Control of Chemoselectivity in Dirhodium(II)-Catalyzed Reaction of 5,6-Dioxygenated 2-Diazo-3-oxohexanoates: C–H Insertion Reaction *versus* Oxonium Ylide Formation

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Methyl (*S*)-2-diazo-4-(3,3-dimethyl-2,4-dioxolan-1-yl)-3-oxobutanoate (1), upon treatment with $Rh_2(OAc)_4$ in boiling dichloromethane, gave methyl (1*S*,5*S*)-2,2-dimethyl-7-oxo-3,8-dioxabicyclo[3.2.1]octane-1-carboxylate (2) *via* oxonium ylide formation/1,2-shift. On the other hand, similar treatment of methyl (*S*)-5,6-bis(*tert*-butyldimethylsilyloxy)-2-diazo-3-oxohexanoate (3a) gave methyl 3-(*tert*-butyldimethylsilyloxy)-5-oxo-1-cyclopentene-1-carboxylate (4a) *via* the C–H insertion reaction.

Key words dirhodium(II) catalyst; C–H insertion reaction; diazoketone; cyclopentenone; oxonium ylide; 1,2-shift

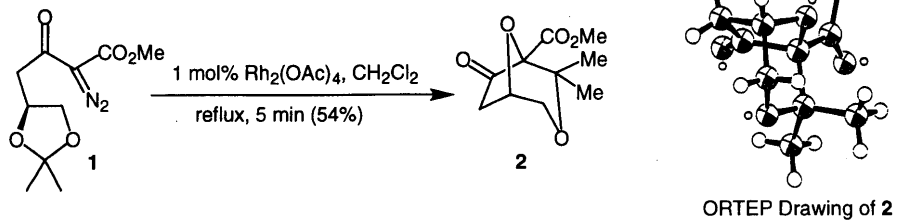
The dirhodium(II)-catalyzed C–H insertion reaction of α-diazocarbonyl compounds has recently been widely used in organic synthesis.[1] However, it is sometimes difficult to control the chemoselectivity because of the high reactivity of the rhodium carbenoid intermediates, which can react with unactivated C–H bonds, C–C multiple bonds, heteroatoms, *etc.* In connection with our studies on the dirhodium(II)-catalyzed C–H insertion reaction of highly functionalized α-diazoketones,[2] we investigated the reaction of 5,6-dioxygenated 2-diazo-3-oxohexanoates (**1** and **3**) in the hope that a new route to 2,3-dioxygenated 5-oxocyclopentanecarboxylates might result. Herein, we report the contrasting behavior of these diazoketones which depends upon the protecting group of the oxygen atoms.

First we examined the reaction of methyl (*S*)-2-diazo-4-(3,3-dimethyl-2,4-dioxolan-1-yl)-3-oxobutanoate (**1**), which was prepared from (*S*)-malic acid.[3] Treatment of **1** with 1 mol% of dirhodium(II) tetraacetate [$Rh_2(OAc)_4$] in dichloromethane (CH_2Cl_2) under reflux for 5 min gave methyl (1*S*,5*S*)-2,2-dimethyl-7-oxo-3,8-dioxabicyclo-[3.2.1]octane-1-carboxylate (**2**)[4] in 54% yield without any C–H insertion products. The structure of **2** was confirmed by X-ray analysis.[5]

Since the reaction of acetonide (**1**) with $Rh_2(OAc)_4$ did not produce any C–H insertion reaction products, we next examined the dirhodium(II)-catalyzed reaction of bis-TBDMSoxy derivatives (**3a** and **3b**), which were also prepared from (*S*)-malic acid.[6] When compound **3a** was heated with $Rh_2(OAc)_4$ in CH_2Cl_2 under reflux for 5 min and the reaction mixture was then passed through a short pad of silica gel, labile methyl (*S*)-3-TBDMSoxy-5-oxo-1-cyclopentene-1-carboxylate (**4a**)[7] was obtained in 68—83% yield. The structure of **4a** was determined by the spectroscopic data and chemical correlations. The IR spectrum showed absorptions due to the cyclopentenone (1760 and 1630 cm^{-1}) and ester groups (1730 cm^{-1}) and the ^{1}H-NMR spectrum exhibited a doublet at δ 8.04 (J = 2.3 Hz) due to the olefinic proton. The reaction of **4a** with lithium dimethylcuprate gave a 8 : 1 mixture of known methyl (1*S*,2*S*,3*S*)-3-(*tert*-butyldimethylsilyloxy)-2-methyl-5-oxocyclopentanecarboxylate (**5**) and its (1*R*,2*R*,3*S*)-isomer (**6**)[2b] in 71% combined yield. A similar reaction of diazosulfone (**3b**) with $Rh_2(OAc)_4$ afforded the corresponding cyclopentenone (**4b**)[8] in 66% yield.

One possible rationalization for the formation of **2** would involve an initial formation of five-membered oxonium ylide (**A**), followed by a 1,2-shift.[9] On the other hand, in the case of **3a** the bulky TBDMS group would restrict the oxonium ylide formation and make the C–H insertion reaction at the C-6 position favorable to form cyclopentanecarboxylate (**B**), which undergoes β-elimination[10] of silanol to give cyclopentenone (**4a**).

In summary, this study revealed that the chemoselectivity of the dirhodium(II)-catalyzed reaction of 5,6-dioxygenated 2-diazo-3-oxohexanoates (**1** and **3**) can be controlled by selecting the protecting groups of the diol: the acetonide derivative (**1**) gave 3,8-dioxabicyclo[3.2.1]-octane (**2**) *via* oxonium ylide formation/1,2-shift, whereas the bis-TBDMSoxy derivatives (**3**) gave the C–H insertion products, cyclopentenones (**4**).



ORTEP Drawing of **2**

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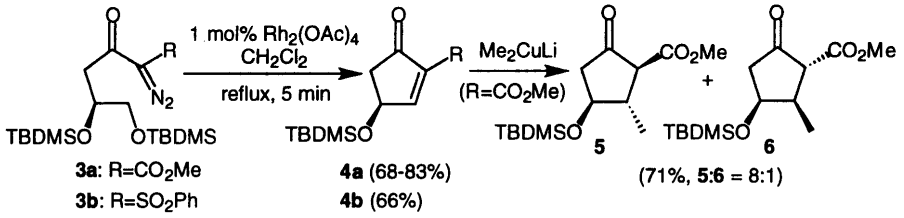

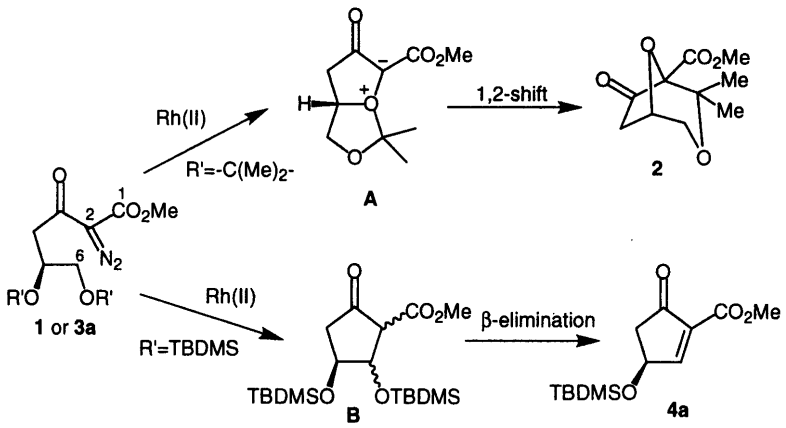

References and Notes

1) For reviews, see: Doyle M. P., *Acc. Chem. Res.*, **19**, 348—356 (1986); Doyle M. P., *Chem. Rev.*, **86**, 919—939 (1986); Adams J., Spero D. M., *Tetrahedron*, **47**, 1765—1808 (1991); Padwa A., Krumpe K. E., *ibid.*, **48**, 5385—5453 (1992); Ye T., McKervey M. A., *Chem. Rev.*, **94**, 1091—1160 (1994); Padwa A., Austin D. J., *Angew. Chem., Int. Ed. Engl.*, **33**, 1797—1815 (1994); Doyle M. P., *Aldrichimica Acta*, **29**, 3—11 (1996); Hashimoto S., Watanabe N., Anada M., Ikegami S., *J. Synth. Org. Chem., Jpn.*, **54**, 988—999 (1996); Zaragoza F., *Tetrahedron*, **53**, 3425—3439 (1997); Doyle M. P., McKervey M. A., *Chem. Commun.*, **1997**, 983—989; Doyle M. P., Forbes D. C., *Chem. Rev.*, **98**, 911—935 (1998).

2) *a*) Yakura T., Yoshida D., Ueki A., Nakao K., Ikeda M., *Chem. Pharm. Bull.*, **45**, 651—658 (1997); *b*) Yakura T., Yamada S., Kunimune Y., Ueki A., Ikeda M., *J. Chem. Soc., Perkin Trans. 1*, **1997**, 3643—3649; *c*) Yakura T., Yamada S., Azuma M., Ueki A., Ikeda M., *Synthesis*, in press.

3) The starting α-diazoketone (**1**) was prepared by homologation of the (*S*)-(3,3-dimethyl-2,4-dioxolan-1-yl)ethanal, prepared from (*S*)-malic acid,[11] with methyl diazoacetate and tin(II) chloride,[2c,12] followed by diazotransfer reaction of the resulting β-ketoester with *p*-toluenesulfonyl azide and triethylamine.

4) Compound **2**; colorless crystals, mp 93.0—94.0 °C (hexane–AcOEt); $[\alpha]_D^{25}$ −37.0° (*c*=1.01, $CHCl_3$); IR (CCl_4): 1770, 1745 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 1.42 (3H, s), 1.43 (3H, s), 2.48 (1H, dd, *J*=17.7, 0.7 Hz), 2.62 (1H, dd, *J*=17.7, 7.7 Hz), 3.47 (1H, dd, *J*=12.0, 1.0 Hz), 3.78 (3H, s), 4.25 (1H, dd, *J*=11.8, 1.8 Hz), 4.76 (1H, ddt, *J*=7.6, 1.8, 0.9 Hz).

5) Some crystal data are as follows. The crystal system was orthorhombic. Space group was $P2_12_12_1$. *R*(*Rw*) was 0.051(0.088). The details will be described elsewhere.

6) The diazoketoester (**3a**) was synthesized starting from methyl (*S*)-3,4-dihydroxybutanoate (**7**);[11] silylation and reduction with diisobutylaluminum hydride, followed by homologation and diazotransfer reaction. The diazoketosulfone (**3b**) was prepared by alkylation of the bis-TBDMSoxy derivative of **7** with methyl phenyl sulfone and lithium diisopropylamide, followed by diazotransfer reaction of the resulting β-ketosulfone.

7) Compound **4a**; a colorless oil; IR (CCl_4): 1760, 1730, 1630 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.14 (3H, s), 0.15 (3H, s), 0.91 (9H, s), 2.44 (1H, dd, *J*=18.3, 2.6 Hz), 2.89 (1H, dd, *J*=18.3, 6.2 Hz), 3.84 (3H, s), 4.98 (1H, dt, *J*=6.2, 2.4 Hz), 8.04 (1H, d, *J*=2.3 Hz).

8) Compound **4b**; colorless crystals, mp 90.0—91.5 °C (hexane–AcOEt); $[\alpha]_D^{26}$ −80.1° (*c*=1.02, $CHCl_3$); IR (CCl_4): 1740, 1630, 1320, 1150 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ: 0.12 (3H, s), 0.14 (3H, s), 0.90 (9H, s), 2.43 (1H, dd, *J*=18.5, 2.6 Hz), 2.88 (1H, dd, *J*=18.5, 6.2 Hz), 5.00 (1H, dt, *J*=6.2, 2.4 Hz), 7.52—7.61 (2H, m), 7.63—7.70 (1H, m), 8.05—8.10 (2H, m), 8.13 (1H, d, *J*=2.3 Hz). Although racemic **4b** was reported in the literature,[13] its spectral data are not available.

9) Very recently Doyle and co-workers reported a similar oxonium ylide formation/1,2-shift of acetonide derivatives with chiral dirhodium reagents, see: Doyle M. P., Ene D. G., Forbes D. C., Tedrow J. S., *Tetrahedron Lett.*, **38**, 4367—4370 (1997).

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