resulting from the rupture of the ring system of the diaziridinone.

Experimental Details

NMR spectra were recorded on a BRUKER AW-80 spectrometer using tetramethylsilane as internal standard. IR spectra were measured on a JASCO IR 700 spectrometer. Elemental analyses were performed on a Perkin-Elmer 2400 CHN Elemental Analyzer. Atomic absorption measurements were performed on a Perkin-Elmer mod. 5000 spectrometer. All melting points are uncorrected.

*General procedure for the synthesis of di-*t*-butylcarbazates 2*

Cobalt(II) chloride (2 mg, 0.015 mmol) was added to the alcohol (5 mL) in a round-bottomed flask, followed by the slow addition of 1,2-di-*t*-butyldiaziridinone (0.25 g, 1.5 mmol). The solution was kept at room temperature during stirring. The excess alcohol was evaporated and chloroform (5 mL), followed by light petroleum ether (10 mL), was added to the resulting mixture. The slightly colored solution was separated from the small amount of solid and filtered through a celite column. The clear solution obtained was evaporated, leaving a colorless oil.

The small amount of solid which precipitated was washed several times with *n*-hexane and dried under vacuum, giving a blue powder which presents 45.9% cobalt (determined by atomic absorption spectrometry; $CoCl_2$ requires 46.10% cobalt). This was dissolved in water, giving a pink solution, and then a white precipitate upon the addition of aqueous silver nitrate solution. These results gave a strong indication that at the end of the reaction cobalt is recovered as $CoCl_2$.

2a- Reaction time was 3 h. This product was obtained in quantitative yield. IR (film) 3340 and 1698 cm^{-1}. ^1H-NMR ($CDCl_3$) 4.20 (q,2H); 4.07 (s,1H); 1.39 (s,9H); 1.26 (t,3H) and 1.07 ppm (s,9H). (Found C,61.01; H,10.98; N,12.80. $C_{11}H_{24}N_2O_2$ requires C,61.11; H,11.11; N,12.96%).

2b- Reaction time was 8 h. Yield 80%. IR (film) 3400 and 1700 cm^{-1}. The ^1H-NMR spectrum of this product was identical to that described in the literature[4]. (Found C,59.10; H,10.80; N,13.70. $C_{10}H_{22}N_2O_2$ requires C,59.40; H,10.89; N,13.86%).

2c- Reaction time was 4 h. Yield 75%. IR (film) 3340 and 1700 cm^{-1}. (Found C,62.70; H,11.35; N,12.20. $C_{12}H_{26}N_2O_2$ requires C,62.20; H,11.30; N,12.17%).

General procedure for the synthesis of 1,3-dialkylureas 8

Cobalt(II) chloride (2 mg, 0.015 mmol) was added to a round-bottomed flask containing the amine (5 mL), followed by the slow addition of 1,2-di-*t*-butyldiaziridinone (0.25 g, 1.5 mmol). The solution was kept at room temperature for 4 h under stirring. After this period light petroleum ether (10 mL) was added and the resulting solution was separated from a small amount of brown precipitate. The solution was maintained in a freezer for 12 h and the crystalline precipitate which appeared was filtered off, washed several times with *n*-hexane, and dried under vacuum, yielding colorless crystals.

The brown precipitates which formed, which gave white precipitate upon the addition of aqueous silver nitrate solution, were washed several times with *n*-hexane and dried under vacuum. The amount of cobalt, determined by atomic absorption spectrometry, in each of these precipitates corresponds to that calculated for the corresponding hexaminecobalt(III) chloride complexes.

8a- Yield 85%. M.p. 240-241° (lit.[4] 241-242°) and an IR spectrum identical to an authentic sample. (Found C,62.50; H,11.59; N,16.18. $C_9H_{20}N_2O$ requires C,62.59; H,11.62; N,16.27%).

8b- Yield 90%. M.p. 189° (lit.[7] 192°) and an IR spectrum identical to an authentic sample. (Found C,58.10; H,11.09; N,19.38. $C_7H_{16}N_2O$ requires C,58.33; H,11.11; N,19.44%).

8c- Yield 92%. M.p. 137-139°. IR(KBr) 3382, 1613 and 1572 cm^{-1}. ^{1}H-NMR ($CDCl_3$) 7.28 (m,10H); 4.42 (t,2H); 3.32 (q,4H) and 2.73 ppm (t,4H). (Found C,76.01; H,7.40; N,10.29. $C_{17}H_{20}N_2O$ requires C,76.12; H,7.46; N,10.44%).

Acknowledgments

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References

1. A. Freund, *Monatsh Chem.* 3, 625 (1882).
2. A. de Meijere, *Angew. Chem. Int. Ed. Engl.* **18**, 809 (1979).
3. F.D. Greene and J.C. Stowell, *J. Am. Chem. Soc.* **86**, 3569 (1964).
4. F.D. Greene, J.C. Stowell and W.R. Bergmark, *J. Org. Chem.* **34**, 2254 (1969).
5. P. Faria dos Santos Filho, H.O. Pastore and A.A. Bellini, *J. Braz. Chem. Soc.* **3 (3)**, 102 (1992); P. Faria dos Santos Filho and H.O. Pastore, *J. Chem. Research* **(S)**, 326 (1989).
6. J.F. Pazos and F.D. Greene, *J. Am. Chem. Soc.* **89**, 1030 (1967).
7. A.W. Hofmann, *Ber.* **15**, 756 (1882).