

Molybdenum-mediated Synthesis of Isoxazole Compounds through a Nitrosyl Insertion into a π -Allyl Ligand

Shie-Hsiung Lin,^a Shie-Ming Peng^b and Rai-Shung Liu*^a

^a Department of Chemistry, National Tsing Hua University, Hsinchu, 30043, Republic of China

^b National Taiwan University, Taipei 30002, Republic of China

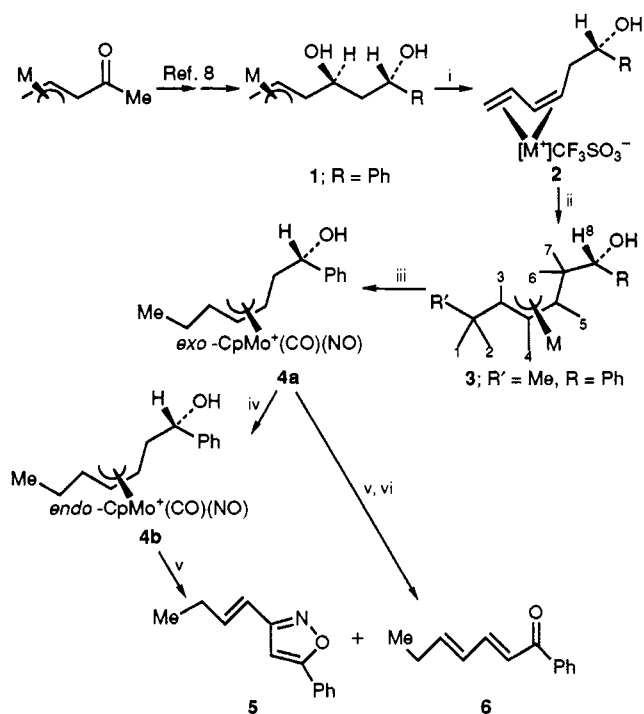
The syntheses of compounds of the type $\text{CpMo}(\text{CO})_2[\eta^3\text{-anti-1-CH}_2\text{CH}(\text{OH})\text{R-syn-3-R}'\text{CH}_2\text{-C}_3\text{H}_3]$ are described; their reactions with excess nitrosonium tetrafluoroborate produce 3-(1'-R'CH₂CH=CH)-5-R-isoxazole, which involves a remarkable nitrosyl insertion into the π -allyl ligand as the key step.

In organic reactions the nitrosonium ion NO^+ is known to act well both for electrophilic nitrosation and as an oxidizing reagent.^{1,2} In contrast, its role in organometallic reactions is merely a synthetic source for the metal–nitrosyl group.³ Little is known of the synthetic utility of the action of NO^+ on a

metal-bound organic moiety. Although efforts in this direction can be achieved through a NO^+ (linear nitrosyl) insertion into a metal–carbon bond, the occurrence³ of this process is not as common as CO insertion, especially on the low-valent metals.⁴ The $[\text{CpMo}(\text{CO})(\text{NO})(\eta^3\text{-allyl})]^+$ cation was first

reported by Faller and Rosan.⁵ Because of their highly electrophilic nature, cations of this type have been widely used as reactive intermediates for the synthesis of α -functionalized alkenes.⁶ We report here that in this NO-cationic system, the η^3 -allyl ligand is capable of undergoing a remarkable nitrosyl insertion,⁷ as a key step to produce isoxazole compounds.

The starting 1,3-diol **1** was conveniently prepared according to our procedure.⁸ Treatment of **1** with $(\text{CF}_3\text{SO}_2)_2\text{O}$ in



Scheme 1 Reagents and conditions: M = CpMo(CO)₂ i, $(\text{CF}_3\text{SO}_2)_2\text{O}$ (1.0 equiv.), Et₂O (−78 °C); ii, R'₂CuLi (6.0 equiv.); Et₂O, NH₄Cl(aq), R' = Me (56%); iii, NOBF₄ (1.2 equiv.), MeCN (−10 °C, 1 h), Et₂O (−10 °C), 90%; iv, MeCN, 28 °C, 10 h; v, NOBF₄ (10.0 equiv.), 0 °C, 6 h; vi, Na₂CO₃(aq), 0 °C

Table 1 M = CpMo(CO)₂ i, NOBF₄ (10.0 equiv.), MeCN, 0 °C 4 h

Entry	R	R'	Product No. (% Yield ^a)
1	Ph	Me (3)	5 (37)
2	Ph	Ph (7)	15 (54)
3	Ph	Bu ⁿ (8)	16 (46)
4	<i>m</i> -C ₆ H ₄ OMe	Bu ⁿ (9)	17 (51)
5	<i>m</i> -C ₆ H ₄ OMe	Me (10)	18 (38)
6	Pr ⁱ	Bu ⁿ (11)	19 (39)
7	Bu ^t	Bu ⁿ (12)	20 (44)
8	Bu ^t	Me (13)	21 (35)
9		(14) ^b	—

^a Yields were calculated based on the amount of the Mo-allyl compounds. ^b Consisting of 1:1 diastereoisomers. ^c All organic products were purified by preparative TLC on silica.

anhydrous diethyl ether (−78 °C) deposited a red precipitate of *s-trans-cis*-1,3-diene cation **2** which reacted *in situ* with Me₂CuLi in diethyl ether (−78 °C) to give 1-*anti*-3-*syn*-allyl compound **3** as a single diastereoisomer (56%). The *exo-anti*, *syn*-configuration of **3** is supported by the ¹H NMR data.[†] Treatment of **3** with nitronium tetrafluoroborate (1.2 equiv.) in MeCN (−10 °C, 1 h) followed by precipitation with anhydrous diethyl ether, afforded the *exo*-3-*anti*, *syn* cation **4a** as a single stereoisomer (90%). At 28 °C, the *exo*-**4a** underwent a slow and irreversible isomerization to the more stable *endo* isomer **4b** (>90%, 10 h). Treatment of **4a** with excess nitronium tetrafluoroborate (10-fold excess, 0 °C) in MeCN, causes demetallation of the metal complex to occur liberating an organic component **5** isolated in 48% yield. Its structure was identified as an isoxazole based on an X-ray diffraction study[§] of its phenyl relative **15** (*vide infra*). According to the ORTEP drawing (Fig. 1) the η^3 -allyl ligand is capable of undergoing a rare nitrosyl insertion which adds regioselectively at the *anti*-allylic terminus. During the course of isoxazole production, an aqueous Na₂CO₃ solution was added to quench the reaction, which gave the dieneone **6** (11%) and **5** (18%). The *endo* isomer **4b** likewise gave the isoxazole in 18% under the same conditions.

As isoxazole belongs to a class of valuable aromatic heterocyclic compounds,⁹ it is important to examine the generalization of this reaction. The results are given in Table 1. The starting *anti*,*syn*-allyl compounds **7–13** were prepared *via* a similar procedure according to Scheme 1. For convenience, the isoxazole synthesis was conducted in a one-pot reaction. The yields were moderate: 35–55%. Of particular interest is the fact that no isoxazole formation is detected for the η^3 -*syn*,*syn*-allyl isomer **14**¹⁰ (entry 9) under the same conditions; the compound remained almost completely as the nitrosyl allyl cation as shown by IR spectra [$\nu(\text{CO})$ 2083vs, $\nu(\text{NO})$ 1711vs cm^{−1}].

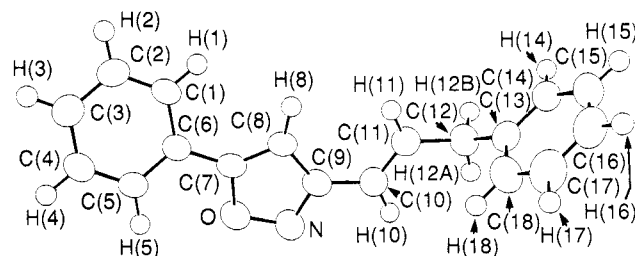
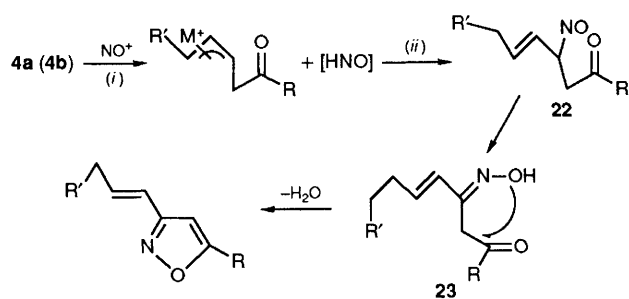


Fig. 1 ORTEP drawing of complex **15**. Pertinent bond distances (Å): C(12)–C(11) 1.498(4), C(11)–C(10) 1.322(5), C(9)–C(10) 1.457(4), N–C(9) 1.314(4), N–O 1.413(3), C(7)–C(8) 1.345(4), C(8)–C(9) 1.410(4), C(7)–O 1.368(4).

[†] The *exo*-conformation of **3** is indicated by the *anti*-H-3 proton resonance at δ 1.83, closer to that (δ 1.67) of the *exo* isomer of CpMo(CO)₂(η^3 -*syn*-1-MeC₃H₄)¹³ than to the corresponding proton resonance of the *endo* isomer at δ 2.76. The *anti*,*syn*-configuration of **3** is supported by the magnitude of the coupling parameter J_{34} 10.4 and J_{45} 8.0 Hz, indicative of *trans*- and *cis*-coupling, respectively. Moreover, the chemical shift of the *syn*-H-5-proton is δ 3.37 far downfield from that of the H-3 proton (δ 1.83).

[‡] The *anti*,*syn*-configuration of **4a** and **4b** is likewise indicated by the magnitude of the coupling constant J_{34} 11–12 and J_{45} = 8–9 Hz.

[§] Complex **15** crystallizes in the monoclinic space group $P2_1/c$. a = 10.3511(13), b = 5.7728(18), c = 24.103(3) Å. β = 101.242(10)°. V = 1400.4(5) Å³, Z = 4, final R = 0.037 and R_w = 0.038 for 1114 reflections with $I > 2\sigma(I)$ out of 1821 unique reflections: 182 parameters. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

Scheme 2 M⁺ = CpMo(CO)NO⁺

We propose the mechanism in Scheme 2. The role of nitronium ion may be twofold (i) to oxidize secondary alcohols to ketones¹¹ and (ii) to promote¹² a nitrosyl insertion into the *anti*-allylic nitroso compounds. Further hydrogen abstraction of the resulting allylic nitroso compound **22**, produces an oximine which is expected to give an isoxazole after an intramolecular cyclization. The details of the insertion step (ii) are not clear at the present stage. Methods to elucidate the mechanism are under investigation.

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