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Chemistry of Ruthenium Azirinyl Complexes and Reversed Regiospecificity of the Carbonyl Insertion Reaction

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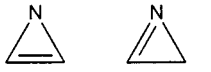
Summary: The three azirinyl complexes [Ru]−C(=NCHR (R = CN, CH=CH$_2$, Ph) are obtained from deprotonation of isonitrile complexes. For R = Ph, three isomers including 1H- and 2H-azirinyl complexes are observed at low temperature. Insertion of C=O groups of acetone, aldehyde, ester, and amide into the azirinyl ligand follows regiospecificity opposite that in the photochemical-induced insertion of the organic azirine system.

Azirine (azacyclopropene) has attracted much attention from the perspective of its strained molecular structure and unique reactivity.[1] There are two isomeric azirines, referred to as 1*H*- and 2*H*-azirine:



1*H*-azirine 2*H*-azirine

The former, known only as a transient intermediate, represents a cyclic conjugated system with four π-electrons. The 2*H*-azirine, however, shows interesting chemical behavior, and many of the reactions can be used in the synthesis of heterocyclic compounds.[2] A photochemical-induced cycloaddition of azirine with ketone or aldehyde may be utilized to prepare oxazoline. The reactivity of 2*H*-azirine is known to be dictated by the ring substituents;[3] however, due to the lack of suitable synthetic methods, the metal-coordinated azirinyl system remains a rare species. We previously described a preparation of cyclopropenyl complexes by deprotonating cationic vinylidene complexes.[4] An extension of this research would be to explore the feasibility of synthesizing azirinyl complexes by deprotonating the isonitrile RuC≡NR system.[5] In this paper we report the synthesis

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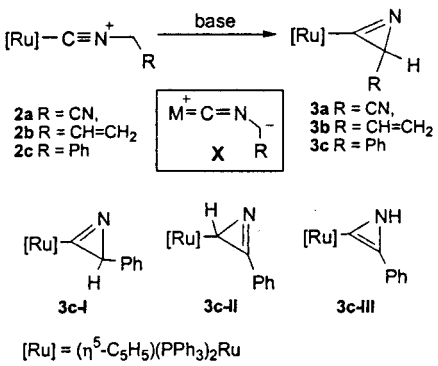
Scheme 1



of several new ruthenium azirinyl complexes and the insertion reaction of the carbonyl group of ketones, aldehydes, or esters into the C−C bond of the azirinyl ring, yielding a metal-coordinated oxazoline complex.[6] The regiospecificity of this insertion is opposite that observed in the organic azirine system and may be used for the coupling of organic halide with carbonyl-containing compounds.[7]

Reactions of [Ru]CN (**1**; [Ru] = (η^5-C_5H_5)(PPh_3)$_2$Ru) with XCH_2R readily gives the green isonitrile complexes {[Ru]$CNCH_2R$}X (**2a**, R = CN, X = Br; **2b**, R = $CH{=}CH_2$, X = I; **2c**, R = C_6H_5, X = Br; **2d**, R = $COOCH_3$, X = Br). Upon treatment with base (*n*-Bu_4NOH or *n*-Bu_4NF) at 0 °C, complexes **2a**−**c** afforded [Ru]$\overline{CNCHR}$ (**3a**−**c**), respectively (Scheme 1). Complexes **3** decompose at room temperature and are characterized by spectroscopic methods. In the ^{1}H NMR spectrum of **3b** the ddd coupling pattern of the resonance at δ 5.73, assignable to the vinyl methine proton, reveals the site of deprotonation at the NCH_2 group. For comparison the corresponding resonance of **2b** exhibits a ddt pattern. Formation of the azirinyl ring should generate a stereogenic center, which is revealed by a pattern of two doublet resonances in the ^{31}P NMR spectra of **3a** and **3b**. The singlet ^{1}H NMR resonance of the ring proton of **3a** appears at δ 2.98, similar to that of organic azirine systems.[8] In the 2D HMQC NMR spectrum this resonance is correlated to the ^{13}C resonance at δ 11.3 assignable to the sp^3 carbon of the azirinyl ring.

A number of general methods[9] are available for the synthesis of organic 2*H*-azirines. These include the modified Neber reaction, thermolysis and photolysis of vinyl azide and isoxazoles, and thermolysis of oxazaphospholines. Using the strategy illustrated in the synthesis of cyclopropenyl complexes, we have prepared the azirinyl complexes **3**. In contrast to the metal vinylidene system with a bent structure at C_β, the isonitrile ligand is linear. Therefore, the deprotonation step should yield a bent transient zwitterionic nitrile ylide X with an anionic charge most likely located at the methyne carbon atom of the isonitrile ligand (see Scheme 1), thus facilitating formation of the azirinyl ring.[10]

At −20 °C, the ^{31}P NMR spectrum of **3c** displays three sets of mutually coupled doublet pairs assigned to three isomers, possibly the 2*H*-azirinyl isomers **3c-I** (δ 51.89, 49.72;) and **3c-II** (δ 51.98, 48.82) and the 1*H*-azirinyl isomer **3c-III** (δ 51.17, 50.15) (Scheme 1), in a ratio of 3:2:2, each with a stereogenic center. In the ^{1}H NMR spectrum two sharp resonances at δ 4.71 and 4.89 are assigned to CH of the azirinyl groups of **3c-I** and **3c-II**, respectively, and a broad resonance at δ 3.23 is assigned to the NH of **3c-III**. Upon addition of D_2O the NH resonance disappears immediately at −20 °C; then within 20 min the two CH resonances also vanish, indicating interconversion of three isomers. As the temperature was lowered to −30 °C, **3c-III** disappears, and then at −40 °C only **3c-I** is observed. The stereogenic nitrogen center in the 1*H*-azirinyl ligand of **3c-III** may originate from hindered pyramidal inversion. A molecular orbital calculation showed that the organic 1*H*-azirine is approximately 30 kcal less stable than 2*H*-azirine because of ring strain and an electronically less favorable structure;[11] previously the presence of 1*H*-azirine was only inferred by indirect evidence.[12] In our system, the Ru center and the phenyl substituent on the ring could stabilize the 1*H*-azirinyl ligand, possibly by an extended conjugation of the phenyl group and metal d electron connected by the C=C double bond of the 1*H*-azirinyl ligand. The M−C(sp^2) bonding in **3c-III** also enhances stability of the 1*H*-azirinyl ligand via a d−π interaction**.** For **3c-I**, a similar d−π interaction combined with the more stable character of the 2*H*-azirinyl ligand leads us to believe that it is the most stable isomer. This explains the fact that, out of three isomers of **3c**, only one is observed at −40 °C. Transition-metal-induced reactions of organic azirine have been reported for Fe,[13] Mo,[14] and Rh, Mo, and Pd.[15]

Treatment of **2d** with *n*-Bu_4NOH afforded [Ru]-$\overline{C{=}NCH_2COO}$ (**4**), which is rationalized by hydrolysis of the ester group followed by oxygen atom attack at C_α. The ^{31}P NMR spectrum of **4** displays a singlet resonance (δ 50.5), unlike the two-doublet pattern of **3**. Previously, in the deprotonation reaction of vinylidene with an ester group, we observed an ester-substituted-cyclopropenyl complex as a kinetic product, which transformed to a furanyl complex as a thermodynamic

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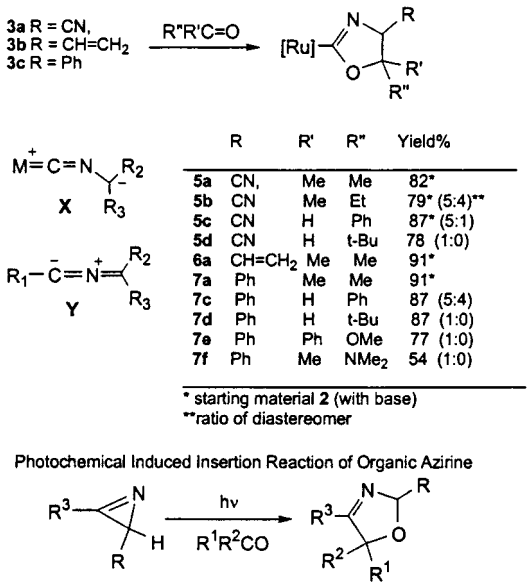
Scheme 2



product. No hydrolysis of the ester group was detected in the cyclopropenyl system. In the deprotonation reaction of the isonitrile system, however, an ester-substituted-azirinyl complex was not detected.

The reaction of **3a** with acetone yields **5a** (Scheme 2), which may also be prepared from the reaction of **2a** in acetone in the presence of *n*-Bu_4NOH. The ^{31}P NMR spectrum of **5a** also displays two doublet resonances at δ 50.0 and 51.0, indicating the presence of a stereogenic center in the cyclic ligand. Thus, the reaction is believed to proceed via insertion of a carbonyl group into the C−C bond of the azirinyl ring. Regiospecificity and diastereoselectivity of this insertion are uncovered by reactions of **3a** with 2-butanone, PhCHO, and Me_3CCHO, yielding **5b** (two diastereoisomers in a 5:4 ratio), **5c** (two diastereomers in a 5:1 ratio), and **5d** (with mild heating only one diastereomer), respectively (Scheme 2). In the ^1H NMR spectrum of **5c** coupling constants of doublet resonances at δ 4.53, 4.15 (major isomer) and δ 4.57, 4.01 (minor isomer) are both in the range of 11 Hz, indicating a $^3J_{H-H}$ interaction, thus revealing C−C bond formation at the sp^3 carbon of the azirinyl ring. Opposite regiospecificity was observed[16] in the photochemical cycloaddition of organic 2*H*-azirines with aldehydes, ketones, and esters, where the C−C bond formation takes place at the sp^2 carbon of the azirine ring. It has been proposed that azirines undergo ring opening by C−C bond cleavage on photoexcitation to give nitrile ylides[17] **Y** (Scheme 2) as an intermediate. Thus, the metal-stabilized nitrile ylide **X** (Scheme 2) can explain the regiochemistry of such a reaction. A comparison of the ratio of diastereomers of **5b**, **5c**, and **5d** implies that the diastereoselectivity is controlled by steric effect. Treatment of **3b** and **3c** with acetone affords **6a** and **7a**, respectively. We have also prepared **7c** (two diastereoisomers in a 5:1 ratio), **7d** (only one diastereomer), **7e** (only one diastereomer), and **7f** (only one diastereomer) (Scheme 2) from reactions of **3c** with PhCHO, Me_3CCHO, $PhCO_2Me$, and $MeCONMe_2$, respectively. For the aldehydes, comparable stereoselectivity was observed. For the ester and the amide, we detected only one diastereomer in the product. It is worth noting that in the organic system insertion of amide into azirine was not observed. Interestingly, the acetone moiety in the oxazoline ring of **5a** is replaced irreversibly by organic aldehyde. Namely, the reaction of **5a** with PhCHO yielded **5b**. In the organic system, such a replacement of the inserted molecule has only been observed in the oxazolone compound resulting from the reaction of azirine with CO_2.[18] The regiochemistry of the C−C bond formation in the insertion reaction is further supported by the formation of organic alcohol from **7**. Treatment of **7a** with $NaBH_3CN$ in MeOH afforded $PhCH_2CMe_2$-OH and **1** in more than 90% yield. In the presence of D_2O the reaction gave $PhCH_2CMe_2OD$. The coordinated cyanide ligand serves as a catalytic center in the coupling reaction of aliphatic halide with ketone.[19]

In conclusion, we have demonstrated the deprotonation reaction of ruthenium isonitrile complexes, yielding metal azirinyl complexes. In the azirinyl system with a phenyl substituent, three isomers could be observed by NMR spectroscopy. Facile insertion of a carbonyl group of ketone, aldehyde, ester, and amide into the ruthenium-bound azirinyl ring gives oxazoline complexes with regiospecificity opposite of that observed in the photolytic organic azirine system. Subsequent hydride reduction releases organic alcohol and the ruthenium nitrile complex. Thus, C−C bond formation between organic halide and a carbonyl group could be induced in a stepwise manner using the coordinated nitrile ligand.

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Supporting Information Available: Text giving spectroscopic and analytical data for the compounds discussed in this paper. This material is available free of charge via the Internet at http://pubs.acs.org.

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