Scope and Pathway of Catalytic Aminomethylation of Olefins

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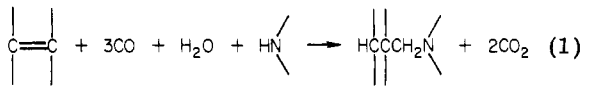
We describe a general and high-yield one-step process for synthesis of tertiary and secondary amines from olefins, carbon monoxide, water, and a nitrogen source in the presence of transition-metal compounds as catalysts. We find this chemistry, initially discovered by W. Reppe, applicable to a wide variety of olefins and nitrogen sources. This chemistry represents a novel general route to secondary and tertiary amines and polyamines. Rhodium-based compounds have been found to be the most effective catalysts.

A one-step, efficient, and general conversion of olefins to amines would be of fundamental importance for synthetic chemistry, but so far this goal had eluded the efforts of organic chemists.

Reaction 1 catalyzed by iron pentacarbonyl was dis-

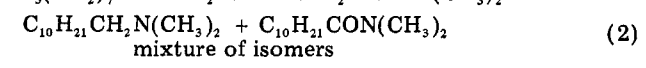


(1)

covered by Reppe[2] to produce amines in low yields. The same system was briefly investigated by Iqbal,[3] who found that rhodium oxide is an effective cocatalyst for reaction 1, and Laine[4] reported that mixed ruthenium/iron carbonyls can also catalyze reaction 1. There are also scattered reports in the patent literature[5] about the feasibility of reaction 1 where hydrogen instead of water is used as a hydrogen source. We believe that the different reactivity of a carbon monoxide/hydrogen system and a carbon monoxide/water system can be explained by the different tendencies toward metal hydride formation in these two systems. An extended discussion of these two approaches will constitute a subject of our future communications.

Synthetic Utility. The generality and wide applicability of this chemistry using readily available starting materials to synthesize amines, previously obtained only by multistep procedures, is illustrated in Table I. Molecules containing linear, branched, and cyclic double bonds, diolefins, and ammonia and primary and secondary amines as nitrogen sources are suitable starting materials for this reaction. Multiple amine isomers, if possible, are generally observed. The catalysts and reaction conditions of this chemistry also promote migration of the double bonds. It is important to note that secondary amine products dominate when primary amines or ammonia are used as a nitrogen source.

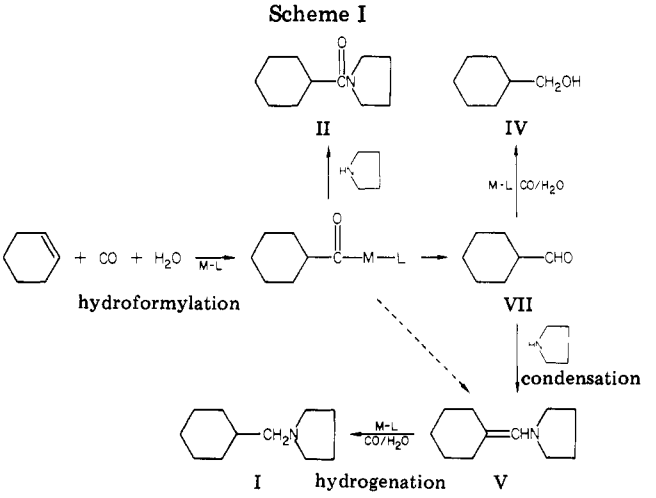
The catalytic utility of several different transition-metal catalysts was evaluated in reaction 2 (Table II). Rhodium



(2)

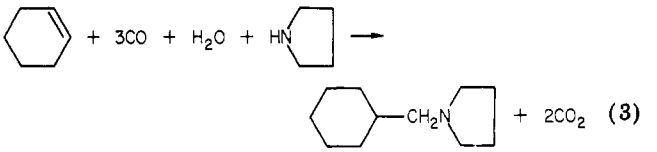
compounds are very effective catalysts for amine formation. The ruthenium and iridium-based catalysts also produce significant amounts of amines with relatively high selectivity toward formation of linear amines. Early quenching of the reaction reveals that the presence of several amine isomers (especially in the case of Rh-based catalysts) is due to the isomerization of the parent olefin prior to the aminomethylation reaction.

Scheme I



The large selection of rhodium and iridium species effectively promoting reaction 2 offers an obvious possibility for optimization of the aminomethylation reaction in any specific case and at the same time creates a challenge for a comprehensive mechanistic understanding of this chemistry.

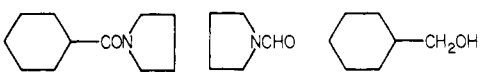
Pathway of the Aminomethylation Reaction. Reaction 3 was selected as a model system for the initial mechanistic study of the catalytic aminomethylation chemistry.



(3)

I

Using a cyclic olefin, cyclohexene, and a secondary amine, pyrrolidine, one precludes the formation of product mixtures (isomers or mixtures of primary, secondary, and tertiary amines). I, II, and III[6] in significant amounts and IV in trace amounts (<1%) were identified as products in reaction 3, accounting for 100 ± 2% of the starting materials. The relative yields of the specific components are a function of the reaction conditions and catalyst system.



II III IV

(1) Most of the data reported in this paper were initially presented at the 2nd International Symposium on Homogeneous Catalysis in Dusseldorf, West Germany.

(2) Reppe, W. *Experientia* **1959**, *5*, 93. German Patents 839 800, 1952; 909 937, 1954; 931 948, 1955.

(3) Iqbal, A. F. M. *Helv. Chim. Acta.* **1971**, *54*, 1440.

(4) Laine, R. M. *J. Org. Chem.* **1980**, *45*, 3370.

(5) U.S. Patents 4 096 150, 3 234 283, 3 513 200.

(6) Amines can be carbonylated to the *N*-formyl derivatives, using ruthenium or iron carbonyls: Byerley, J. J.; Rempel, G. L.; Takebe, N. *Chem. Commun.* **1971**, 1482. Dombek, B. D.; Angelici, R. J. *J. Catal.* **1977**, *48*, pp 433. We find rhodium carbonyls to catalyze formation of formamides as well.

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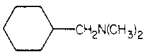
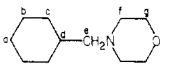
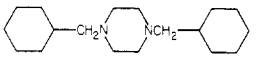
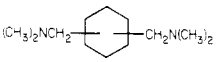
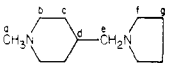
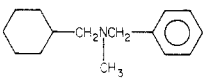
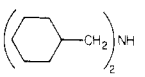
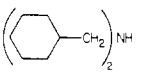
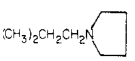
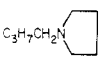
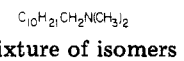
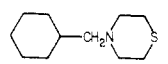
Table I

olefin	amine	product	% yield	MS, ^{13}C NMR, ^{1}H NMR data
cyclohexene [b]	dimethylamine		90	mass spectrum, *m/e* 14.158; ^{1}H NMR ($CDCl_3$) (s) 2.17, (d) 2.05 ppm
cyclohexene	morpholine		60	^{13}C NMR ($CDCl_3$) 67.01 (g), 66.13 (e), 54.24 (f), 34.74 (d), 31.83 (c), 26.85 (a), 26.13 ppm (b)
cyclohexene [b]	piperazine		70	mass spectrum, *m/e* 278.195; ^{1}H NMR ($CDCl_3$) 2.08 (d), 2.37 ppm (s)
1,4-cyclohexadiene [b,d]	dimethylamine	 mixture of isomers	50	mass spectrum, *m/e* 198, 154, 140
1-methyl-1,2,3,6-tetrahydropyridine [c]	pyrrolidine		20	^{13}C NMR ($CDCl_3$) 62.81 (e), 55.80 (b), 54.35 (f), 46.44 (a), 34.79 (d), 31.15 (c), 23.44 ppm (g)
cyclohexene [b]	*N*-methylbenzylamine		90	^{1}H NMR ($CDCl_3$) 7.23 (5 H), 3.40 (2 H), 2.11 ppm (5 H)
cyclohexene [b]	cyclohexene-methylamine		85	^{1}H NMR ($CDCl_3$) 2.40 (d); mass spectrum, *m/e* 209, 126
cyclohexene [a,e]	ammonia		50	^{1}H NMR ($CDCl_3$) 2.40 (d); mass spectrum, *m/e* 209, 126
isobutylene [a]	pyrrolidine		70	
trans-2-butene [b]	pyrrolidine	 2 isomers	70	
1-decene [c]	dimethylamine	 mixture of isomers	65	
cyclohexene	thiomorpholine		55	mass spectrum, *m/e* 199, 116, 88

[a] 1.23×10^{-4} mol of Rh_2O_3 as catalyst. [b] 2.46×10^{-4} mol of $[Rh(NBD)((CH_3)_2PPh)_3]^+PF_6^-$ as catalyst. [c] 0.41×10^{-4} mol of $Rh_6(CO)_{16}$ as catalyst. [d] 6.15×10^{-2} mol of cyclohexadiene. [e] 1.23 mol of NH_3, 1600 psi of carbon monoxide.

Table II [a]

catalyst	conversion, %	total amines, %	total amides, %	rel isomer distribution of amines, % α	β	γ	δ	ε
$RhCl_3(Py)$	90	72	12	35	31	12	11	10
$[(NH_3)_5RhCl]SO_4$	84	72	12	37	31	11	10	10
$[Rh(NBD)((CH_3)_2PPh)_3]^+PF_6^-$		66	3	32	38	13	10	8
$Rh_6(CO)_{16}$	84	71	10	37	30	12	10	10
$Ru_3(CO)_{12}$	38	38		73	25	2		
$IrBr((CO)OPPh_3)_2$	55	49	2	53	34	9	4	1

[a] Reactor: 10-mL SS Hoke cylinder placed in a 160 °C preheated shaker bath for 8 h; 1-decene, 5.29×10^{-3} mol; dimethylamine, 5.56×10^{-3} mol; H_2O 5.55×10^{-3} mol; *N*-methylpyrrolidine, 1 mL. [Rh-], [Ru-], and [Ir-] catalysts ≡ [olefin] 500^{-1} (number of Me atoms)$^{-1}$. Conversion, total amines, and total amides calculated on the basis of the starting amount of 1-decene. Amine isomer distribution (α, β, γ, δ, α = linear) normalized for the total amine yield. All analytical data obtained by GC internal standard method.

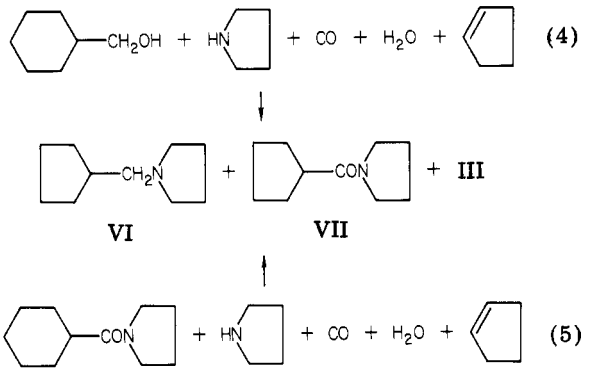
While the intimate mechanistic details of reaction 3 are still under investigation, the chemistry depicted in Scheme I is consistent with our experimental findings. Laine[5] also suggested the feasibility of the pathway depicted in Scheme I for reaction 1. We believe that the following arguments prove it convincingly.

The overall aminomethylation process can be formally divided into three reactions. The first is hydroformylation leading to the formation of aldehyde or metal acyl species followed by condensation, resulting in the intermediate formation of Schiff's base or enamine, and subsequent hydrogenation of the C=N or C=C—N bond, respectively, producing the desired end product amine.

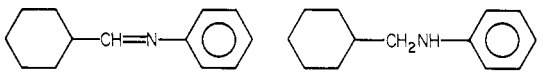
The possibility of amide II or alcohol IV being intermediates to I was eliminated by the results of the experiments, best described by eq 4 and 5, where II and IV were used as starting materials. While VI, VII, and III are formed in high yields, the amine I has not been detected and II as well as IV is completely recovered.[7]

The intermediacy of the aldehyde and enamine species either free or metal coordinated is strongly suggested by several lines of evidence: (a) The origin of the alcohol is best explained by the hydrogenation of the corresponding aldehyde. (b) The isomer distribution of the amine

(7) The presence of cyclopentene in reactions 4 and 5 elminates the possibility that an activation of the catalyst by an olefin is required. Also the rates of formation of I and V in separate experiments are comparable, $k_I/k_V = 0.7$, and they do not complicate the interpretation of the results of reactions 4 and 5.

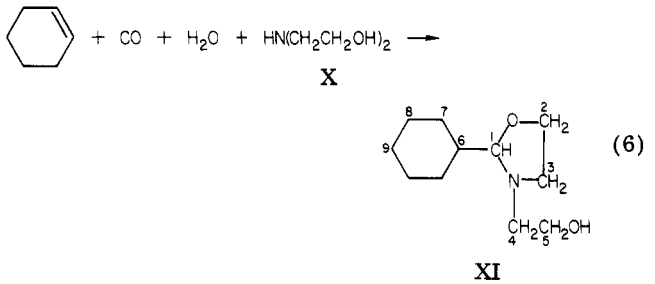


products in reaction 2 is similar to that for hydroformylation products from the same olefin. Aminomethylation of isobutylene with pyrrolidine yields exclusively *N*-(3-methylbutyl)pyrrolidine, where the hydroformylation leads exclusively to 3-methylbutanal.[8] (c) Enamines are known to form readily from aldehydes and secondary amines under these conditions,[9,10] The enamine V is easily quantitatively hydrogenated in this system to the corresponding amine. When ammonia or primary amines are used, an imine intermediate may also be important. For example, the aminoethylation of cyclohexane with aniline yields both imine VIII and amine IX. VIII



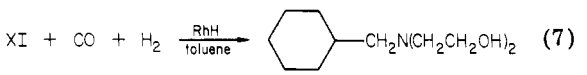
VIII IX

was also hydrogenated under these reaction conditions with 30% yield. When diethanolamine (X) is used as a nitrogen source in reaction 6, oxazolidine XI is obtained as a major



XI

product (yield 70%). The condensation of aldehyde VII and diethanolamine leads also to a quantitative formation of XI. XI can be subsequently hydrogenated (eq 7) to the corresponding amine XII. Also consistent with Scheme



XII

I is the fact that carbazole does not undergo the aminomethylation reaction with cyclohexene as one would expect, considering the lack of enamine formation in reaction of carbazole with cyclohexanecarbaldehyde (VII).

The aldehyde/amine condensation[10] and subsequent hydrogenation can also occur independently from hydroformylation.[11] Although it is not certain that aldehyde appears as a distinct intermediate in 1, Scheme I implies at least a common intermediate (R–CO–M–L) for hydroformylation and aminomethylation reactions.

One can thus conclude that the feasibility of olefin hydroformylation and condensation of corresponding aldehyde with the nitrogen source are primary criteria for the aminomethylation of olefins.

Experimental Section

Reagents and solvents were reagent grade and used without further purification. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Varian EM 390 (90 MHz) and are reported relative to internal Me_4Si. ^{13}C NMR were taken on a JEOL FX 100 (100 MHz). The mass spectra were recorded at 70 eV on an AEI MS 12 mass spectrometer.

General Procedures. Unless otherwise indicated, 0.123 mol of olefin, 0.25 mol of amine, 0.25 mol of water, 25 mL of *N*-methylpyrrolidine, and catalysts were placed in a 150-mL stainless steel cylinder that was subsequently pressurized with 1000 psi of carbon monoxide and placed in an oil shaker bath at 140 °C for 6 h. Unless otherwise mentioned, $[Rh(NBD)((CH_3)_2PPh)_3]^+PF_6^-$ was used as catalyst. The mole amount of a catalyst used was calculated according to the following formula: mole amount of olefin 500^{-1} (number of Rh atoms in a molecule)$^{-1}$. The quantitative results were obtained by GC internal standard analysis, using 10% Carbowax 20M, 2% KOH, 80/100 Chromosorb WAW glass column from Supelco.

Hydrogenation of Enamine V and Schiff's Base VIII. V was synthesized by mixing equivalent amounts of pyrrolidine and cyclohexanecarbaldehyde at ambient temperature and subsequent vacuum distillation [^{1}H NMR ($CDCl_3$) 5.51 ppm]. Except for the absence of olefin and amine, the reaction conditions described in the general procedure were used for hydrogenation of V (yield 100%). The same procedure was used for hydrogenation of VIII. IX: ^{1}H NMR ($CDCl_3$) 2.87 (d, 2 H), 3.58 ppm (s, 1 H).

Oxazolidine Formation (7). XI has been vacuum distilled and characterized: ^{13}C NMR 101.07 (d), 64.08 (t), 56.77 (t), 52.34 (t), 60.82 (t), 41.57 (t), 29.38–26.07 ppm (t), five signals (asymmetric center at C1); mass spectrum, *m/e* 198, 116.

Hydrogenation of XII (8). CO/H_2 (1:1) mixture (1000 psi) in the presence of $[Rh(NBD)((CH_3)_2PPh)_3]^+PF_6^-$ (1/500) and toluene as a solvent was used for hydrogenation of XII at 150 °C for 5 h: ^{1}H NMR 4.06 (s, 2 H), 3.55 (t, 4 H), 2.59 (t, 4 H), 2.27 ppm (d, 2 H).

Acknowledgment. We thank Dr. J. L. Gove and Mr. M. W. Smith for their valuable assistance in analytical work.

Registry No. I, 5005-27-6; V, 6815-55-0; VIII, 62582-99-4; IX, 79952-92-4; X, 111-42-2; XI, 55135-29-0; XII, 79952-93-5; *N*-methylpyrrolidine, 120-94-5; cyclohexanecarbaldehyde, 2043-61-0; cyclohexene, 110-83-8; 1,4-cyclohexadiene, 628-41-1; 1-methyl-1,2,3,6-tetrahydropyridine, 694-55-3; isobutylene, 115-11-7; *trans*-2-butene, 624-64-6; 1-decene, 872-05-9; dimethylamine, 124-40-3; morpholine, 110-91-8; piperazine, 110-85-0; pyrrolidine, 123-75-1; *N*-methylbenzylamine, 103-67-3; cyclohexenemethylamine, 32917-19-4; ammonia, 7664-41-7; thiomorpholine, 123-90-0; *N*,*N*-dimethylcyclohexanemethylamine, 16607-80-0; *N*-(cyclohexylmethyl)-morpholine, 5005-25-4; 1,4-bis(cyclohexylmethyl)piperazine, 79952-94-6; bis[(*N*,*N*-dimethylamino)methyl]cyclohexane, 79953-29-0; 1-methyl-4-[(pyrrolidin-1-yl)methyl]piperidine, 79970-14-2; *N*-(cyclohexylmethyl)-*N*-methylbenzylamine, 79952-95-7; *N*-(cyclohexylmethyl)cyclohexanemethylamine, 3309-27-1; *N*-(3-methylbutyl)-pyrrolidine, 4462-08-2; *N*-pyrrolidinylbutane, 79953-30-3; (dimethylamino)undecane, 79953-31-4; *N*-(cyclohexylmethyl)thiomorpholine, 79952-96-8; $RhCl_3(py)_3$, 15617-30-8; $[(NH_3)_5RhCl]SO_4$, 21360-80-5; $[Rh(NBD)((CH_3)_2PPh)_3]^+PF_6^-$, 32761-50-5; $Rh_6(CO)_{16}$, 28407-51-4; $Ru_3(CO)_{12}$, 15243-33-1; $IrBr(CO)(OPPh_3)_2$, 79953-37-0.

(8) Gankin, V. Y.; Genender, L. S.; Rudkovskii, D. M. "Carbonylation of Unsaturated Hydrocarbons"; Rudkovskii, D. M., Ed.; Leningrad, 1968; p 61.
(9) Bergman, E. D. *Chem. Rev.* **1953**, *53*, 309.
(10) Cook, A. G., Ed.; "Enamines"; Marcel Dekker: New York, 1969.
(11) Watanabe, Y.; Shim, S. C.; Mitsudo, T.; Yamashita, M.; Takegami, Y. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2301.