Origin of the Deactivation in Styrene Aziridination by Aryl Azides, Catalyzed by Ruthenium Porphyrin Complexes. Structural Characterization of a Δ^2-1,2,3-Triazoline Ru^{II}(TPP)CO Complex

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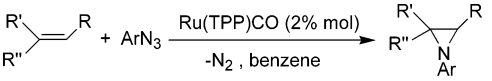
Summary: The reaction of Ru(TPP)CO (TPP = dianion of tetraphenylporphyrin) with 1-(p-nitrophenyl)-5-methyl-5-phenyl-1,2,3-triazoline yielded a Δ^2-1,2,3-triazoline ruthenium(II) porphyrin complex, which is responsible for the catalyst deactivation in the aziridination reaction of α-methylstyrene by p-nitrophenyl azide.

The transition-metal-catalyzed aziridination of alkenes is an area of active investigation, owing to the utility of the aziridine ring in organic synthesis.[1] This reaction is efficiently catalyzed by porphyrin metal complexes using mainly PhI=NSO_2Ar as the nitrogen source.[2] However, while the mechanism of related epoxidation and cyclopropanation reactions has been deeply investigated, relatively little is known on the mechanism of aziridination,[3] especially concerning the role of possible organic reaction intermediates.

We have recently reported that the catalytic amination of benzylic C−H bonds forms amines and imines using aryl azides as aminating agents in the presence of cobalt(II) porphyrin complexes.[4] Aryl azides represent a versatile class of aminating reagents, also active in the reaction with styrenes to form *N*-arylaziridines using Ru(TPP)CO (TPP = dianion of tetraphenylporphyrin) as catalyst.[5] To improve the yields and purity of the aminated products, we have performed an optimization study of the experimental conditions for the reaction between *p*-nitrophenyl azide and several olefins (Scheme 1). Some results obtained under the improved conditions are reported in Table 1. The aziridination reactions were followed by IR spectroscopy, monitoring the intensity of the 2121 cm^{-1} absorption of the N_3 group of the azide. All reactions showed a first-order dependence of the rate on azide concentration, and the corresponding kinetics constants are also reported in Table 1.

Scheme 1



Ar = *p*-nitrophenyl

Table 1. Ru(TPP)CO-Catalyzed Aziridination of Selected Olefins by *p*-Nitrophenyl Azide[a]

run	substrate	yield (%)[b]	k/[Ru] (s^{-1} M^{-1})[c]
1	styrene	98	0.81
2	α-methylstyrene	99	2.20
3	2-allylphenol	32	2.00
4	*trans*-anethole	62	1.98
5	diphenylethylene	90	2.50

[a] Experimental conditions: Ru(TPP)CO (9 mg, 0.012 mmol) in 30 mL of refluxing benzene; Ru(TPP)CO/ArN_3/olefin ratio 1/50/250. [b] Determined by ^{1}H NMR (2,4-dinitrotoluene as internal standard) at complete conversion of the starting azide. [c] k was determined using the equation $\ln A = \ln A_0 - kt$ (A = IR absorbance value at time t and A_0 = IR absorbance value at zero time).

To clarify the mechanism of the aziridination, we performed a kinetic study of the model reaction between α-methylstyrene and *p*-nitrophenyl azide catalyzed by Ru(TPP)CO. The kinetics is always first order in azide concentration and also shows a first-order dependence on catalyst concentrations. A first-order dependence of the rate on α-methylstyrene concentration is also observed up to 30% (v/v) of olefin.[6] At higher olefin concentrations the reaction rate is lower than could be expected on the basis of this kinetics (Figure 1).

To better understand these results, we studied the uncatalyzed reaction between α-methylstyrene and *p*-nitrophenyl azide at 75 °C. The kinetics is first order in both aryl azide and α-methylstyrene, and 1-(*p*-nitrophenyl)-5-methyl-5-phenyl-1,2,3-triazoline (**1**) was isolated in 73% yield (Scheme 2).[7]

The one- and two-dimensional ^{1}H NMR spectra of **1** showed the presence in solution of only one of the two

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(6) Since the boiling point of the solvent mixture changes as the fraction of α-methylstyrene increases, all reactions were run at 75 °C. Other experimental conditions are as given in the caption to Table 1.

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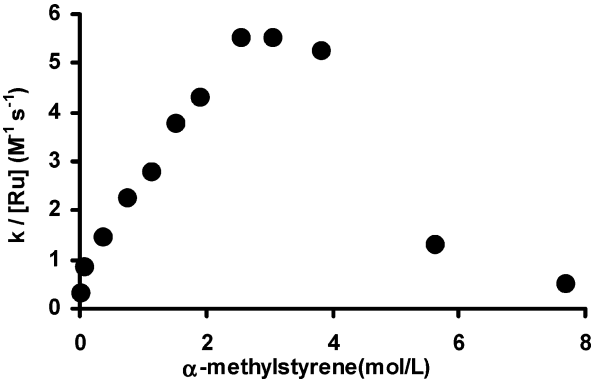
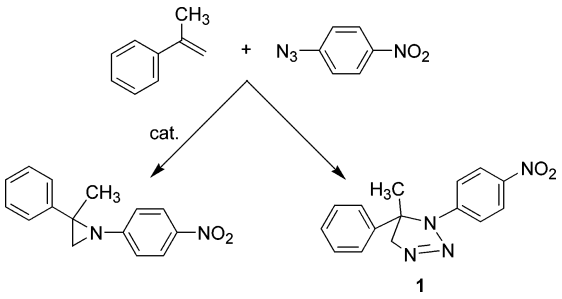


Figure 1. Dependence of the aziridination rate on α-methylstyrene concentration. Experimental conditions are as in the caption to Table 1, except for the α-methylstyrene concentration, which varies.

Scheme 2



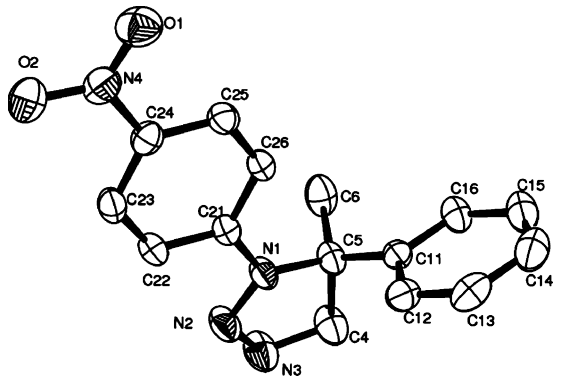


Figure 2. Ortep drawing of **1**. Selected bond lengths (Å): N3−N2 = 1.244(3); N2−N1 = 1.373(2); N1−C5 = 1.483(2); C4−C5 = 1.546(3); C4−N3 = 1.452(3). See the Supporting Information for details.

possible regioisomers, that having the substituent-bearing nitrogen of the aryl azide (N1) bonded to the carbon bearing the phenyl and methyl groups (C5).

It should be emphasized that **1** is unusually stable, and this allowed us to determine its molecular structure by single-crystal X-ray diffraction analysis (Figure 2) (see below).

In fact, despite the great number of 4,5-dihydro-1,2,3-triazoles (Δ^2-1,2,3-triazoline) synthesized,[8,9] only a few of them have been structurally chacterized.[10] Moreover, most of the cycloadditions reported in the literature give impure products and azido compounds react efficiently only with electron-poor or strained alkenes, whereas simple alkenes either do not react or react very slowly.

To investigate whether aziridine can be formed from **1** by N_2 elimination, we analyzed the thermal and photochemical stability of the triazoline molecule. Compound **1** was heated at 180 °C in vacuo, and a decomposition process was observed, but without the formation of aziridine; *p*-nitroaniline, propiophenone, and 1-phenylpropan-2-one (the last two in a 1/6 ratio) were the only detected products. The presence of ketones in the reaction mixture, formed by hydrolysis of the corresponding imines obtained via dinitrogen elimination,[8,11] was confirmed by ^{1}H NMR and GC-MS analyses. The thermolysis of **1** probably did not afford the corresponding aziridine because of the presence of the methyl group on carbon 5 of the triazoline ring. It is known[8b] that the nature of the decomposition products of triazolines also depends on the electronic nature of the substituents on the carbon atoms. If an alkyl group is present on carbon 5, the rearrangement can also proceed through a migration of the alkyl group from the 5- to the 4-carbon of the triazoline ring to afford an imine, rather than by ring contraction to give an aziridinine.

The decomposition temperature (150 °C) was identified afterward by means of a TGA (thermal gravimetric analysis) experiment.

Compound **1** was also irradiated with a low-pressure mercury lamp at room temperature, but only decomposition products were observed, probably due to competing processes associated with the excited aromatic nitro group.[12] The reaction of 1 equiv of **1** with Ru(TPP)CO at room temperature was monitored by IR and ^{1}H NMR spectroscopy. The formation of aziridine was never observed. Conversely, an immediate shift of the CO stretching frequency and the ^{1}H NMR triazoline signals to higher field were respectively registered. These data indicate that triazoline is not the precursor of aziridine in the catalytic cycle. To confirm this hypothesis, we investigated the reactivity of **1** with some Ru^{II}(Porph)CO complexes normally used as catalysts (eq 1).

$$Ru^{II}(Porph)CO + L \rightarrow Ru^{II}(Porph)(L)CO \qquad (1)$$

L = **1**; Porph = TPP (**2**), *p*-ClTPP (**3**), *p*-MeOTPP (**4**)

Again, in all cases the formation of aziridine was not observed, whereas triazoline ruthenium porphyrin complexes were isolated in high yields (∼80%). Complexes

(7) Synthesis of **1**: *p*-nitrophenyl azide (100 mg, 0.61 mmol) was dissolved in α-methylstyrene (30 mL). The resulting yellow solution was stirred at 75 °C for 28 h, the solvent evaporated in vacuo, and the residue purified by flash chromatography on silica gel (eluent dichloromethane/*n*-hexane (9/1)) (73%). Recrystallization of the residue from dichloromethane/methanol (1/1) gave crystals of **1** suitable for a structural determination.

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Table 2. Dependence of the Ratio $k_{\text{catalytic reaction}}/k_{\text{uncatalyzed reaction}}$ on α-Methylstyrene Concentration[a]

α-methylstyrene concn (mol/L)	$k_{\text{catalytic reaction}}/k_{\text{uncatalyzed reaction}}$
1.92	370
3.84	186
5.77	37
7.69	9

[a] Experimental conditions: 100 mg of *p*-nitrophenyl azide (0.610 mmol). In the catalyzed reaction, Ru(TPP)CO (9 mg, 0.012 mmol) was also present. The reactions were run in 30 mL of benzene/α-methylstyrene at 75 °C.

2,[13] **3**, and **4** were characterized by elemental analysis and IR and NMR spectroscopy (see the Supporting Information). Complex **2** was also characterized by X-ray crystal analysis (see below). The most notable feature in the ^{1}H NMR spectra is a strong high-field shift of the signals relative to the two C4 protons and to the methyl group of the triazoline moiety due to the porphyrin ring current effect.

To better understand the role of triazoline in the catalytic cycle, a reaction was carried out between α-methylstyrene (1.9 M in benzene) and *p*-nitrophenyl azide using complex **2** as catalyst or with the addition of a slight excess of **1** to the reaction mixture containing a catalytic amount of Ru(TPP)CO. In both cases the reaction rate decreased drastically, strongly indicating that **1**, rather than being an intermediate, is an inhibitor of the catalytic cycle (k(Ru(TPP)CO)/k(**2**)/k(Ru(TPP)CO/**1**=1:1.11) = 36/3.5/1). These data suggest a competition between **1** and *p*-nitrophenyl azide for the coordination to the catalytic center. To support this hypothesis, the ^{1}H NMR of a mixture of **2** and aryl azide at 75 °C was analyzed. The formation of 14% of free triazoline strongly points to a ligand substitution reaction. The presence of free triazoline was also confirmed by a GC-MS analysis of the reaction mixture.

The kinetics of the triazoline formation indicates that, at high olefin concentration, **1** is formed at a rate competitive with that of the catalytic reaction and can react with Ru(TPP)CO to generate **2**. As reported in Table 2, the decrease of the ratio $k_{\text{catalytic reaction}}/k_{\text{uncatalyzed reaction}}$ is proportional to the increase of α-methylstyrene concentration. The GC-MS analysis of the reaction mixture after a catalytic reaction run with α-methylstyrene (7.69 M) showed the presence of **1**, whereas the ^{1}H NMR analysis of the residue after evaporation of all volatiles revealed the presence of the typical signals of the aliphatic protons of **2** at negative field.

The formation of the catalytically inactive complex **2** reduces the active catalyst amount and consequently the reaction rate, thus explaining the effect observed when the solution contains more than 30% (v/v) of α-methylstyrene (see Figure 1).

To the best of our knowledge, complex **2** is the second reported transition-metal complex of a neutral triazoline. The first one, a triazoline complex of palladium(II), was obtained by one of us some years ago by reacting *cis*-cyclooctene with phenyl azide in the presence of palladium chloride.[14] It must be noted that examples of Δ^2-1,2,3-triazolines employed as ligands for transition metals are extremely rare, and in almost all of them the metal center is σ-bonded to an anionic nitrogen of the heterocycle. These triazoline complexes were synthesized directly in the coordination sphere of the metal by the reaction of azido complexes with olefins.[15]

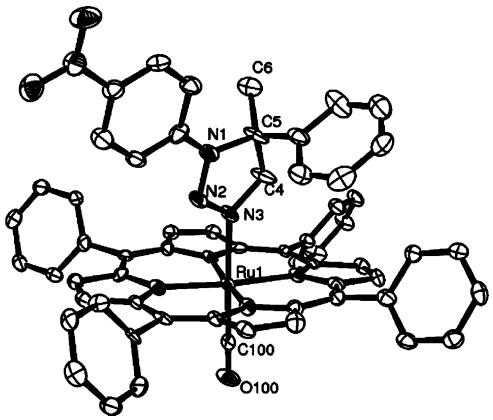

Figure 3. Ortep drawing of **2.** Selected bond lengths (Å) and angles (deg): Ru−N3 = 2.143(5); N3−N2 = 1.280(98); N2−N1 = 1.365(8); N1−C5 = 1.48(1); C4−C5 = 1.55(1); C4−N3 = 1.468(9); Ru−C1 = 1.829(7); C1−O1 = 1.157(8); $<$Ru−$N_{porph}>$ = 2.053; Ru−N3−N2 = 121.3(4); Ru−N3−C4 = 128.1(4); Ru−C1−O1 = 179.0(6). See the Supporting Information for details.

The Ru(TPP)(L)CO (L = **1**) complex has a remarkable thermal stability, compared with that of free **1**. The TGA and DSC (differential scanning calorimetry) analyses showed that **2** decomposes, in a multistep process, only above 250 °C: i.e. 100 °C over the free triazoline (vide supra).

Complex **2** is not stable in the presence of strong donor ligands, and a ligand substitution occurs. The reaction of **2** with *tert*-butyl isocyanide or dimethyl sulfoxide afforded **1** and Ru^{II}(TPP)(^{t}BuNC)$_2$ (**5**)[16] and Ru^{II}(TPP)(DMSO)CO (**6**), respectively, which were isolated and characterized (see the Supporting Information).

An interesting comparison between the molecular geometries of the isolated and complexed triazoline is possible, having determined the structures of both **1** and **2** (Figures 2 and 3, respectively) by single-crystal X-ray diffraction experiments.

While **1** spontaneously resolves during the crystallization process (in the orthorhombic space group $P2_12_12_1$), giving rise to a racemate, the reaction in eq 1

(13) Synthesis of **2**: **1** (125 mg, 0.44 mmol) was added to a benzene (50 mL) suspension of Ru(TPP)CO (311 mg, 0.42 mmol). The resulting red solution was stirred at 75 °C for 15 min and concentrated to 5 mL, and *n*-hexane (30 mL) was added. The resulting violet solid was collected by filtration, washed with *n*-hexane, and dried in vacuo (85%). Recrystallization of **2** from ethyl ether gave crystals suitable for a structural determination.

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produces a solid-state phase of **2**, probably tetragonal and acentric, but of very low crystallinity. Any attempt to solve that structure (and even to unambiguously identify the crystalline system) was unsuccessful, but, after recrystallization in Et_2O, a racemic phase (monoclinic *C*2/*c*) including the clathrated solvent was obtained and could be solved, despite poor diffraction by the crystals. The coordination of the triazoline to Ru occurs via N3, which is more basic and less sterically hindered than N2. The N2−N3 bond is elongated upon complexation (1.244(3) Å in **1**, 1.279(8) Å in **2**), suggesting that some π-bonding redistribution occurs after coordination. The Ru−CO bond distance (1.828(7) Å) lies in the range of Ru porphyrins with axial coordination to a monoaza heterocyclic ligand (such as pyridine).[17]

The conformation of the triazoline about the Ru−N bond is very likely imposed by the crystal packing more than by intramolecular effects. Molecules of **2** pack in columns elongated along the monoclinic axis *b* (although the molecular principal axis and *b* are not aligned but form an angle of 28°) and leave channels, again parallel to *b*, where the solvent is hosted, though disordered. For further information about the X-ray characterization see the Supporting Information.

In conclusion, we have reported a new aspect in the chemistry of Δ^2-1,2,3-triazolines. Thermal and photochemical reactions of triazolines that afford aziridines, by ring contraction and evolution of dinitrogen, have been widely reported in the literature.[8b,12,18] On the other hand, nothing is known about the role of triazoline when the reactions between azides and olefins are performed in the presence of a metal catalyst.[19] The identification of **2**, the first example of a ruthenium porphyrin complex of a neutral triazoline, allowed us to study for the first time the influence of triazoline on the catalytic aziridination of olefins. We have shown that in the present system, quite unexpectedly, the triazoline is not an intermediate in the catalytic cycle and may even act as an inhibitor. It is worth pointing out that in the present case the aziridine cannot be obtained without the assistance of the metal, and a more in-depth mechanistic study of the aziridination reaction is in progress. Preliminary kinetic data suggest that an azide complex of the type $Ru(TPP)CO(ArN_3)$ is the active species involved in the amination step, rather than an imido complex such as Ru(TPP)(CO)(NAr). It is important to note that the ^1H NMR and IR spectra recorded at the end of the catalytic reaction revealed the presence of the unmodified catalyst Ru(TPP)CO.

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Supporting Information Available: Text, tables, and figures giving synthetic procedures, characterization data, and X-ray crystal structure data; X-ray data are also given as CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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