

# Ruthenium route to reaction

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CARBON–hydrogen bonds are ubiquitous in organic chemistry. Yet although the organic chemist has a wide repertoire of reactions that are highly specific for transformations of various functional groups, the ability to react  $sp^2$ - and  $sp^3$ -hybridized C–H bonds is limited. There are virtually no reagents that can choose between similar C–H bonds in a complex organic molecule and add a functional group to a specific site; developing catalysts for this is one of the great challenges of modern chemistry. A big step towards this goal is described on page 529 of this issue by Murai *et al.*<sup>1</sup>, who have found ruthenium complexes that can efficiently and selec-

tively catalyse the insertion of olefins into specific C–H bonds of arylketones.

Organometallic chemistry, which has given rise to many of the most useful and specific catalysts for organic reactions, has long been considered promising for catalytic functionalization of C–H bonds. Numerous reactions of organotransition-metal complexes with C–H bonds have been discovered in the past two decades<sup>2</sup>. Many of these reactions have attractive selectivity patterns; for example, several examples of specific attack on the terminal position of *n*-alkanes have been found<sup>3</sup>. But incorporating such reactions into catalytic cycles has proved difficult; although some catalytic examples have been discovered (for example, alkane dehydrogenation<sup>4</sup>, as in equation (1), and the insertion of CO (equation (2), ref. 5) or isocyanides<sup>6</sup> into C–H bonds), selectivity and yields have generally been much too low for organic synthesis<sup>7</sup>.

As organometallic catalysts are widely used to effect the addition of H<sub>2</sub> (H–H bonds) to olefins, a logical step was to try the analogous insertion of olefins into C–H bonds. Unlike the reactions in refs 4–6, olefin insertion is thermodynamically very favourable. In 1989 Jordan and Taylor discovered a cationic zirconium complex that could catalyse the insertion of ethylene, propene or 1-butene into the *ortho* C–H bond of picoline<sup>8</sup>, as shown in equation (3).

The system that Murai and co-workers now report, although related, seems to be much more general. It may prove to be the first synthetically useful example of an organometallic-catalysed transformation of a C–H bond. H<sub>2</sub>Ru(CO)<sub>2</sub>L<sub>2</sub> and Ru(CO)<sub>2</sub>L<sub>3</sub> (where L is P(C<sub>6</sub>H<sub>5</sub>)<sub>3</sub>) are found to catalyse the reaction of a huge variety of aromatic ketones with a wide range of olefins, according to equation (4).

The reactions are highly efficient. Up to 50 mol of product is obtained per mol

of ruthenium. More important, in many cases quantitative yields of product are obtained based on both olefin and aromatic ketone. In all previous examples of the catalytic functionalization of unactivated C–H bonds, a large excess of at least one reagent has been required; in most cases the substrate containing the C–H bond has been used as the solvent.

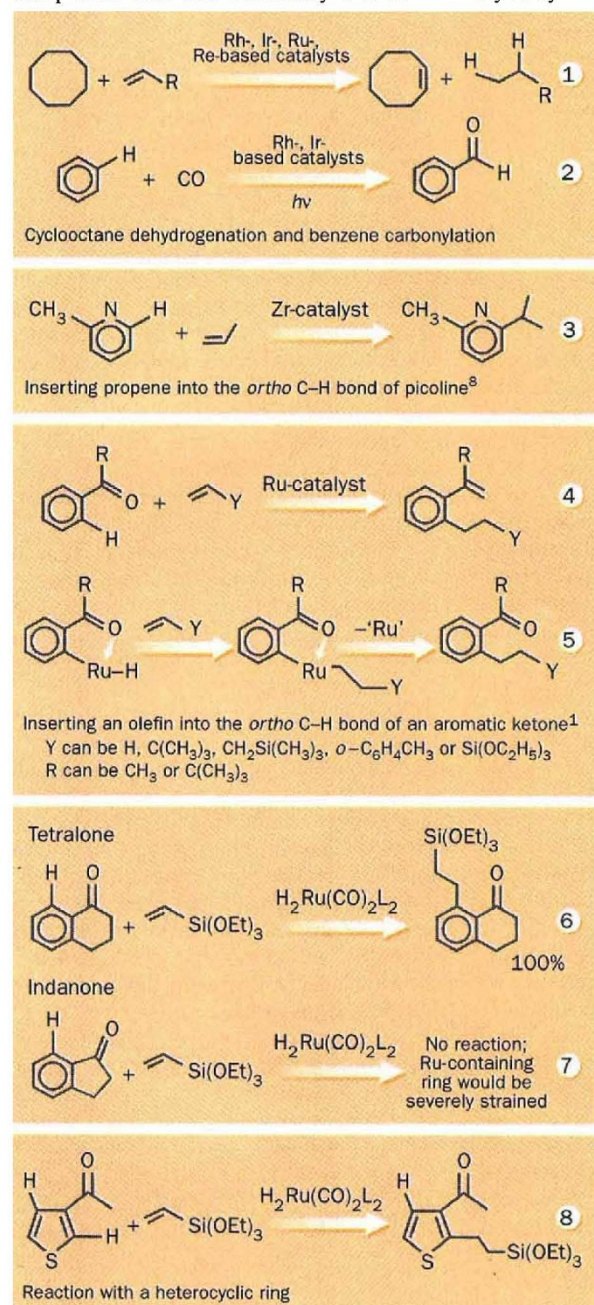
Substitution reactions specific to the *ortho* position are unusual. Electronic effects that favour *ortho* rather than *meta* attack inevitably also favour attack at the *para* position, and steric effects generally favour *para* attack over *ortho*. The key to the site-specificity of the reaction demonstrated by Murai *et al.* presumably involves coordination of the ketone carbonyl group, positioning the ruthenium to react with the *ortho* C–H bond. The olefin then inserts into either the Ru–aryl or the Ru–H bond (shown), and the product is eliminated (equation (5)).

The carbonyl-bound ruthenium–aryl complex is strongly implicated by a comparison of the reactivity of tetralone (equation (6); 100 per cent yield) with indanone (equation (7); no reaction). In the case of indanone the ruthenium-containing ring would be highly strained.

For synthesis, another important aspect of the reaction's high selectivity is the direction of addition. The aryl group is added to the less hindered side of the olefin. This is presumably because of steric effects that keep the Y group away from the crowded ruthenium centre during the olefin insertion. Additionally, and rather surprisingly, where two inequivalent *ortho* C–H bonds are present, Murai and colleagues find that selectivity is virtually complete for one of the two (equation (8)).

The next question, of course, is how general these reactions are. What other functional groups (on either substrate) can be tolerated? What other types of olefin can be inserted into the C–H bond? The answers will largely determine the range of applications that the reaction will find in organic synthesis. More broadly, for either this ruthenium catalyst or other organometallic complexes, it remains to be seen what other functional groups will act to 'direct' the functionalization of specific C–H bonds. □

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- Murai, S. *et al.* *Nature* **366**, 529–531 (1993).
- Crabtree, R. H. *Chem. Rev.* **85**, 245 (1985).
- Bergman, R. G. *Science* **223**, 902 (1984).
- Burk, M. J. & Crabtree, R. H. *J. Am. chem. Soc.* **109**, 8025–8032 (1987).
- Kunin, A. J. & Eisenberg, R. *J. Am. chem. Soc.* **108**, 535–536 (1986).
- Jones, W. D., Foster, G. P. & Putinas, J. M. *J. Am. chem. Soc.* **109**, 5047–5048 (1987).
- Davies, J. A., Watson, P. L., Liebman, J. F. & Greenberg, A. *Selective Hydrocarbon Activation* (VCH, New York, 1990).
- Jordan, R. F. & Taylor, D. F. *J. Am. chem. Soc.* **111**, 778–779 (1989).