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Allylic Amination of Cyclohexene Catalyzed by Ruthenium Complexes. A New Reaction Involving an *Inter*molecular C−H Functionalization

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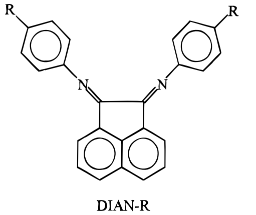
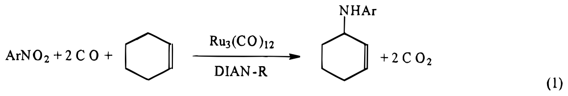
Transition-metal-mediated *inter*molecular activation and functionalization of C−H bonds is a topic of high current interest. From another perspective, the functionalization of a simple olefin by an external amine is also a topic that has attracted much interest. However, the direct *inter*molecular addition of an amine to an unactivated olefin, either metal-mediated or not, has met with only very limited success.[2] As far as allylic amines are considered as products, most reported synthetic procedures proceed *via* a palladium or nickel allyl complex. However, the synthesis of these intermediates usually requires the availability of a prefunctionalized starting material, such as an allyl acetate. A few methods have been reported in the literature, which afford an allylic amine by a C−H activation reaction.[3−6] Stoichiometric reactions have been performed employing sulfur or selenium imino compounds (RN═X═NR; X = S, Se),[3] or molybdenum oxaziridines.[4] A few catalytic processes have also been reported employing PhI═NTs[5] or PhNHOH[6] as the nitrogen-containing compound, but the turnover numbers are quite low and the aminating reagents are not readily available.

In this paper, we report on a new synthetic way to produce allylic amines, employing a simple unactivated olefin, cyclohexene, and an aromatic nitro compound as the aminating reagent, under reducing conditions (CO pressure). Although the method requires the use of a high-pressure apparatus, the reagents are bulk, cheap commercial products which do not need to be purified (although a higher selectivity can be achieved by purifying the olefin), the experimental operation is easy, the selectivity is high (up to 81.9% *under unoptimized conditions*), and the turnover numbers are higher than those reported for most C−H activation reactions. Only one precedent exists for an analogous reaction also examined in our laboratories,[7] but only trace amounts of allylic amine were obtained in that case, the main products being ureas and anilines.[8]

The reduction of aromatic nitro compounds by CO catalyzed by Ru$_3$(CO)$_{12}$ in the presence of DIAN-R, in commercial cyclohexene as solvent and at 160 °C and 40 bar, gives the corresponding allylamine derivatives as the main products (eq 1, Table 1). By-products of the reaction are the anilines corresponding to the nitro compounds. With a substrate/catalyst ratio of 50, only in the case of Ar = 4-MeOC$_6$H$_4$ is a complete conversion not achieved (entry 1). Moreover, in this case the reaction shows a poor selectivity. In the other cases, a complete conversion is also accompanied by a much better selectivity. The selectivity increases with an increase in the electron-withdrawing power of the substituent on the nitroarene (Table 1, entries 1−5) (Figure 1, Supporting Information).



DIAN-R
(R = H, CH$_3$, OCH$_3$, Cl)



(1)

The amount of aniline formed during the reaction is quite insensitive to the nature of the substituents.[9] This observation may be explained by the high tendency of some intermediate complex formed during the reaction to react with adventitious moisture more rapidly than any further step of the catalytic reaction. We have already shown that the Ru$_3$(CO)$_{12}$/DIAN-Me system is one of the best catalysts for the reduction of nitrobenzene to aniline by CO/H$_2$O.[10] However, when we employed cyclohexene purified by distillation over Na/benzophenone ketyl under the conditions of entry 5 in Table 1, the selectivity in aniline was slightly changed, although the selectivity in allylic amine increased to 81.9% (with a mass balance of 98.4%). Moreover, we could detect (by GC−MS) the formation of benzene and cyclohexadiene in the volatile fraction after the end of the reaction. The same two products were not present in the starting solvent, and their formation indicates that the substrate itself is responsible for at least part of the aniline formed, but moisture in the undried solvent plays a negligible role. The higher selectivity obtained with the purified substrate also indicates that, although the commercial olefin is a suitable substrate, it contains some impurities which lower the selectivity, affording unidentified, high-boiling products.

We also examined the effect of changing the substituent in the *para* position of the aryl rings of the ligand. In all the cases, the conversion was complete, but the selectivity in allylamine followed the order R = H > Me > OMe > Cl (entries 5 and 8−10). The less basic ligand clearly disfavors the formation of the allylamine, but there is no correlation with the Hammet σ constant. Use of 3,4,7,8-tetramethyl-1,10-phenanthroline (TMPhen) as the ligand in place of DIAN-R gave much poorer results (entry 7). Phosphines are even less efficient as ligands,

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Table 1[a]

entry	nitroarene	ligand	allylamine selectivity (%)[b]	aniline selectivity (%)[b]
1[c]	$4\text{-MeOC}_6H_4NO_2$	DIAN-Me	26.3	15.1
2	$4\text{-MeC}_6H_4NO_2$	DIAN-Me	55.0	27.4
3	$PhNO_2$	DIAN-Me	58.9	22.8
4	$4\text{-FC}_6H_4NO_2$	DIAN-Me	63.8	26.3
5	$3,4\text{-Cl}_2C_6H_3NO_2$	DIAN-Me	71.1	20.7
6[d]	$3,4\text{-Cl}_2C_6H_3NO_2$	DIAN-Me	75.8	20.7
7	$3,4\text{-Cl}_2C_6H_3NO_2$	TMPhen	22.4	34.4
8	$3,4\text{-Cl}_2C_6H_3NO_2$	DIAN-H	77.4	23.4
9	$3,4\text{-Cl}_2C_6H_3NO_2$	DIAN-OMe	61.8	30.5
10	$3,4\text{-Cl}_2C_6H_3NO_2$	DIAN-Cl	57.7	29.1
11[e]	$3,4\text{-Cl}_2C_6H_3NO_2$	DIAN-Me	74.3	25.5
12[f]	$3,4\text{-Cl}_2C_6H_3NO_2$	DPPE	26.2	42.7

[a] Experimental conditions: amount of $Ru_3(CO)_{12}$, 0.01 mmol; amount of ligand, 0.03 mmol; amount of $ArNO_2$, 0.5 mmol, T = 160 °C, P_{CO} = 40 bar; t = 6 h; in cyclohexene (10 mL). Conversion 100%. [b] Calculated with respect to the converted nitroarene; GC analysis. [c] Conversion 78.3%. [d] Amount of DIAN-Me, 0.047 mmol. [e] Amount of $3,4\text{-Cl}_2C_6H_3NO_2$, 1 mmol, conversion 86.0%. [f] $Ru(CO)_3(DPPE)$ (0.03 mmol) was used as catalyst, without any added ligand; conversion 51.6%.

even when the preformed complex (see later) $Ru(CO)_3(DPPE)$ (DPPE = 1,2-bis(diphenylphosphino)ethane) was employed (entry 12). Use of other catalytic systems such as Pd(2,4,6-trimethylbenzoate)$_2$/TMPhen[11] or $Rh_4(CO)_{12}$/Bipy[11] also afforded much poorer yields.

The results above reported for the $Ru_3(CO)_{12}$/DIAN-R catalytic system suggest that the reaction rate depends on the nitroarene concentration. The reaction conducted on $3,4\text{-Cl}_2C_6H_3NO_2$ under the usual catalytic conditions was also followed by using a high-pressure IR cell. Plotting the ln(absorbance) for the ν_{as,NO_2} at 1540 cm^{-1} *versus* time gave a straight line ($r^2 = 0.996$), clearly indicating a first order dependence of the reaction rate on the nitroarene concentration. This first-order dependence indicates that the initial activation of the nitroarene is the rate-determining step of the catalytic cycle, and the fact that the only substrate for which a complete conversion was not achieved is the one with a *p*-methoxy group, that is, the one with the most electron-releasing group among those tested, suggests that, analogously to all other investigated Ru, Rh, Fe, and Ni systems,[12] this activation is an electron transfer from the complex to the nitroarene.

The rate was also found to be a function of the olefin concentration. Use of mixtures of cyclohexene and toluene as solvents led to the observation that the reaction rate linearly increases as the olefin concentration is increased from 5% of the total volume to 75%, but then decreases when only the olefin is used as solvent, indicating a positive effect of the presence of a small amount of toluene that we still need to examine in more detail. The data collected (see Figures 2 and 3 in the Supporting Information) show that the rate follows the equation $-d[3,4\text{-Cl}_2C_6H_3NO_2]/dt = [3,4\text{-Cl}_2C_6H_3NO_2](k[\text{cyclohexene}] + c)$, with $k = 0.186$ L h^{-1} mol^{-1}, $c = 0.331$ L h^{-1}, and $r^2 = 0.9994$ (at 160 °C and under 40 bar of CO). This equation indicates the rate is also first order in olefin, but the nonzero intercept in Figure 3 indicates that there is a contribution from an olefin-independent reaction (see also later).

In order to ascertain if the aniline is only a byproduct and not an intermediate of the reaction,[13] one experiment was carried out by using $3,4\text{-Cl}_2C_6H_3NO_2$ as substrate, but also adding unsubstituted aniline to the reaction mixture. Only the adduct deriving from the substituted aryl ring and no adduct derived from aniline was detected among the products. Thus, aniline is clearly not an intermediate in the reaction.

The reaction is not limited to cyclohexene as substrate, and preliminary results show that cyclopentene, cyclooctene, and α-methylstyrene also afford a high yield of the desired adduct. However, 1-hexene gave only poor yields of a mixture of isomeric adducts, accompanied by isomerization of the unreacted olefin to a mixture of 1-, 2-, and 3-hexene, and allyl alcohol reacted as an alcohol to afford the carbamate $3,4\text{-Cl}_2C_6H_3\text{-}NHCOOCH_2CH{=}CH_2$, as is common in this kind of system.

In order to obtain some more information on the identity of the catalytically active species, we have undertaken a preliminary IR study of the $Ru_3(CO)_{12}$/DIAN-Me system. It is known that $Ru_3(CO)_{12}$ reacts in refluxing hexane with a nonrigid alkyldiazabutadiene derivative, *i*PrN=C(Me)C(Me)=N*i*Pr (*i*Pr-DAB), to give a mononuclear complex (eq 2).[14] When the same

$$Ru_3(CO)_{12} + 3i\text{Pr-DAB} \xrightarrow[N_2]{\text{hexane, reflux}} 3Ru(CO)_3(i\text{Pr-DAB}) + 3CO \quad (2)$$

reaction was performed using DIAN-Me instead of R-DAB, a complex was obtained which we formulate as $Ru(CO)_3$(DIAN-Me) on the basis of the IR and ^{1}H NMR data. The same IR spectrum was observed, by use of a high-pressure IR cell, at 160 °C and 40 bar of CO in hexane as solvent, together with absorptions due to $Ru(CO)_5$ and $Ru_3(CO)_{12}$, but the same bands were not observed under the same conditions if cyclohexene was used as solvent (a strong band at 1992 was observed instead), while $Ru(CO)_5$ and $Ru_3(CO)_{12}$ were unchanged. These data support the view, previously suggested by the catalytic experiments, that the olefin is also bound to the metal complex before the activation of the nitroarene and indicates that the active species should be a mononuclear complex of the kind $Ru(CO)_2$(DIAN-R)(cyclohexene). A rapid preequilibrium of this species with $Ru(CO)_3$(DIAN-R) would explain the observed first-order dependence of the rate on both the nitroarene and olefin concentrations, while the direct reaction of $Ru(CO)_3$(DIAN-R) with the nitroarene is proposed to account for the olefin-independent term in the rate equation.

Further studies are in progress to ascertain the scope and limits of this new amination reaction and to better understand its mechanism.

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Supporting Information Available: Figures 1−3 and IR and ^{1}H NMR data for $Ru(CO)_3$(DIAN-Me) (3 pages). See any current masthead page for ordering and Internet access instructions.

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