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Synthesis and Aldol Reactivity of *O*- and *C*-Enolate Complexes of Nickel

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The development of transition metal enolates has provided important contributions to organic synthesis.[1] The reactivity of these compounds is often characterized by high levels of selectivity or stereoselectivity, which may be tuned by modifying the nature of the metal center and the ancillary ligands. Obviously, these factors also determine the coordination mode of the enolate fragment, which in turn exerts a major influence on its reactivity.[2] Enolate σ-coordination is predominant, with *O*-binding being almost the only coordination mode observed for the early transition metals.[3] In contrast, both *O*- and *C*-coordination have been ascertained for the middle and late transition metal enolates,[4] the latter being more common for the heavier elements of the last groups.[5] It is frequently observed that *C*-bound enolates display low enolate-like reactivity and behave instead as sort of stabilized metal alkyls,[5c] undergoing typical reactivity such as migratory insertion.[3,6] However, aldol-type additions of *C*-bound enolates, although rare, are not unknown.[7] In these cases, the participation of undetected *O*-bound tautomer cannot be ruled out, since the energy difference between isomers is usually small. This prevents establishing unambiguously if the coordination mode of the enolate ligand could have an influence not only in the reaction rate but also in its selectivity. To obtain some clear indications on the relative reactivities of *C*- and *O*-bound enolates, we set out to prepare σ-coordinated enolate complexes of nickel, in which the interconversion between the two modes is hindered under normal conditions. To this end, we devised the cyclic complex **1**, in which the enolate functionality is part of a rigid metallacyclic structure. Herein we describe the synthesis of the enolate complex **1** and its thermal equilibration with its isomeric *C*-bound enolate **2**, as well as their reactivity toward enolizable and nonenolizable aldehydes (MeC(O)H and PhC(O)H).

Treatment of a THF solution of Ni(C_6H_4-*o*-C(O)CH_3)(Cl)(dippe) with 1 equiv of KO^{t}Bu allows the preparation of the nickel enolate[8] **1** in good isolated yields (ca. 60%). *O*-Coordination of the enolate fragment can be proposed on the basis of the NMR spectra. Thus, the terminal methylene group gives rise to two signals in the ^{1}H spectrum, at δ 4.62 and 4.79 that correlate (^{1}H−^{13}C HETCOR experiment) with a ^{13}C resonance at 75.9 ppm which exhibits no coupling to phosphorus. In addition, the formulation of **1** has been confirmed by a single-crystal diffraction study, as illustrated in the ORTEP diagram shown in Figure 1. Although the quality of the diffraction data is not high, the molecular structure is well-defined and the bond lengths and angles are comparable to those found in related complexes, particularly in the analogous derivative Ru(OC(=CH_2)-*o*-C_6H_4)(PMe_3)$_4$.[4c]

Even if *C*-enolate coordination is prevalent among compounds of the heavier group 10 elements Pd and Pt,[5] both *C*- and *O*-coordination are encountered in the corresponding Ni derivatives,[7b,9] as expected for a metal center with intermediate hard/soft character. Under the experimental conditions described above, the *O*-enolate is the major if not the exclusive tautomer that forms, but upon heating at 50 °C, the solutions of **1** in different solvents undergo slow conversion (ca. 12 h) to equilibrium mixtures of **1** and the *C*-enolate **2** (Scheme 1). The isomer ratio varies very little in the solvents used (**2**/**1** = 0.30 in THF; ca. 0.60 in C_6D_6 or cyclohexane) and does not change when the sample is cooled to room temperature. Unfortunately, all attempts to separate **2** by fractional crystallization have proved unsuccessful. Despite this, the identity of **2** is unambiguously deduced from the ^{13}C{^{1}H} NMR spectrum of the mixture, which displays a characteristic doublet of doublets at 47.7 ppm ($^2J_{CP}$ = 40, 16 Hz), due to the metal-bound CH_2 group of **2**. Kinetic measurements carried out in C_6D_6 between 52 and 92 °C showed that the equilibration process follows first-order kinetics, with $\Delta H^{\ddagger}$ = 18.5(3) kcal mol^{-1}, $\Delta S^{\ddagger}$ = −22(1) cal mol^{-1} K^{-1}, and $\Delta G^{\ddagger}$(298 K) = 25.3(3) kcal mol^{-1}. In view of the negative value of the activation entropy, a concerted mechanism, with a highly ordered η^3-oxoallyl transition state, seems likely. η^3-Oxoallyl complexes have been proposed before as intermediates in the interconversion between the *C*-and *O*-coordination modes of enolates.[4c]

Enolate **1** reacts with 1 equiv of PhC(O)H or MeC(O)H at room temperature, giving rise to the condensation products **4** and **5**, respectively (Scheme 2). The NMR spectra of these compounds share many features with those of **1** and indicate the presence of a

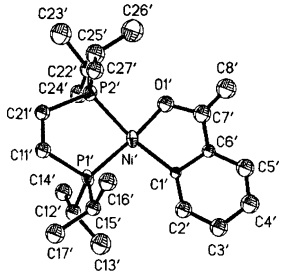
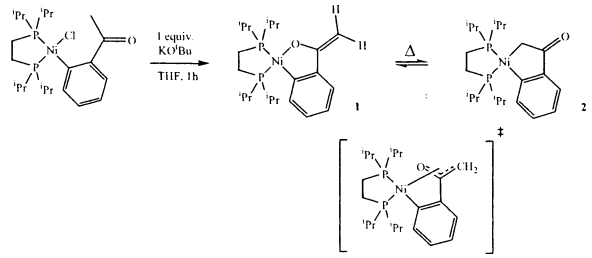


Figure 1. Structure of the complex **1**.

Scheme 1



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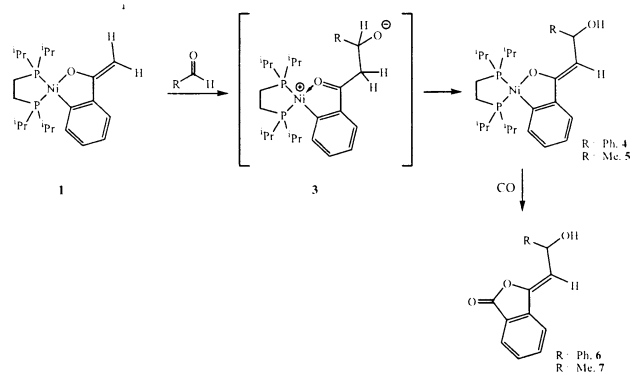
Scheme 2



substituted enolate ligand. For instance, they display a singlet resonance in their ^{1}H NMR spectra (δ 5.48, **4**; 4.73, **5**) which is assigned to an olefinic methyne proton. The corresponding carbon atom resonates at 97.4 and 97.3 ppm for **4** and **5**, respectively ($^1J_{CH}$ ca. 140 Hz). The hydroxyl group can be detected both in the ^{1}H NMR (**4**, 6.91; **5**, 5.77 ppm) and in the IR spectra (ca. 3200 cm^{-1}). The two products display low thermal stability. This has prevented us from gathering good analytic data for **5**, but both **4** and **5** are quantitatively carbonylated to the stable lactones **6** and **7**, which have been isolated and characterized. It is noteworthy that compounds **4**−**7** are selectively obtained as a single isomer that displays a *Z* double-bond substitution pattern. This is unambiguously established from their 2D NOESY spectra which exhibit clear NOE cross-peaks between the olefin proton and the H 5′ aromatic resonance. Although **4** and **5** retain an enolate functionality, they do not react further with aldehydes. As the presence of substituents on the double bond is not expected to decrease the nucleophilic character of the enolate, we assume that this lack of reactivity is due to steric effects.

To compare the reactivity of **1** and **2** toward aldehydes, ca. 2:1 mixtures of **1** and **2** have been reacted, at room temperature, with PhC(O)H and MeC(O)H. Monitoring these chemical changes by ^{31}P{^{1}H} NMR spectroscopy over a period of 24 h shows full consumption of **1**, whereas **2** remains unaltered. This result evinces that under the above conditions only the *O*-bound enolate has enough nucleophilic character to add to aldehydes, while the *C*-bound enolate lacks this reactivity.

One final aspect of the reactivity of **1** which is worthy of note concerns the nature of the aldehyde reaction products **4** and **5**. It is widely accepted that in aldol reactions induced by transition metal compounds, aldehyde coordination precedes the C−C bond-forming step.[2b,c,3a−f] As the metallacyclic nature of enolate **1** would impose considerable strain to achieve the C−C bond-making transition state, its reactions proceed otherwise. Hence the products **4** and **5** are not classical aldolates but instead new enolate derivatives that may result from aldehyde attack by the nucleophilic enolate carbon, followed by a proton shift (rather than Ni^{2+} shift) in the resulting dipolar intermediate **3** of Scheme 2. Another consequence of the cyclic structure of **1** is its ability to react with enolizable carbonyl compounds, a reaction that is often hampered by acid−base exchange of the added reagent and the coordinated enolate ligand.[2b,7b,10]

In summary, we have shown that the metallacyclic oxygen-bound nickel enolate **1** can be prepared in a straightforward manner and can be thermally isomerized to the corresponding *C*-bound enolate. Both tautomers display different reactivity, with only the former being capable of undergoing aldol additions to enolizable and nonenolizable aldehydes. Research in our laboratories continues to investigate this and related reactivity, in particular that of cyclic enolates in Michael additions to α,β-unsaturated carbonyl compounds.

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Supporting Information Available: Synthetic procedures and spectroscopic and analytical data for compounds **1**−**7** and X-ray crystallographic data (cif) for **1**. This material is available free of charge via the Internet at http//pubs.acs.org.

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