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Dirhodium(II) Tetra(triphenylacetate): A Highly Efficient Catalyst for the Site-selective Intramolecular C-H Insertion Reactions of α-Diazo β-Keto Esters

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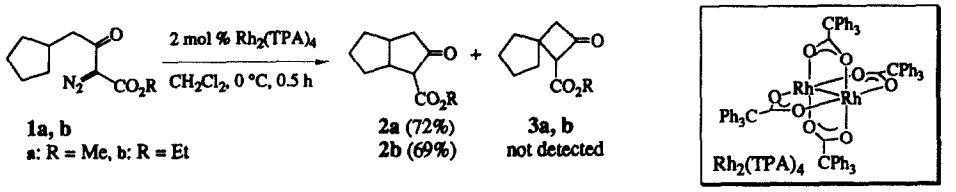
Abstract: Dirhodium(II) tetra(triphenylacetate), $Rh_2(TPA)_4$, featured by a bulky bridging ligand has been demonstrated to exhibit an exceptionally high order of selectivity for C-H insertion into methylene over methine in catalytic decompositions of α-diazo β-keto esters tethered to a cyclic system, thus providing an expedient and general entry to bicyclic compounds in preference to spirocyclic compounds. The efficiency is verified well by high-yield and site-controlled construction of bicyclo[3.3.0]octane derivative, a pivotal intermediate for the convergent synthesis of (+)-isocarbacyclin.

Dirhodium(II) complexes-catalyzed intramolecular C-H insertion reaction of α-diazo carbonyl compounds is currently emerging as potentially a powerful method for the construction of carbocycles and heterocycles, featuring C-C bond formation at an unactivated carbon atom.[1-5] It is well documented that cyclization of the electrophilic rhodium-carbene complexes leads to the preferential formation of five-membered rings in an acyclic, conformationally mobile system,[3a] in which the order of reactivity of the target C-H site is methine > methylene >> methyl.[3b] However, there have recently been reported an increasing number of interesting examples of C-H insertions leading to four- and six-membered rings as well as facile insertion into a methyl C-H bond in a constrained rigid system[4] and even in an acyclic system.[5] These results clearly show that the site-selectivity depends on the type of α-diazo carbonyl compounds, and also suggest that it is governed by steric and conformational factors as well as electronic factors. Given that the site-control based on the modification of the substrate by tuning the above factors is possible,[2r,4c] we are intrigued by the feasibility of the control based on the variation of the bridging ligands of the rhodium(II) catalysts.[3b,5a] While dirhodium(II) carboxylates such as dirhodium(II) tetraacetate, $Rh_2(OAc)_4$, have been widely used as catalysts in intramolecular C-H insertion reactions, Doyle and his coworkers have recently introduced dirhodium(II) tetraacetamidate,[6] $Rh_2(HNAc)_4$, as the electronically selective catalyst.[5c,d] Herein we wish to report that dirhodium(II) tetra(triphenylacetate), $Rh_2(O_2CCPh_3)_4$ [abbreviated to $Rh_2(TPA)_4$], featured by the steric bulk of the bridging ligand on the rhodium exhibits an exceptionally high order of selectivity for C-H insertion into methylene over methine in catalytic decompositions of α-diazo β-keto esters tethered to a cyclic system, with which the competitive C-H insertions take place by the aid of the commonly used catalysts.

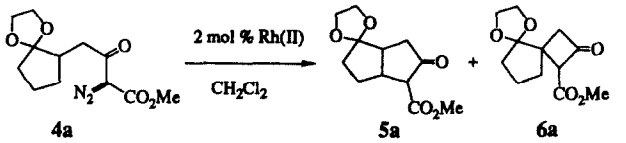
$Rh_2(TPA)_4$,[7] dark green prisms, was prepared from $Rh_2(OAc)_4$ by carboxylate exchange reaction with triphenylacetic acid according to the method of Callot.[8] An initial experiment with this catalyst was focused on decomposition of the α-diazo β-keto esters **1a,b**, because Taber and Cane independently reported that the insertion of the rhodium-carbene complex generated from **1a,b** and $Rh_2(OAc)_4$ into the C-H bond on a



cyclopentyl ring led to the formation of the bicyclo[3.3.0]octane derivatives **2a,b** and the spirocyclic compounds **3a,b** in ratios of 2:1 and 1.5:1, respectively. We were pleased to find that exposure of **1a,b** to 2 mol % of $Rh_2(TPA)_4$ in CH_2Cl_2 at 0 °C led to smooth conversion into **2a,b**[9] with no detectable amount of **3a,b**. The absence of **3a,b** was further confirmed by converting the crude product into the α,β-unsaturated esters (i, $NaBH_4$, MeOH, -50 °C, 1 h; ii, MsCl, Et_3N, CH_2Cl_2, -20 °C, 0.5 h; iii, DBU, benzene, 10 °C, 7 h). The virtually complete selectivity in insertion into the methylene C-H bond seemed to be ascribed to the steric bulk of the bridging ligand on the rhodium, suggesting the superiority of this catalyst to $Rh_2(OAc)_4$ in the C-H insertion reaction into a cyclic system.

On this positive note, we next turned our attention to the construction of the bicyclic β-keto ester **5**, key intermediate for the synthesis of (+)-isocarbacyclin.[4c,10] We previously reported that $Rh_2(OAc)_4$-catalyzed C-H insertion of the ethylene acetal **4a** produced a mixture of the desired bicyclic compound **5a** and the spirocyclic compound **6a** in a ratio of 37:63 and 64% yield, whereas the catalytic decomposition of the acetals **4b,c** of (±)-2,3-butanediol afforded **5b,c** without any sign of the formation of **6b,c** in 64% and 62% yields, respectively.[4c,10a] These results could be accounted for by the difference in steric shielding by the acetal moieties. Consequently, it became of particular interest to examine the site-selectivity with **4a**, in that the more

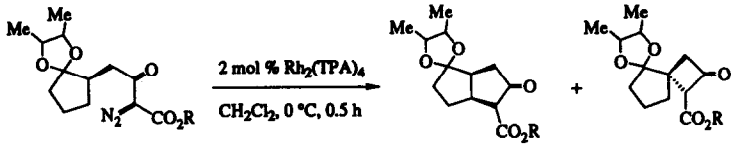
Table 1. Effects of the Bridging Ligands of Dirhodium(II) Catalysts on Site-selectivities [a]



entry	catalyst	temp, °C	time, h	% yield[b]	5a:6a[c]
1	$Rh_2(OAc)_4$	24	1	64	37:63
2	$Rh_2(O_2CCF_3)_4$	0	1	49	56:44
3	$Rh_2(HNAc)_4$	28	1	72	14:86
4	$Rh_2(O_2CCMe_3)_4$	0	1	67	37:63
5	$Rh_2(O_2CPh)_4$	0	0.5	74	54:46
6	$Rh_2(O_2CCHPh_2)_4$	0	0.5	68	64:36
7	$Rh_2(O_2CCMePh_2)_4$	0	0.5	72	82:18
8	$Rh_2(TPA)_4$	0	1.5	75	96:4

[a] Dirhodium(II) catalyst (0.02 mmol) was added in one portion to a stirred solution of **4a** (1 mmol) in CH_2Cl_2 (12 mL) at the indicated temperature under argon atmosphere. After the reaction was complete, the mixture was concentrated *in vacuo*, and chromatographed directly to give a mixture of **5a** and **6a**. [b] Isolated total yield. [c] The ratios were determined by ^1H NMR analysis of a mixture of the corresponding α,β-unsaturated esters.

precise profile of this catalyst might be obtained. Toward this end, intramolecular C-H insertion reaction of **4a** was performed by using a variety of rhodium(II) catalysts including $Rh_2(TPA)_4$, the results of which are summarized in Table 1. As seen from the table, $Rh_2(TPA)_4$ proved to be the catalyst of choice for exhibiting the highest selectivity in insertion into the methylene C-H bond. While neither $Rh_2(O_2CCF_3)_4$[11] nor $Rh_2(O_2CPh)_4$[12] showed any selectivity, the selectivities obtained by the use of $Rh_2(O_2CCMe_3)_4$,[13] $Rh_2(O_2CCHPh_2)_4$,[14] or $Rh_2(O_2CCMePh_2)_4$[14] were found to be modest, in which $Rh_2(O_2CCMe_3)_4$ still favored **6a** over **5a** as was the case with $Rh_2(OAc)_4$. The latter findings confirm that the exceptional bulkiness of the bridging triphenylacetate ligands on the rhodium is responsible for the remarkably high order of bicyclo-selectivity. It is also worthy of note that $Rh_2(HNAc)_4$ favored predominantly the C-H insertion into the methine over the methylene due to the electronically discriminating ability as mentioned by Doyle.[5c,d] Hence, $Rh_2(TPA)_4$ endowed with the sterically discriminating ability can be complementary to $Rh_2(HNAc)_4$ for the site-selective C-H insertion reactions. As might be expected, $Rh_2(TPA)_4$-catalyzed C-H insertions of **4b,c** led to the exclusive formation of the bicyclic β-keto esters **5b,c**, in which even higher yields (75% and 78%, respectively) than those with $Rh_2(OAc)_4$ could be attained. In particular, the result with **4c** makes our convergent synthesis of (+)-isocarbacyclin and its analogues more efficient.[10]

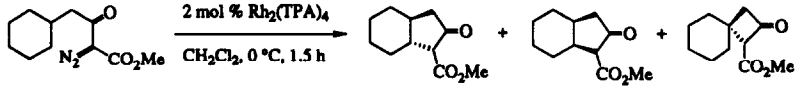


4b, c
b: R = Me, **c**: R = Bn

5b (75%)
5c (78%)

6b, c
not detected

Apart from the preferential construction of the bicyclo[3.3.0]octane derivatives, the superiority of $Rh_2(TPA)_4$ to the commonly used catalysts was also demonstrated by the insertion into a cyclohexyl ring.[15] Thus, $Rh_2(TPA)_4$-catalyzed C-H insertion of **7** furnished the *trans*-bicyclo[4.3.0]nonane derivative **8**, its *cis*-isomer **9**, and the spirocyclic compound **10** in a ratio of 94:1:5 and 89% yield,[16] whereas the ratio dropped to 50:19:31 with $Rh_2(OAc)_4$. It is noteworthy that the excellent *trans* selectivity as well as the selective insertion into the methylene C-H bond could be achieved with $Rh_2(TPA)_4$.



7

8 (84%)

9 (1%)

10 (4%)

In conclusion, $Rh_2(TPA)_4$ has emerged as a catalyst of choice for hitherto difficult site-selective intramolecular C-H insertion reactions of α-diazo β-keto esters to form bicyclic compounds in preference to spirocyclic compounds. Further studies on the scope and potential of this catalyst are currently in progress.

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References and Notes

1. For reviews, see: (a) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919; *Acc. Chem. Res.* **1986**, *19*, 348. (b) Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765.
2. (a) Wenkert, E.; Davis, L. L.; Mylari, B. L.; Solomon, M. F.; da Silva, R. R.; Shulman, S.; Warnet, R. J.; Ceccherelli, P.; Curini, M.; Pellicciari, R. *J. Org. Chem.* **1982**, *47*, 3242. (b) Taber, D. F.; Raman, K. *J. Am. Chem. Soc.* **1983**, *105*, 5935. (c) Taber, D. F.; Petty, E. H.; Raman, K. *ibid.* **1985**, *107*, 196. (d) Taber, D. F.; Schuchardt, J. L. *ibid.* **1985**, *107*, 5289. (e) Taber, D. F.; Ruckle, R. E., Jr. *Tetrahedron Lett.* **1985**, *26*, 3059. (f) Rao, V. B.; George, C. F.; Wolff, S.; Agosta, W. C. *J. Am. Chem. Soc.* **1985**, *107*, 5732. (g) Sakai, K.; Fujimoto, T.; Yamashita, M.; Kondo, K. *Tetrahedron Lett.* **1985**, *26*, 2089. (h) Hrytsak, M.; Etkin, N.; Durst, T. *ibid.* **1986**, *27*, 5679. (i) Monteiro, H. J. *ibid.* **1987**, *28*, 3459. (j) Corbel, B.; Hernot, D.; Haelters, J.-P.; Sturtz, G. *ibid.* **1987**, *28*, 6605. (k) Nakatani, K. *ibid.* **1987**, *28*, 165. (l) Adams, J.; Frenette, R. *ibid.* **1987**, *28*, 4773. (m) Taber, D. F.; Schuchardt, J. L. *Tetrahedron* **1987**, *43*, 5677. (n) Matsumoto, M.; Watanabe, N.; Kobayashi, H. *Heterocycles* **1987**, *26*, 1479. (o) Hrytsak, M.; Durst, T. *J. Chem. Soc., Chem. Commun.* **1987**, 1150. (p) Taber, D. F.; Raman, K.; Gaul, M. D. *J. Org. Chem.* **1987**, *52*, 28. (q) Doyle, M. P.; Shanklin, M. S.; Pho, H. Q.; Mahapatro, S. N. *ibid.* **1988**, *53*, 1017. (r) Stork, G.; Nakatani, K. *Tetrahedron Lett.* **1988**, *29*, 2283. (s) Mikolajczyk, M.; Zuranwinski, R.; Kielbasinski, P. *ibid.* **1989**, *30*, 1143. (t) Adams, J.; Poupart, M.-A.; Grenier, L. *ibid.* **1989**, *30*, 1753. (u) Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Rosati, O.; Wenkert, E. *J. Org. Chem.* **1990**, *55*, 311. (v) Etkin, N.; Babu, S. D.; Fooks, C. J.; Durst, T. *ibid.* **1990**, *55*, 1093. (w) Hashimoto, S.; Watanabe, N.; Ikegami, S. *Tetrahedron Lett.* **1990**, *31*, 5173. (x) Kennedy, M.; Mckervey, M. A.; Maguire, A. R.; Roos, G. H. P. *J. Chem. Soc., Chem. Commun.* **1990**, 361. (y) Doyle, M. P.; van Oeveren, A.; Westrum, L. J.; Protopopova, M. N.; Clayton, T. W., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 8982. (z) Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Rosati, O.; Wenkert, E. *J. Org. Chem.* **1991**, *56*, 7065.
3. (a) Taber, D. F.; Petty, E. H. *J. Org. Chem.* **1982**, *47*, 4808. (b) Taber, D. F.; Ruckle, R. E., Jr. *J. Am. Chem. Soc.* **1986**, *108*, 7686.
4. (a) Cane, D. E.; Thomas, P. J. *J. Am. Chem. Soc.* **1984**, *106*, 5295. (b) Brown, P.; Southgate, R. *Tetrahedron Lett.* **1986**, *27*, 247. (c) Hashimoto, S.; Shinoda, T.; Shimada, Y.; Honda, T.; Ikegami, S. *ibid.* **1987**, *28*, 637. (d) Sonawane, H. R.; Bellur, N. S.; Ahuja, J. R.; Kulkarni, D. G. *J. Org. Chem.* **1991**, *56*, 1434. (e) Ceccherelli, P.; Curini, M.; Marcotullio, M. C.; Rosati, O. *Tetrahedron* **1991**, *47*, 7403.
5. (a) Doyle, M. P.; Shanklin, M. S.; Oon, S.-M.; Pho, H. Q.; van der Heide, F. R.; Veal, W. R. *J. Org. Chem.* **1988**, *53*, 3384. (b) Adams, J.; Poupart, M.-A.; Grenier, L.; Schaller, C.; Ouimet, N.; Frenette, R. *Terahedron Lett.* **1989**, *30*, 1749. (c) Doyle, M. P.; Taunton, J.; Pho, H. Q. *ibid.* **1989**, *30*, 5397. (d) Doyle, M. P.; Bagheri, V.; Pearson, M. M.; Edwards, J. D. *ibid.* **1989**, *30*, 7001. (e) Lee, E.; Jung, K. W.; Kim, Y. S. *ibid.* **1990**, *31*, 1023. (f) Box, V. G. S.; Marinovic, N.; Yiannikouros, G. P. *Heterocycles* **1991**, *32*, 245. (g) Doyle, M. P.; Pieters, R. J.; Taunton, J.; Pho, H. Q.; Padwa, A.; Hertzog, D. L.; Precedo, L. *J. Org. Chem.* **1991**, *56*, 820.
6. Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K.-L. *J. Am. Chem. Soc.* **1990**, *112*, 1906.
7. A mixture of $Rh_2(OAc)_4$ (700 mg, 1.58 mmol), triphenylacetic acid (3.61 g, 12.5 mmol), and chlorobenzene (200 mL) was heated at reflux with vigorous stirring, while the solvent was distilled off at a rate such that 30 mL of the solvent was removed per an hour. After completion of the reaction (3 h) was confirmed by TLC analysis, the mixture was concentrated to ca. 30 mL followed by diluting with CH_2Cl_2 (100 mL). The resulting dark green solution was washed with saturated aqueous $NaHCO_3$, water, and brine, and then dried over anhydrous Na_2SO_4. Filtration and evaporation *in vacuo* furnished the crystalline residue, which was recrystallized from CH_2Cl_2 followed by drying *in vacuo* at 80 °C for 10 h to give $Rh_2(TPA)_4{\cdot}2H_2O$ (1.86 g, 85%) as dark green prisms: mp >300 °C; IR ($CHCl_3$) 1590, 1365 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.5-7.2; ^{13}C NMR (100MHz, $CDCl_3$) δ 69.14, 126.66, 127.30, 127.60, 130.41, 130.51, 142.99, 193.29; Anal. Calcd for $C_{80}H_{60}O_8Rh_2{\cdot}2H_2O$: C, 69.07; H, 4.64. Found: C, 69.14; H, 4.68. Further drying of the dihydrate complex *in vacuo* (150 °C, 20 h) gave the anhydrous $Rh_2(TPA)_4$ as yellow-green powder, which readily picked up water from the laboratory atmosphere. By this reason, the dihydrate complex was used throughout the present experiments.
8. Callot, H. J.; Metz, F. *Tetrahedron* **1985**, *41*, 4495.
9. All compounds exhibited satisfactory spectral (IR, 400 MHz ^1H NMR) and high-resolution mass spectral characteristics.
10. (a) Hashimoto, S.; Shinoda, T.; Ikegami, S. *J. Chem. Soc., Chem. Commun.* **1988**, 1137. (b) Hashimoto, S.; Miyazaki, Y.; Shinoda, T.; Ikegami, S. *Tetrahedron Lett.* **1989**, *30*, 7195.
11. Johnson, S. A.; Hunt, H. R.; Neumann, H. M. *Inorg. Chem.* **1963**, *2*, 960.
12. Legzdins, P.; Mitchell, R. W.; Rempel, G. L.; Ruddick, J. D.; Wilkinson, G. *J. Chem. Soc. (A)* **1970**, 3322.
13. Cotton, F. A.; Felthouse, T. R. *Inorg. Chem.* **1980**, *19*, 323.
14. The catalyst was prepared in a similar manner to $Rh_2(TPA)_4$.
15. Taber and Ruckle, Jr. reported that Rh(II)-catalyzed C-H insertion of **7** gave the *trans*- and *cis*-bicyclo[4.3.0]nonane derivatives **8** and **9** with the ratios dependent on the Rh(II) catalysts used (**8** to **9** ratio: $Rh_2(OAc)_4$, 3:1; $Rh_2(O_2CC_7H_{15})_4$, 5:1; tetraphenylporphyrinrhodium chloride, 15:1).[3b] However, the formation of the spirocyclic compound **10** was not mentioned.
16. These structures were further confirmed by demethoxycarbonylation of the products to the known ketones,[17] and the exact ratios were determined by ^1H NMR analysis of the corresponding α,β-unsaturated esters.
17. (a) Moriconi, E. J.; George, J. P. S.; Forbes, W. F. *Can. J. Chem.* **1966**, *44*, 759. (b) Wenkert, E.; Golob, N. F.; Hatch, R. P.; Wenkert, D.; Pellicciari, R. *Helv. Chim. Acta* **1977**, *60*, 1.

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