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$RuCl_2(PPh_3)_3$: A New Catalyst for Diazocarbonyl Insertions into Heteroatom-Hydrogen Bonds

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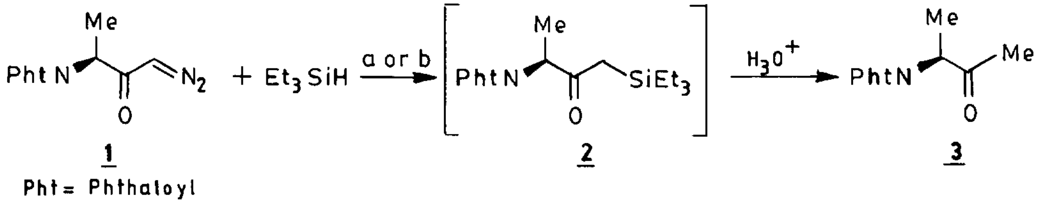
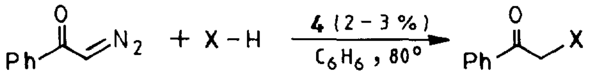
Abstract : The first ever use of $RuCl_2(PPh_3)_3$ as a catalyst for diazoketone insertions into heteroatom-hydrogen bonds is described. Copyright © 1996 Published by Elsevier Science Ltd

In a program directed towards synthesis of peptide isosteres, we recently initiated a study on the intermolecular insertion reactions of amino acid derived α-diazoketones (e.g.**1**).[1] We were especially interested in their insertion reaction with silanes,[2] since the resultant α-silylketones (e.g.**2**) promised to be attractive intermediates for further elaboration via asymmetric aldol reactions. Towards this end, we investigated the $Rh_2(OAc)_4$ catalyzed reaction of **1** with Et_3SiH which gave only 35% yield of the silylketone **2** (isolated as the methyl ketone **3**) along with considerable amount of polar side products (**Scheme 1**).



Scheme 1. a : $Rh_2(OAc)_4$ (1-2%), CH_2Cl_2, RT (35%)
b: $RuCl_2(PPh_3)_3$ (2-3%), C_6H_6, 80° (30%)

While searching for milder catalysts, our attention was drawn to a number of recent reports on ruthenium-catalyzed[3] cyclopropanation reactions with diazoacetates which prompted us to examine $RuCl_2(PPh_3)_3$ (**4**) as a catalyst for the above reaction. However, silane insertion to **1**, when catalyzed by **4**, gave very much the same results, the methyl ketone **3** being isolated in 30% yield (**Scheme 1**). Nevertheless, the fact that $Rh_2(OAc)_4$ and **4** showed comparable catalytic activity in the above reaction led us to speculate that the latter could be a potential alternative to the more expensive Rh-carboxylates as diazocarbonyl insertion catalyst, in general. Since nothing was known on Ru-catalyzed diazocarbonyl insertion reactions, we took this opportunity to investigate the catalytic behaviour of **4** in such reactions, preliminary results of which are described in this Letter.



5

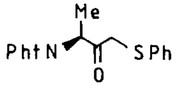
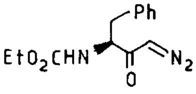
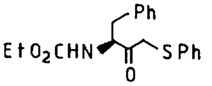
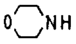
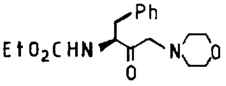
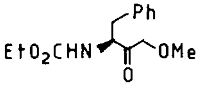
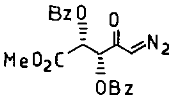
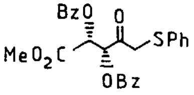
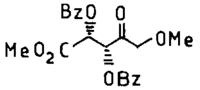
6a : X = OMe (70 %)
6b : = OPh (74 %)
6c : = SPh (80 %)
6d : = $SiEt_3$ (70 %)

Scheme 2

α-Diazoacetophenone **5** was chosen as a model substrate whose insertion reactions with methanol, phenol, thiophenol and Et_3SiH were studied with 2 - 3 mol% of 4 as catalyst in refluxing benzene (**Scheme 2**). Indeed, **4** turned out to be an efficient catalyst for these reactions producing the respective adducts **6a - d** in good yields. Benzene was found to be the ideal solvent for these reactions whereas CH_2Cl_2 or THF was totally ineffective for the purpose. This Ru-catalyst seemed to be somewhat less reactive than $Rh_2(OAc)_4$ since no reaction was observed with the former at room temperature, although under the conditions described above, the yields compared favourably with those reported with $Rh_2(OAc)_4$.[1a]

Having $RuCl_2(PPh_3)_3$ established as an efficient catalyst for diazoketone insertion reactions, we turned towards our original goal i.e. intermolecular insertion reaction of α-aminodiazoketones (e.g. **1** & **8**) into heteroatom-hydrogen bond and examined the efficacy of this catalyst for such reactions (**Table 1**). Ru-Catalyzed reaction of both the N-phthaloyl diazoketone **1** (entry 1) and N-CO_2Et protected diazoketone **8** (entry 2) with thiophenol gave 50% yield of the corresponding adducts **7** and **9**, respectively. The yields were somewhat inferior to that obtained from the simpler diazoketone **5** with thiophenol (cf.Scheme 2) and may be attributed to the nitrogenous functionalities present in **1** and **8.** However, it was quite interesting to note that during thiol insertion to **8**, no intermolecular NH-insertion was observed at all. In fact, control experiments with **8** (2 - 3% **4**, 0.2 M in benzene, 80°) failed to produce any intramolecular NH-insertion product, the diazoketone **8** being mostly recovered unchanged. That it was not a general inhibition by **4** towards NH-insertion was later shown by the successful intermolecular insertion reaction of **8** with morpholine (entry 3). This unique feature of **4** which sharply differs from Rh-catalyzed intramolecular NH-insertion in analogous α-aminodiazoketones[4] promises much broader synthetic ramifications, further exemplified by the selective intermolecular insertion of methanol to **8** (entry

Table1. Ru-Catalyzed insertion reactions of functionalized α - diazoketones.

Entry	Diazoketone	X – H	P r o d u c t	Yield (%)[a]
1.	(**1**)	PhSH	 (**7**)	50
2.	 (8)	PhSH	 (9)	50
3.	(**8**)		 (10)	47
4.	(**8**)	MeOH	 (11)	45
5.	 (12)	PhSH	 (13)	65
6.	(12)	MeOH	 (14)	60

[a] Isolated yields

4). The mild nature of this new catalyst (**4**) was also useful for insertion reactions to the tartarate-based α-diazoketone **12** (entries 5,6). Interestingly, **12** devoid of any nitrogenous functionalities gave better yields than those obtained from **1** and **8**. In all the reactions involving **8** and **12** , insertions yields are somewhat moderate (45 - 65%) due to formation of polar by-products. Nevertheless, **4** remained the catalyst of choice since $Rh_2(OAc)_4$ despite providing similar yields gave a number of side-products which required tedious separation from the desired adducts.

In summary, $RuCl_2(PPh_3)_3$, in lieu of the more expensive $Rh_2(OAc)_4$, has been shown to be an effective catalyst for diazoketone insertion into heteroatom-hydrogen bonds.[5] Significantly, for carbamate protected α-aminodiazoketones (and perhaps for other monoprotected α-aminodiazoketones) this new catalyst is uniquely selective towards intermolecular insertion into S-H, O-H, and N-H bonds with no competition whatsoever from the intramolecular N-H insertion pathway . Synthesis of peptide-isosteric substrates utilizing this unique characteristic of Ru-catalyzed diazoketone insertion reaction is currently underway.

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References :

1. General reviews on α-diaxocarbonyl compounds : a) Ye, T. ; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091 ; b) Padwa, A. ; Austin, D. J. *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1797 ; c) Padwa, A. ; Krumpe, K. E. *Tetrahedron* **1992** , *48*, 5385 ; d) Adams, J. ; Spero, D. M. *ibid* **1991**, *47*, 1765 ; e) Doyle, M. P. *Chem.Rev* **1986**, *86*, 919.
2. a) Andrey, O. ; Landais, Y. ; Planchenault, D. ; Weber, V. *Tetrahedron* **1995**, *51*, 12083 ; b) Andrey, O. ; Landais, Y. ; Planchenault, D. *Tetrahedron Lett.* **1993**, *34*, 2927 ; c) Bagheri, V. ; Doyle, M. P. ; Taunton, J. ; Claxton, E.E. *J. Org. Chem.* **1988**, *53*, 6158.
3. a) Demonceau, A. ; Dias, E. A. ; Lemoine, C. A. ; Stumf, A. W. ; Noels, A. F. ; Pietraszuk, C. ; Gulinski, J. ; Maccinics, B. *Tetrahedron Lett.* **1995**, *36*, 3519. b) Demonceau, A. ; Lemoine, C. A. ; Noels, A. F. ; Chizhevsky, I. T. ; Sorokin, P. V. *ibid* **1995**, *3b*, 8419 ; c) Nishiyama, H. ; Itoh, Y. ; Matsumoto, H. ; Park, S. B. ; Itoh, K. *J. Am. Chem. Soc.* **1994**, *116* 2223 ; d) Demonceau, A. ; Noels, A. F. ; Saive, E. ; Hubert, A. J. ; *J. Mol. Cat.*, **1992**, *76*, 123 ; e) Demonceau, A. ; Saive, E. ; de Froidmont, Y. ; Noels, A. F. ; Hubert, A. J. ; Chizhevsky, I. T. ; Lobanova, I. A. ; Bregadze, V. I. *Tetrahedron Lett.* **1992**, *33*, 2009 .
4. a) Hanessian, S. ; Fu, J. -M. ; Chiara, J. -L. ; Difabio, R. *Tetrahedron Lett.* **1993**, *34*, 4157 ; b) Burger, K. ; Rudol ph, M. ; Fehn, S. ; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 285 ; c) Ko, K. -Y.; Lee, K. -I. ; Kim, W. -J. *Tetrahedron Lett.* **1992**, *33*, 6651 ; also see ref. 1a, esp. 1105ff.
5. All compounds gave satisfactory spectral (IR, NMR) data in accordance to the proposed structure. Representative procedure: To a refluxing solution of PhSH (0.27 g, 2.43 mmol) and **4** (0.018 g, 0.018 mmol) in benzene (12 ml) was added dropwise to a solution of **8** (0.15 g, 0.60 mmol) in CH_2Cl_2 (6 ml) over a period of 3h. After addition was complete, the solution was refluxed for an additional 15 min after which it was diluted with ether, washed with water, dil. NaOH soln. and again water and dried (Na_2SO_4). Removal of solvent followed by silica-gel chromatography (5 - 15% EtOAc in light petroleum) gave **9** (0.08 g, 50%); $[\alpha]_D^{28}$ - 15.72 (c=0.5, $CHCl_3$); IR (cm^{-1}): 3420, 1700 (br), 1500, 1210; ^{1}HNMR($CDCl_3$): 1.19 (3H, t, J 7), 2.99(2H, m), 3.65 (2H, s), 4.07 (2H, q, J 7), 4.80 (1H, m), 5.20 (1H, br), 6.99 - 7.53 (10H, m).

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