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

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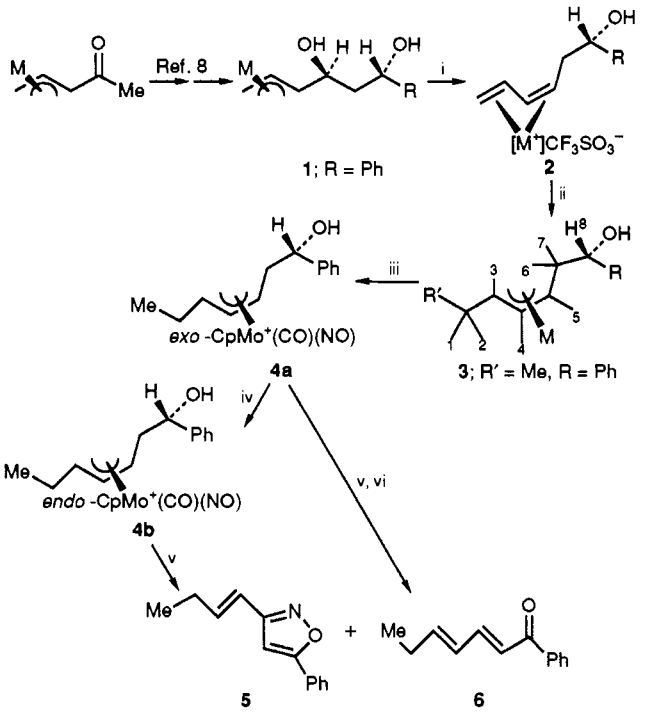
The syntheses of compounds of the type $CpMo(CO)_2[\eta^3$-*anti*-1-$CH_2CH(OH)R$-*syn*-3-$R'CH_2$–$C_3H_3]$ are described; their reactions with excess nitrosonium tetrafluoroborate produce 3-(1′-$R'CH_2CH$=CH)-5-R-isoxazole, which involves a remarkable nitrosyl insertion into the π-allyl ligand as the 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 occurrence[3] of this process is not as common as CO insertion, especially on the low-valent metals.[4] The $[CpMo(CO)(NO)(\eta^3$-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.

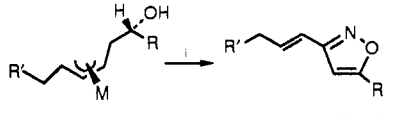
The starting 1,3-diol **1** was conveniently prepared according to our procedure.[8] Treatment of **1** with $(CF_3SO_2)_2O$ in anhydrous diethyl ether (−78 °C) deposited a red precipitate of s-*trans*-*cis*-1,3-diene cation **2** which reacted *in situ* with Me_2CuLi in diethyl ether (−78 °C) to give 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 nitrosonium 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 nitrosonium 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 Na_2CO_3 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.

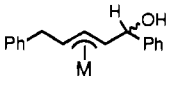
As isoxazole belongs to a class of valuable aromatic heterocyclic compounds,[9] it is important to examine the generalization of this reaction. The results are given in Table 1. The starting *anti,syn*-allyl compounds **7–13** were prepared *via* a similar procedure according to Scheme 1. For convenience, 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 [ν(CO) 2083vs, ν(NO) 1711vs cm^{-1}].



Scheme 1 *Reagents and conditions*: M = $CpMo(CO)_2$ i, $(CF_3SO_2)_2O$ (1.0 equiv.), Et_2O (−78 °C); ii, R'_2CuLi (6.0 equiv.); Et_2O, NH_4Cl(aq), R′ = Me (56%); iii, $NOBF_4$ (1.2 equiv.), MeCN (−10 °C, 1 h), Et_2O (−10 °C), 90%; iv, MeCN, 28 °C, 10 h; v, $NOBF_4$ (10.0 equiv.), 0 °C, 6 h; vi, Na_2CO_3(aq), 0 °C

Table 1 M = $CpMo(CO)_2$ i, $NOBF_4$ (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	*m*-C_6H_4OMe	Bu^n (**9**)	**17** (51)
5	*m*-C_6H_4OMe	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.

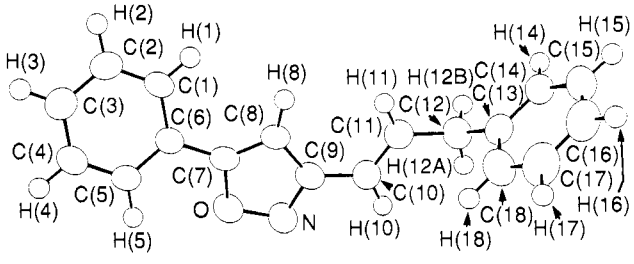
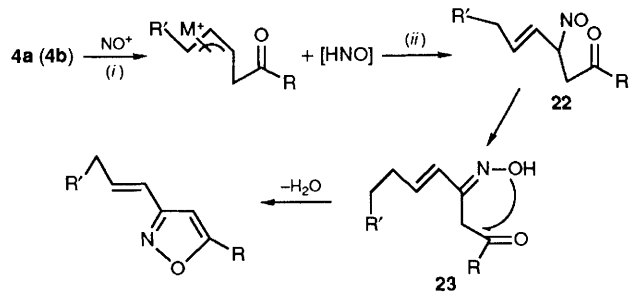


Fig. 1 ORTEP drawing of complex **15**. Pertinent bond distances (Å): C(12)–C(11) 1.498(4), C(11)–C(10) 1.322(5), C(9)–C(10) 1.457(4), N–C(9) 1.314(4), N–O 1.413(3), C(7)–C(8) 1.345(4), C(8)–C(9) 1.410(4), C(7)–O 1.368(4).

† 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 $CpMo(CO)_2(\eta^3$-*syn*-1-$MeC_3H_4)$[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) Å^3, 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 nitrosonium ion may be twofold (*i*) to oxidize secondary alcohols to ketones[11] and (*ii*) to promote[12] a nitrosyl insertion into the *anti*-alllic 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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