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Rhodium(II)-catalyzed nitrene transfer with phenyliodonium ylides

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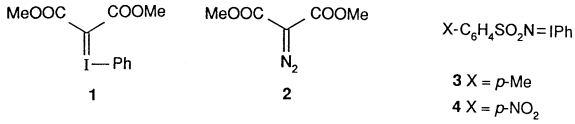
ABSTRACT: The [$Rh_2(OAc)_4$]-catalyzed decomposition of NsN=IPh {[*N*-(*p*-nitrobenzenesulfonyl)imino]phenyliodinane} affords aziridines in the presence of olefins and insertion products with compounds having activated CH bonds. The aziridination is stereospecific, and the insertion proceeds with retention of configuration. With chiral Rh(II) complexes, enantioenriched products result. A one-step mechanism involving a metal-complexed nitrene is proposed for both reactions. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: rhodium(II)-catalyzed nitrene transfer; phenyliodonium ylides

INTRODUCTION

Phenyliodonium methylides (**1**) are useful substitutes for diazo compounds (**2**) (Scheme 1) in transition metal-catalyzed carbenoid reactions.[1] The possibility of realizing analogous nitrene transfer with the corresponding nitrogen containing phenyliodonium ylides such as TsN=IPh {[*N*-(*p*-toluenesulfonyl)imino]phenyliodinane (**3**)} was first recognized about 15 years ago. Mansuy's group discovered the aziridination of olefins on metalloporphyrin-catalyzed decomposition of **3**.[2] Aziridination using TsN=IPh (**3**) and Cu(I)-based catalysts was subsequently developed and optimized to become an efficient synthetic method.[3] Cu(I) catalysts with chiral bis(oxazoline)[4] or salen[5] ligands provided aziridinations with enantioselectivities of up to 98% in selected cases.

The observation of almost enantiomerically pure pruducts in olefin aziridination with **3** in the presence of chiral Cu catalysts is consistent with a mechanism where nitrene transfer occurs in close vicinity of the metal. The intermediacy of metal-complexed nitrenes in the Cu-catalyzed aziridinations was unambiguously demonstrated by Li *et al*.[5] The details of the nitrene transfer from the metal to the substrate are, however, less clear. Aziridination may be a one-step process, in analogy with olefin epoxidation or cyclopropanation with peracids[6] or carbenes,[7] respectively, but a two-step process proceeding *via* biradical or even zwitterionic intermediates may not be ruled out *a priori*. The partial loss of stereospecificity in the Cu-catalyzed aziridination of *cis*-*β*-methylstyrene suggests a two-step mechanism,[5] where the *cis/trans* ratio of the aziridines is determined by the relative rates for ring closure and cyclization of an intermediate biradical. A similar situation prevails in the [Mn^V(salen)]-catalyzed epoxidation of olefins.[8]



Scheme 1.

The first metal-catalyzed inter- and intramolecular nitrene insertions into CH bonds by iminophenyliodinanes in the presence of metalloporphyrins or [$Rh_2(OAc)_4$] were reported by Breslow and Gellman.[9] Mansuy's group[10] investigated insertions of olefins with TsN=IPh (**3**) and Fe- or Mn-porphyrins. As in aziridination, the overall insertion may proceed in a single step in analogy with the CH insertion of singlet carbenes[11] and Rh-carbenoids,[12] but could also be the result of a two-step mechanism involving hydrogen abstraction/radical recombination with concomitant loss of stereochemical integrity. The investigations by Mansuy's group suggest that the latter mechanism should apply to the metal porphyrin-catalyzed insertions with **3**.)

RHODIUM(II)-CATALYZED AZIRIDINATION OF OLEFINS

We have previously reported the development and main characteristics of the Rh(II)-catalyzed aziridination with NsN=IPh {[*N*-(*p*-nitrobenzenesulfonyl)imino]phenyliodinane (**4**)}[13,14] Aziridines are formed in up to 85%

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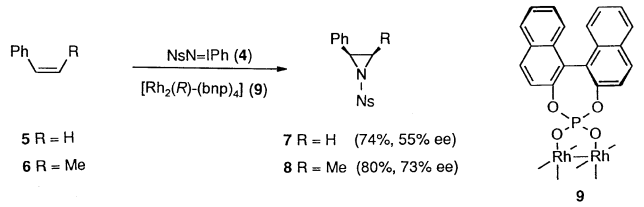
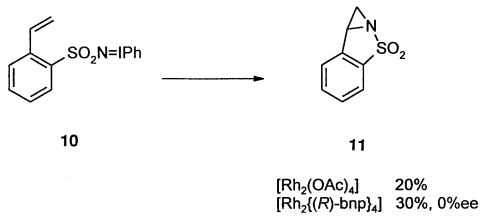


Scheme 2.



Scheme 3.

yield when styrene (**5**) (20 equiv.) is exposed to suspended NsN=IPh (**4**) (1.0 equiv.) in dichloromethane containing $[Rh_2(OAc)_4]$ (0.02 equiv.). The yields are decreased if the double bond carries electron-attracting groups, or if it is sterically hindered.[15] The aziridination of hex-2-ene and *β*-methylstyrene is stereospecific, but that of stilbene is not. The Hammett plot for aziridination of substituted styrenes exhibits a reaction constant $= -0.60$ (*vs* σ^+). With Rh(II) catalysts having chiral ligands the aziridination is enantioselective. Thus, styrene (**5**) and *cis*-*β*-methylstyrene (**6**) afforded the aziridines **7** and **8** having *ee*s of 55 and 73%, respectively, in the presence of Pirrung's bis(naphthol)phosphate catalyst **9** $\{Rh_2[(R)\text{-}(-)\text{-bnp}]_4\}$ (Scheme 2).[16] In contrast, the Rh(II) carboxamidate catalysts of Doyle and McKervey,[7,17] which have performed very successfully in carbenoid reactions, were less satisfactory in enantioselective aziridinations.

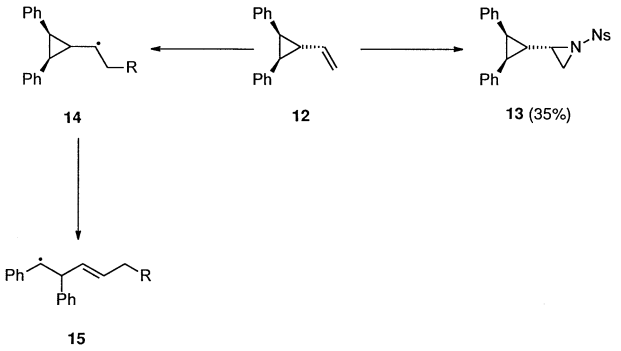
The metal-catalyzed aziridinations with TsN=IPh (**3**) and NsN=IPh (**4**) are accompanied by decomposition of the iodinane, which ultimately affords the corresponding sulfonamide $ArSO_2NH_2$ as a secondary product. This reaction is partially suppressed when the olefin is used in excess over iodinane. In the [Fe-porphyrin]-catalyzed aziridination this secondary reaction consists in hydrolysis of TsN=IPh to iodosylbenzene (PhI=O) and $TsNH_2$. The iodosylbenzene generated in this way, in turn, converts *cis*-stilbene stereospecifically to the *cis*-epoxide in an [Fe-porphyrin]-catalyzed oxidation. Alternatively, hydrolysis of the putative Fe^V=NTs intermediate may result in the formation of an [Fe–oxo porphyrin], capable of olefin epoxidation. The yields of aziridine are improved when the reaction is carried out under strictly analogous conditions in the presence of molecular sieves.[2,10] In contrast, no epoxides were formed upon aziridination of *cis*-stilbene or other olefins with $[Rh_2(OAc)_4]$, even under conditions under which $NsNH_2$ was isolated. Control experiments revealed that $[Rh_2(OAc)_4]$ does not catalyze the epoxidation of stilbene with iodosylbenzene. Since decomposition of the iodinane also occurs in the absence of water, the intermediacy of iodosylbenzene appears unlikely. An alternative pathway for $NsNH_2$ formation involving the hydrolysis of an intermediate of as yet unknown structure may exist. Attempts to trap and identify the primary decomposition product of the iodinane have so far been unsuccessful. The possibility of the intervention of a radical pathway for iodinane decomposition was tested by carrying out the aziridination of styrene (**5**) in the presence of toluene, but no products resulting from radical dimerization (bibenzyl) or from formal nitrene insertion into the CH_3 group of toluene could be detected.

Addition of a small amount of sulfolane (0.5%) to CH_2Cl_2 was beneficial for the yield of the aziridination. Under these conditions, aziridination of styrene (**5**) with an equimolar amount of NsN=IPh (**4**) and 2% of $[Rh_2(OAc)_4]$ afforded a 64% yield of aziridine **7**. Both smaller and larger amounts of sulfolane were detrimental, however. Unfortunately, these reaction conditions were not optimum for the aziridination of other olefins or for nitrene insertion into activated CH bonds (see below).

In the intramolecular aziridination, an excess of olefin may not be used, but the aziridination reaction profits from a high local olefin concentration owing to the immediate vicinity of the double bond with respect to the nitrene. In spite of this, the reaction of **10** proceeded with poor yield to **11**, 20% with $[Rh_2(OAc)_4]$, 30% with **9** (Scheme 3). No induction was observed when the reaction was catalyzed with Pirrung's Rh(II) bisnaphthol-phosphate catalyst **9**.

The aziridination of the *cis*-diphenyl-substituted vinylcyclopropane **12** proceeded in 35% yield to **13** (Scheme 4). No products except unreacted **12**, $NsNH_2$ and PhI were found in the crude reaction mixture. Aziridination of **12** *via* a radical pathway would result in the formation of the secondary radical **14**, which radical is known to undergo ring opening to **15** (Scheme 4) with a rate constant of 2×10^{10} s^{-1}.[18] The absence of products derived from **15** suggests a concerted as opposed to a stepwise radical mechanism for aziridination. This mechanism is consistent with the stereospecificity observed in the aziridination of hex-2-ene and *β*-methylstyrene.[13–15] It does not explain, however, the loss of stereospecificity in the case of stilbene, and a stepwise mechanism in which radical cyclization occurs fast in comparison with bond rotation in the intermediate radical cannot be ruled out.

Experiments similar to those reported by Li *et al.*[5] for the Cu-catalyzed aziridination with TsN=IPh were carried out with NsN=IPh–[Rh(II) bis(naphthol)phosphate] **9** in order to establish the intermediacy of a metal-complexed nitrene. Aziridination of styrene (**5**) proceeds in 74% yield and with 55% *ee* (Scheme 5). Photo-



Scheme 4.

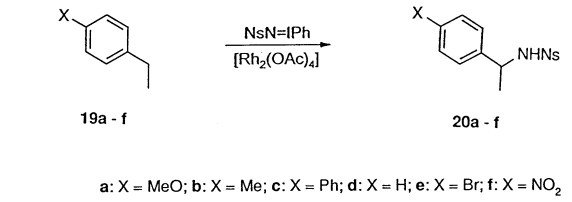
chemical decomposition of sulfonyl azides is known to produce nitrenes.[19] When NsN_3 (**16**) was decomposed photolytically in the presence of styrene (**5**) and the Rh(II) bis(naphthol)phosphate catalyst **9**, the resulting aziridine **7**, which was formed in 9% yield, had an enantiomeric excess of 17%. The azide **16** underwent no change when exposed to **9** under the conditions of the experiment. The result implies that at least part of the reaction must proceed *via* a metal-complexed nitrene **17**. The trapping efficiency of the Rh(II) catalyst is, however, significantly below that of 100% observed by Li *et al.* in the Cu–TsN_3 system. Under our reaction conditions the major proportion of the photochemically generated nitrene **18** reacts directly with **5** to afford racemic aziridine **7** and only about 30% of **18** is delivered *via* the metal-complexed species **17**.

RHODIUM(II)-CATALYZED NITRENE INSERTION INTO CH BONDS

The metal-catalyzed aziridination of olefins is often accompanied by insertion products in various amounts, which derive from competing secondary reactions. In the case of the [Mn(TPP)]-catalyzed allylic insertions, all available evidence indicates a radical mechanism. Most significantly, sulfonamidation of *cis*-hex-2-ene with **3** resulted in a product distribution typical of hydrogen abstraction from the allylic positions, followed by *cis–trans* isomerization of the intermediate allylic radicals before further reaction.[2,10] Intra- and intermolecular insertions have also been realized upon [$Rh_2(OAc)_4$]-catalyzed decomposition of iminophenyliodinanes, although the mechanism was not investigated.[9]

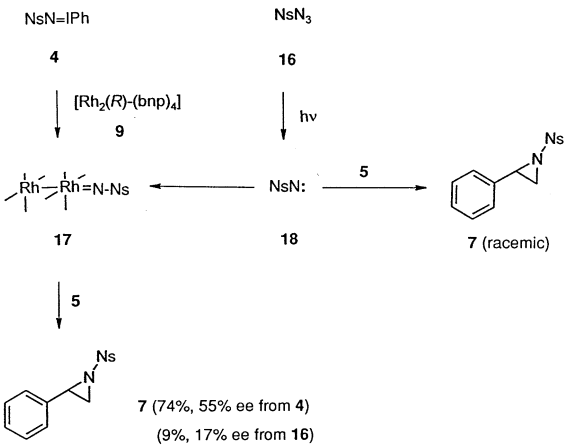
In previous papers we have reported the discovery and scope of CH insertions with the Rh(II)–NsN=IPh system.[13–15] Reaction of cyclohexene-d_1 afforded a product distribution consistent with a one-step insertion of the nitrene. The [$Rh_2(OAc)_4$]-catalyzed sulfonamidation of adamantane-1,3-d_2 exhibits an intramolecular isotope effect of 3.5.[20] Unfortunately, considering the large variation of isotope effects in the oxidation of adamantane with PhI=O–metalloporprphyrin systems (2.83–8.71),[21] this value cannot safely be assigned to a specific mechanism. The relative reactivities for sulfonamidation of substituted ethylbenzenes **19a–f** to the corresponding sulfonamides **20** with NsN=IPh–[$Rh_2(OAc)_4$] (Scheme 6) were determined by competition experiments and afforded a Hammett plot (*vs* σ^+) with a reaction constant $\rho = -0.90$ (Fig. 1), higher than that observed for aziridination of substituted styrenes with the same system.[15]

The possible intervention of radicals in the insertions



a: X = MeO; **b**: X = Me; **c**: X = Ph; **d**: X = H; **e**: X = Br; **f**: X = NO_2

Scheme 6.



Scheme 5.

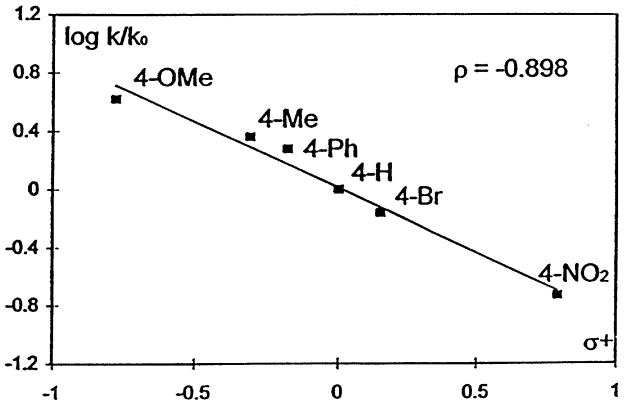
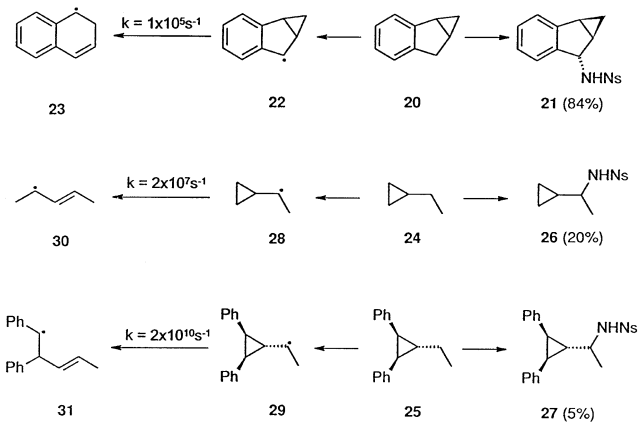


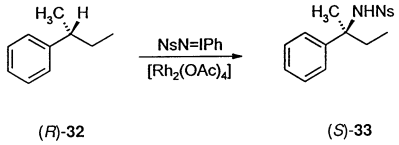
Figure 1. Hammett plot (*vs* σ^+) for sulfonamidation of substituted ethylbenzenes (**19a–f**) with NsN=IPh (**4**)–[$Rh_2(OAc)_4$]. $\rho = -0.90$ ($r = 0.989$).



Scheme 7.

was tested by means of radical clocks. Sulfonamidation of cyclopropa[*a*]indane **20** proceeded in 84% yield without ring opening to the unrearranged product **21** (Scheme 7). This result supports a one-step mechanism for insertion. However, the secondary radical **22** derived formally from hydrogen abstraction of **20** opens to **23** with a rate constant of only 1×10^5 s^{-1}.[22] Since this rate constant is low, the experiment is only partially conclusive. Indeed, radical recombination could be faster than ring opening. In order to exclude this second possibility, the cyclopropanes **24** and **25** were subjected to sulfonamidation to afford **26** and **27**. The rate constants for ring opening of the corresponding radicals **28**–**30** ($k = 2 \times 10^7$ s^{-1}) and **29**–**31** ($k = 2 \times 10^{10}$ s^{-1}) are significantly higher.[23] Unfortunately, the cyclopropane ring provides only weak activation for insertion into the adjacent CH bonds and, as a consequence, the yield of insertion products **26** and **27** was low (21 and 5%, respectively). However, no ring-opened products could be detected in the reaction mixture, which contained, in addition to insertion products, only unreacted starting cyclopropanes and $NsNH_2$. This implies that the reaction mechansim should either be single step, or in two steps with the second step very fast.

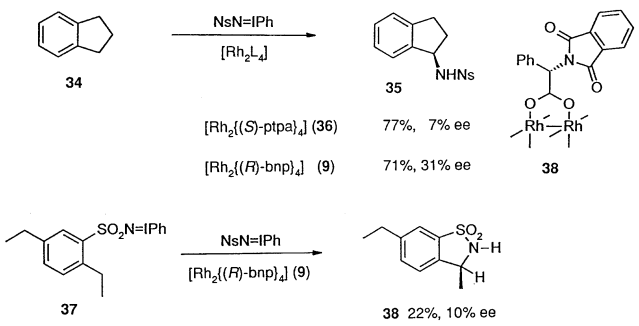
The stereospecificity of the reaction was examined with (*R*)-2-phenylbutane (**32**) as substrate. Although sulfonamidation of tertiary hydrocarbons is known to afford only poor yields of insertion products,[13–15] **32** was selected because an unambiguous result was expected from its reaction. The amidation product **33** (Scheme 8) was isolated in 3% yield and was optically active, having $[\alpha]_D^{20} = -10.2$ ($CHCl_3$, $c = 0.50$). An independently prepared sample[24] of the (*R*)-sulfonamide (*R*)-**33** had $[\alpha]_D^{20} = 8.8$ ($CHCl_3$, $c = 0.34$). The sulfonamidation product derived from (*R*)-**32** therefore has an *S*-configuration. This corresponds to retention of configuraton for the insertion, the change from *R* of phenylbutane **32** to *S* in **33** being due to the change in CIP priorities of the substituents.



Scheme 8.

Although the results of these individual experiments are not entirely satisfactory because of the low product yields, they are without exception consistent with a one-step insertion mechanism as opposed to a two-step hydrogen abstraction–radical recombination mechanism. However, a two-step mechanism where the recombination step proceeds at very high rate cannot definitely be ruled out. Conceivably, if the radical pair formed *via* hydrogen abstraction is in the singlet state, recombination could be faster than reorientation of the radicals. It is clear, however, that this mechanism would have no bearing on the possibility of enantioselective nitrene insertions. On the other hand, a mechanism involving a free nitrene in the triplet state is expected to be non-specific.

The participation of the catalyst in the product-forming step is evidenced by the observation of asymmetric induction in the sulfonamidation of indane **34** with the optically active catalysts of Ikegami $\{Rh_2[(-)\text{-ptpa}]_4\}$ (**36**) and Pirrung $\{Rh_2\{(R)\text{-}(-)\text{-bnp}\}_4\}$ (**9**) (Scheme 9). The sulfonamide **35** was formed with an enantiomeric excess of 7 and 31%, respectively. The intramolecular insertion of **37**, in turn, proceeded to **38** with an *ee* of 10% with **9**. These modest levels of induction are of little value for synthetic applications, but they are nevertheless mechanistically significant. The observation of asymmetric induction in the Rh(II)-catalyzed insertion demonstrates that the catalyst is involved not only in the decomposition of NsN=IPh (**4**), but also in the transfer of the nitrene. This is clearly different from the the [Mn(TPP)]-catalyzed insertion of TsN=IPh (**3**), which proceeds *via* a stepwise radical mechanism.[2,10]



Scheme 9.

Acknowledgments

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