Nitrene-transfer to olefins catalyzed by methyltrioxorhenium: a universal catalyst for the [1+2] cycloaddition of C-, N-, and O-atom fragments to olefins

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Methyltrioxorhenium (MTO) was found to catalyze the transfer of the nitrene unit of [*N*-(*p*-tolylsulfonyl)imino]-iodobenzene to a number of olefins providing aziridines in moderate to good yields, establishing MTO as a universal catalyst for the [1 + 2] cycloaddition of carbene, nitrene, and oxo units to olefins.

The metal-catalyzed [1 + 2] cycloaddition of small functional groups to olefins to yield 3-membered rings comprises a very important class of reactions in organic syntheses.[1,2] Most important among this class of reactions is the addition of isoelectronic second row (ISR) fragments, *e.g.* carbene, nitrene, and oxo species, to olefins to produce cyclopropanes, aziridines, and epoxides, respectively. From a valence-shell electron consideration, it is quite reasonable to propose that these ISR moieties may behave similarly toward olefins in the presence of the *same* metal catalyst. In particular, we were intrigued by the possibility that there may exist a "universal" catalyst which can transfer all three of these ISR species to olefins. The development of a common catalyst for multiple organic reactions is a powerful concept in synthesis. Its significance lies in the possibility that the ligand framework developed for one reaction may be applied to other reactions without further modification of the catalyst system. The advantages are most apparent in the case of enantioselective reactions catalyzed by soluble metal complexes, where the most labor-intensive research is the development of the required chiral ligands. Perhaps the most prominent example of this strategy is the work by Sharpless and coworkers on the osmium-catalyzed asymmetric olefin aminohydroxylation,[3–6] where a chiral alkaloid ligand used in the asymmetric olefin dihydroxylation reaction is applied to the synthesis of chiral β-aminoalcohols. In the area of [1 + 2] cycloadditions, the developers of Cu[2,7–9] and Rh[2,10] catalysts have utilized this strategy to some degree in that both aziridination and cyclopropanation can be carried out by the same metal catalyst.

We report herein the aziridination of olefins catalyzed by methyltrioxorhenium[11] (MTO). Combined with the known olefin epoxidation[12–14] and cyclopropanation[15] catalyzed by the same metal complex, our work establishes *the unique activity of MTO as a 'universal' catalyst for the [1 + 2] cycloaddition of carbene, nitrene, and oxo units to olefins*. To our knowledge, this is the first instance where a single catalyst can be used for three different [1 + 2] cycloaddition reactions.

In the olefin aziridination experiments, we utilized [*N*-(*p*-tolylsulfonyl)imino]iodobenzene (PhINTs) as the nitrene source. General experimental conditions involved the mixing of PhINTs (1 equiv.), olefin (5 equiv.), and MTO (10 mol% relative to PhINTs) in MeCN at the appropriate temperature (Table 1). Although the polymeric PhINTs was initially insoluble, the mixture became homogeneous as the reaction proceeded. The complete consumption of the nitrene source signaled the end of the reaction. In the absence of MTO no reaction occurred, as evidenced both by the lack of dissolution of PhINTs as well as by GC analysis of the reaction solution which shows trace $TsNH_2$ as the only nitrogen-containing product.

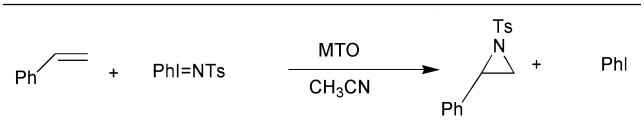
As depicted in Table 1, reaction conditions were varied to elucidate their effect on the catalyst activity with respect to the aziridination of styrene. In general, higher substrate concentrations gave better yields in shorter reaction times. A reaction of 40 equiv. of styrene relative to the nitrene source resulted in the highest yield of aziridine (45%, Table 1, entry 5). In refluxing MeCN (*ca.* 82 °C, Table 1, entries 6 and 7), the reaction was essentially instantaneous. There was no noticeable change in yield compared to those at room temperature.

Nitrile solvents (both MeCN and benzonitrile) were the most suitable for this system. In most other solvents, such as Et_2O, CH_2Cl_2 PhMe, THF, and pyridine, aziridine did not form, and all of the nitrene precursor was converted to $TsNH_2$. In the absence of nitrile solvents (neat conditions), the yield of aziridine was 27% based on PhINTs.

In all cases, $TsNH_2$ was the major side product of the aziridination reaction. To determine the hydrogen atom sources for $TsNH_2$ formation, a series of labeling experiments was conducted. A 10:1 mixture of styrene and PhINTs with MTO (10 mol% relative to PhINTs) in deuterated solvent (CD_3CN, rigorously dried and distilled) was allowed to react for 4 h, and the product mixture was analyzed by GC–MS. If the solvent was the major hydrogen source, $TsND_2$ or TsNDH would have been expected to form. However, the product from hydrogen abstraction was mostly $TsNH_2$ with a small amount of TsNDH. When styrene-d_8 in MeCN was used, the byproduct consisted mostly of $TsND_2$ (*m/z* 173) and TsNDH (*m/z* 172). Although both MeCN and styrene can supply hydrogen atoms for the $TsNH_2$ formation, the labeling experiments indicate that the substrate is the major hydrogen source leading to the formation of the $TsNH_2$ side product.

To investigate the scope of the MTO catalyzed aziridination reaction, several substituted olefins were examined using the conditions optimized for the aziridination of styrene (Table 2). In general, electron-withdrawing substituents at the *para* position of styrenes slowed down the overall reaction although yields remained essentially the same (Table 2, entries 1–4). For conjugated aromatic olefins, substitution patterns affected both

Table 1 Substrate concentration effect in the aziridination of styrene catalyzed by MTO



Entry	Substrate[a]	Temperature/°C	Reaction time[b]	Yield (%)[c]
1	5	rt	4–5 h	28
2	10	rt	2–3 h	33
3	20	rt	2–3 h	34
4	30	rt	1–2 h	39
5	40	rt	1–2 h	45
6	10	82	3 min	35
7	20	82	< 2 min	38

[a] Number of equiv. of substrate to PhINTs. [b] Time for complete dissolution of PhINTs. [c] HPLC yield (calibrated with an internal standard) based on the amount of PhINTs. All reactions were performed with PhINTs (0.2 mmol) and MTO (10 mol% relative to PhINTs) in CH_3CN (1 mL) at room temp.

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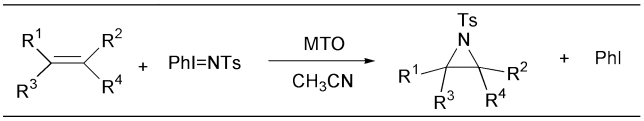
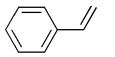
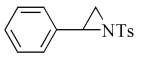
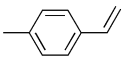
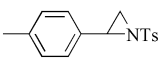
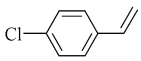
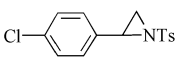
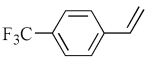
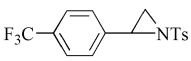
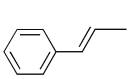
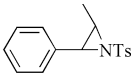
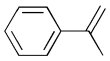
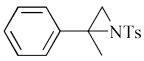
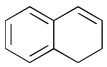
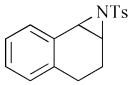
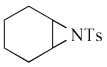
Table 2 Scope of the aziridination reaction catalyzed by methyltrioxorhenium (MTO)

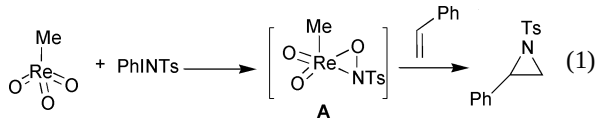


Entry	Substrates	Reaction time[a]/h	Aziridines	Yield (%)[b]
1		4–5		28
2		3		24
3		9–10		33
4		43		32
5		10		17
6		1		70[c]
7		4–5		43
8		4–5		12

[a] Time for complete dissolution of PhINTs. [b] HPLC yield based on the amount of PhINTs. All reactions were performed with PhINTs (0.2 mmol), MTO (10 mol% relative to PhINTs), and substrate (5 equiv. relative to PhINTs) in CH_3CN (1 mL) at room temp. [c] Isolated yield of a mixture of the desired aziridine and the rearranged *N*-Ts-2-phenylpropylidenimine product (*ca.* 4:3).

reaction time and yield. While (*E*)-β-methylstyrene only yielded 17% of the desired *trans*-product after 10 h (Table 2, entry 5), the *cis*-substituted 1,2-dihydronaphthalene showed faster conversion, producing 43% aziridine after 4–5 h (Table 2, entry 7). Aziridination of α-methylstyrene was fastest (1 h reaction time) among the substrates examined, and a mixture of aziridine and *N*-tosyl-2-phenylpropylidenimine was isolated (Table 2, entry 6). Finally, cyclohexene, a substrate known to be very sluggish in atom-transfer reactions, was transformed to the corresponding aziridine in low, but finite, yield (Table 2, entry 8).

Although identification of a complete mechanism accounting for the yields and products obtained from this family of reactions is beyond the scope of this initial communication, we believe that a 3-membered rhenoxaziridine intermediate **A**, formed from the coupling of [NTs] with MTO, is a reasonable common first intermediate (eqn. (1)).[15] This intermediate **A** could then react with olefins to form aziridines or undergo other transformations, such as hydrogen abstraction from the substrate to yield $TsNH_2$.



(1)

To summarize, we have demonstrated that MTO can act as a catalyst for the transfer of nitrene to olefins. This reactivity, taken together with the known MTO-catalyzed epoxidation[12–14] and cyclopropanation,[15] represents the first example of three different [1 + 2] cycloadditions of ISR fragments catalyzed by a single metal complex. Further studies, including the isolation and characterization of reaction intermediates, a complete elucidation of the reaction mechanism, the extension of the scope of this reaction to other rhenium(VII) oxo compounds and olefin substrates, as well as the asymmetric version of the MTO-catalyzed olefin aziridination are currently in progress and will be the topic of future reports.

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