Substituent effects in the cobalt-catalyzed oxidative carbonylation of aromatic amines

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Abstract

The N,N-bis(salicylidene)ethylenediaminocobalt(II)-catalyzed oxidative carbonylation of *ortho*-, *meta*- and *para*-substituted aromatic primary amines in methanol gives ureas, isocyanates, carbamates, azoderivatives. The conversion is correlated for six substrates with Hammett σ giving a $\rho = -0.5$. This suggests the electrophilic attack of carbon monoxide at a nitrogen anion complexed to cobalt in the transition state. Force field calculations show that octahedral *trans*-di-aminocobalt(III)salen intermediates have stability very similar to that of the corresponding *cis* derivatives. These latter are suggested to be intermediates in the formation of ureas. Steric effects in an unknown transition state may explain the fact that high yields in ureas are obtained only using *para*-substituted anilines as starting materials.

Keywords: Cobalt; Carbonylation; Oxidation; Urea; Force field; Aromatic amine

1. Introduction

The reaction of phosgene with amines is one of the most important industrial methods for the formation of isocyanates, carbamates and ureas [1]. The environmental risk connected with the use of phosgene could be avoided using alternative methods with low environmental impact.

In previous experiments the treatment of certain aromatic primary amines with carbon monoxide (1 atm) and dioxygen (1 atm) in methanol in the presence of N,N-bis(salicylidene)ethylenediaminocobalt(II) as a catalyst led to the formation of azo derivatives, deriving

from an oxidation reaction; carbamates and ureas, deriving from oxidative carbonylation. The selectivity in the oxidative carbonylation reaction was not high. An isocyanate was intermediate in these reactions, and could be evidenced by performing the oxidative carbonylation in methylene chloride [2]. At increased oxygen and carbon monoxide ureas were formed in good yields, with only small amounts of carbamates and azo derivatives. Aromatic amines having certain *ortho*-substituents also gave cyclic ureas via a metal-induced oxidative carbonylation–cyclization pathway [3].

An aliphatic primary amine lacking α-hydrogens was also submitted to these reaction conditions and gave moderate amounts of the corresponding carbamate. Performing the reaction under pressure of both reactant gases gave higher

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selectivity in carbamate and allowed operation with a smaller amount of catalyst [4].

This homogeneous catalytic system seemed to have advantages over the well known synthesis of ureas and carbamates via phosgene [1], and seemed to be complementary to another modern non-phosgene route for the carbonylation of amines: the use of dimethylcarbonate [5]. A more systematic study was needed in order to optimize the cobalt-catalyzed oxidative carbonylation reaction of aromatic primary amines.

2. Results and discussion

Five groups of *ortho*-, *meta*- and *para*-substituted anilines were submitted to the cobalt-catalyzed oxidative carbonylation. The first group was constituted by 2-, 3-, 4-chloroaniline (1–3). These substrates were poorly converted under these reaction conditions. Reaction products were the isocyanates (4, 5) and the carbamates (6, 7) in the *ortho*- and the *meta*-substituted substrate (Table 1). The *para*-substituted substrate gave the carbamate (8) only in trace amounts. All these amines formed the ureas (9–11) in amounts which followed the series:

para ≫ *meta* > *ortho*

The urea was the main reaction product with the *para*-substituted compounds. The azoderivatives (12, 13) were present in trace amounts.

A very similar situation occurred with 2-, 3- and 4-fluoroaniline (14–16). Isocyanates (17, 18) and carbamates (19, 20) were the main reaction products with the *ortho*- and the *meta*-isomer. The urea (24) was preferentially formed with the *para*-isomer.

A much higher reactivity was shown by the three isomeric methylanilines (26–28). Again, the urea (36) was the most important product in the *para*-isomer, the isocyanate and the carbamate with the other two isomers.

Methoxyanilines (40–42) were less reactive than methylanilines, but the formation of the urea was again favored by the presence of the *para*-substituent. The two bromoanilines (55, 56) were poorly reactive. The distribution of reaction products was similar to the other substrates.

Conversion values of six *para*- and *meta*-substituted substrates were correlated with the electronic effect of the substituents expressed in terms of Hammett σ [6] (Fig. 1). *ortho*-substituted substrates cannot be included in this correlation because of steric effects. The sensitivity of the reaction to the electronic effects of

Table 1
Conversion and selectivity in the cobalt-catalyzed oxidative carbonylation of aromatic amines

| Substrate	Selectivity in reaction products %				
	conversion%	isocyanate	carbamate	urea	azoderivative
2-chloroaniline (1)	27	(4): 68	(6): 30	(9): 2	(12): traces
3-chloroaniline (2)	29	(5): 44	(7): 22	(10): 21	
4-chloroaniline (3)	13		(8): traces	(11): 85	(13): traces
2-fluoroaniline (14)	42	(17): 39	(19): 43	(22): 18	
3-fluoroaniline (15)	41	(18): 34	(20): 42	(23): 22	
4-fluoroaniline (16)	96		(21): 3	(24): 80	(25) 1
2-methylaniline (26)	75	(29): 28	(31): 51	(34): 14	(37): 1
3-methylaniline (27)	70	(30): 57	(32): 26	(35): 12	(38): 1
4-methylaniline (28)	92		(33): 9	(36): 64	(39) 4
2-methoxyaniline (40)	25	(43): 76	(46): 11	(49): 11	(52): 1
3-methoxyaniline (41)	31	(44): 28	(47): 25	(50): 27	(53): 6
4-methoxyaniline (42)	31	(45): 43	(48): 2	(51): 53	(54): 1
3-bromoaniline (55)	9	(57): 25	(58): 32	(60): 21	(62): traces
4-bromoaniline (56)	16		(59): traces	(61): 88	(63): traces
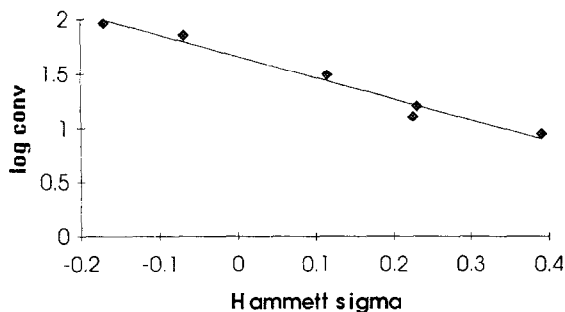
Fig. 1. Hammett plot of the conversion of 4-chloro-, 3-chloro-, 3-methyl-, 4-methyl-, 3-bromo-, 4-bromoaniline versus σ.

the substituents (ρ) was calculated to be -0.5 ($r^2 = 0.97$).

These data allow to suggest a mechanism for this reaction.

The reactivity of primary amines with N,N-bis(salicylidene)ethylenediaminocobalt(II) [Co(II)salen] (64):
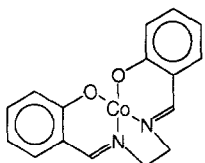

(64)

in the presence of dioxygen is believed to derive from an initial complexation of the amine to give a Co(II)amino complex (65) [7]. Complex (65) is in equilibrium with the amido complex (66):

$$Ph-NH_2 + Co(II)L_5$$

$$\rightleftharpoons Ph-NH_2-Co(II)L_5 \rightleftharpoons Ph-NH-Co(II)L_5$$
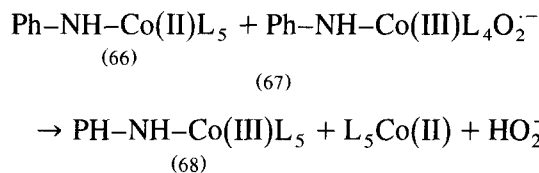$$\qquad (65) \qquad\qquad\qquad (66)$$
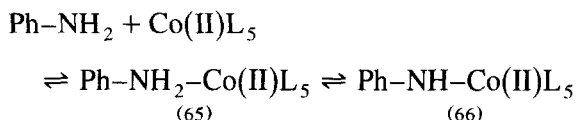
Such Co(II) complexes react easily with dioxygen and are transformed into the corresponding Co(III) superoxo complexes (67) [8], which are fairly basic [9].

$$Ph-NH-Co(II)L_5 + O_2$$
$$\qquad (66)$$

$$\rightleftharpoons Ph-NH-Co(III)L_4O_2^{\cdot-}$$
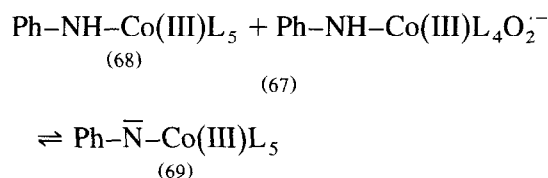$$\qquad (67)$$
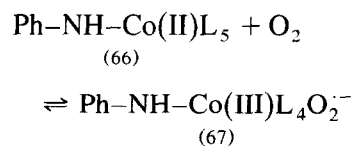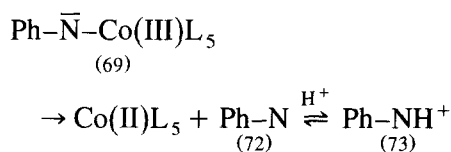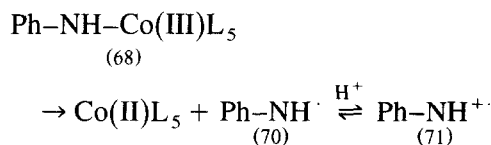
The superoxo complex (67) will act as an

oxidant toward the Co(II) species, forming Co(III) species such as (68) which have an acidic hydrogen owing to the presence of the cobalt(III) atom attached to nitrogen.
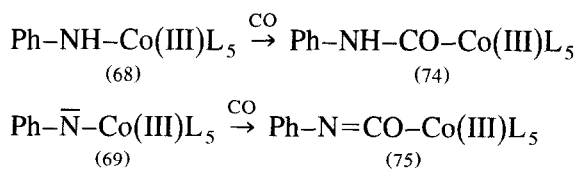
$$Ph-NH-Co(II)L_5 + Ph-NH-Co(III)L_4O_2^{\cdot-}$$
$$\qquad (66) \qquad\qquad\qquad (67)$$

$$\rightarrow PH-NH-Co(III)L_5 + L_5Co(II) + HO_2^-$$
$$\qquad (68)$$

Hence, they are deprotonated by the basic superoxo complex to give the anion (69):

$$Ph-NH-Co(III)L_5 + Ph-NH-Co(III)L_4O_2^{\cdot-}$$
$$\qquad (68) \qquad\qquad\qquad (67)$$

$$\rightleftharpoons Ph-\overline{N}-Co(III)L_5$$
$$\qquad (69)$$

Complexes (68) and (69) are respectively amino radicals (70) and nitrenes (72) coordinated to cobalt. These species are in acid–base equilibrium with the corresponding protonated forms, aminiumyl radicals (71) or nitrenium ions (73) respectively.

$$Ph-NH-Co(III)L_5$$
$$\qquad (68)$$

$$\rightarrow Co(II)L_5 + Ph-NH^{\cdot} \overset{H^+}{\rightleftharpoons} Ph-NH^{+\cdot}$$
$$\qquad\qquad\qquad (70) \qquad\qquad (71)$$

$$Ph-\overline{N}-Co(III)L_5$$
$$\qquad (69)$$

$$\rightarrow Co(II)L_5 + Ph-N \overset{H^+}{\rightleftharpoons} Ph-NH^+$$
$$\qquad\qquad\qquad (72) \qquad\quad (73)$$

Both cobalt-centered complexes (68) and (69) undergo carbonylation. In the case of the amido complex or its anion, they will give respectively a carbamoyl complex (74) or an isocyanato complex (75):

$$Ph-NH-Co(III)L_5 \overset{CO}{\rightarrow} Ph-NH-CO-Co(III)L_5$$
$$\qquad (68) \qquad\qquad\qquad (74)$$

$$Ph-\overline{N}-Co(III)L_5 \overset{CO}{\rightarrow} Ph-N=CO-Co(III)L_5$$
$$\qquad (69) \qquad\qquad\qquad (75)$$

Isocyanates were found in high yield in the oxidative carbonylation of these aromatic

amines, in spite of the fact that isocyanates are readily transformed into methyl carbamates when heated in methanol. This suggests that isocyanates coordinated to cobalt are formed in the reaction, and that coordination to cobalt prevents hydrolysis. Isocyanates could derive from the carbonylation of the anion (69) or of a nitrene. Nitrenes are known to react with carbon monoxide to give isocyanates [10], but this reaction is known to occur at high temperatures and high carbon monoxide pressure. Hence, the anion (69) could be the intermediate.

The negative ρ value of -0.5 for the reaction of some substrates is in line with this interpretation. In fact, this value suggests that the negative nitrogen atom of the intermediate undergoing carbonylation effects the nucleophilic attack to carbon monoxide. This generates a loss of negative charge at nitrogen in the transition state. Hence, the reaction occurs through a rate-determining electrophilic carbonylation of a cobalt-centered amido anion to give an isocyanato complex.

Hence, the Co(II)salen-catalyzed oxidative carbonylation of primary aromatic amines seems to occur with a mechanism different from the Co(II)salen-catalyzed oxidative N-dealkylation of n-butylanilines [11].

The selectivity in urea was high when a para-substituted aniline was the substrate. Minor amounts of ureas were obtained using meta-substituted anilines, and lower yields were obtained using ortho-substituted substrates. In order to explain this behavior, the possibility that the cobalt atom could act as a template in an intramolecular cyclization reaction leading to
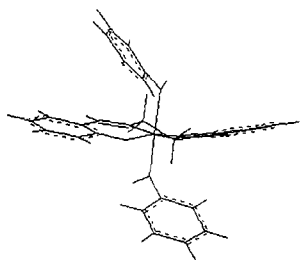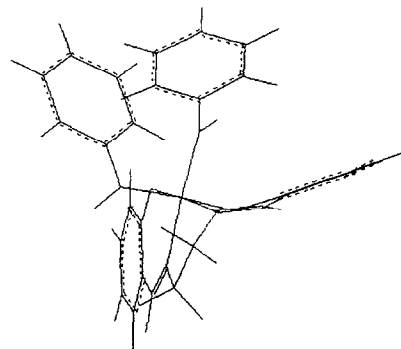

Fig. 2. Force field calculated trans-anion (69).

Fig. 3. Force field calculated cis-anion (69).

an urea was considered and steric effects which could be important in this reaction were studied.

The Co(III)-centered amino complexes are probably a mixture of trans and cis structures. This behavior has been shown for other Co(III)salen complexes such as K[Co(III)salenCO₃] [12] for [Co(III)L(acac)] [13] and for complexes deriving from the reduction of hydroxo Co(III)-Schiff base complexes with alcohols [14].

Figs. 2 and 3 show models of the trans and cis structure of the anion (69) obtained using force field calculations. The influence of steric effects on the stability of cobalt-centered intermediates was studied performing force field calculations on the dependence of the steric minimum energy of the cis- and the trans-isomers of the anions (69) from the size of the nuclear substituents. In fact, cis-complexes, having a non-planar salen ligand, could act as templates for the formation of products involving the reaction of two molecules of substrate, i.e. azo derivatives and ureas. The action of the metal center as a template has also been suggested in other cases. In fact, lead tetraacetate oxidation of aromatic amines gives oxidative dimerization to azoderivatives by an intramolecular reaction of two molecules of amine bound to the Pb(IV) atom [15].

The fact that the urea is the primary product for many oxidative carbonylations suggests that a carbonylated intermediate such as the isocyanato complex is attacked by an amino ligand
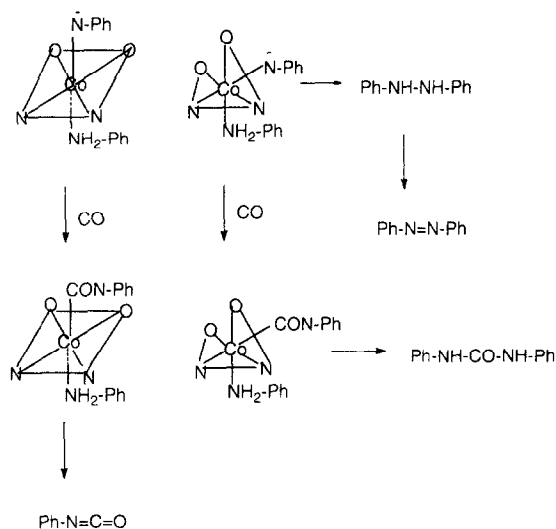
Scheme 1.

from a proximal site in a complex having a *cis* octahedric structure and two proximal nitrogen ligands, as shown in Scheme 1. The isocyanato complex could be formed by carbonylation of the anion (69). This could be present in *trans–cis* equilibrium. The *trans*-isomer could undergo carbonylation to a cobalt-isocyanate complex which could release isocyanate or be solvolyzed to a carbamate. The *cis* isomer could undergo carbonylation to a *cis* cobalt isocyanate which could rearrange to an urea through a

nucleophilic attack of the amino ligand to the isocyanate carbon. Alternatively, the nucleophilic attack of the negative nitrogen on the electrophilic nitrogen of the coordinated amine could form an azoderivative.

Force field calculations shown in Table 2 excluded that the *cis*- and the *trans*-isomer are in equilibrium. In fact, the barrier for *cis–trans* isomerization was too high if compared with the reaction temperature (60°C). Hence, the *cis:trans* ratio was kinetically controlled. This led to the consideration that the dependence from the position of the nuclear substituent of the ratio between the bimolecular process leading to ureas and the monomolecular process leading to isocyanates and carbamates did not derive from steric factors within the coordination sphere of cobalt in the intermediates shown in Figs. 1 and 2. Hence the preference for the formation of ureas in *para*-substituted substrates and of isocyanate–carbamate in *ortho*-substituted substrates appears to be due to kinetic control in the rate-determining carbonylation of the intermediate *cis*- and *trans*-anions shown in Scheme 1.

The presence of steric effects both in the conversion and in the selectivity for ureas was studies plotting the steric factor E_s with conversion and selectivity with three *ortho*-substituted

Table 2

The dependence from the size of the nuclear substituents of the steric minimum energy of the *cis*- and the *trans*-isomers of the anions (69)

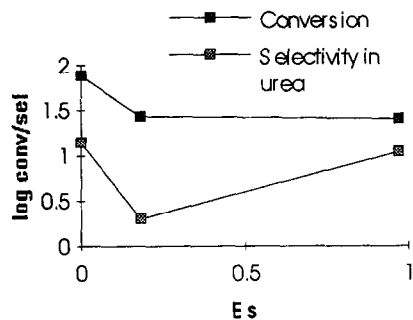| $X-C_6H_4-NH-CoL_4-N^--C_6H_4-X$ $X =$	*Trans*-isomer (kcal/mol Å)	*Cis*-isomer (kcal/mol Å)	Difference (kcal/mol Å)	Selectivity in. urea (%)
4-Cl	57.41	67.28	9.87	85
3-Cl	57.16	66.92	9.77	21
2-Cl	59.73	68.60	8.87	2
4-F	57.69	67.55	9.86	80
3-F	57.61	67.48	9.83	22
2-F	58.14	67.79	9.65	18
4-Me	62.35	72.27	9.92	64
3-Me	61.97	71.30	9.33	12
2-Me	63.47	74.82	11.35	14
4-OMe	71.07	80.56	9.49	53
3-OMe	70.80	80.90	10.10	27
2-OMe	68.51	79.71	11.2	11
4-Br	56.84	66.71	9.87	88
3-Br	56.52	66.22	9.70	21

Fig. 4. Steric effects in the conversion and selectivity in urea for the Co(salen)-catalyzed oxidative carbonylation of 2-methyl, 2-chloro- and 2-methoxyaniline.

anilines. Fig. 4 shows that steric effects seemed not to play an important role.

In conclusion, the cobalt-catalyzed oxidative carbonylation of aromatic primary amines is achieved in high yield, with simple and low-cost environmentally compatible reactants and procedures under mild conditions. This reaction seems to be complementary for the preparation of ureas and carbamates to the palladium-catalyzed oxidative carbonylation of aromatic amines [16], the ruthenium-catalyzed reductive carbonylation of aromatic nitroderivatives [17], the indirect electrochemical carbonylation of aromatic amines with a palladium catalyst [18].
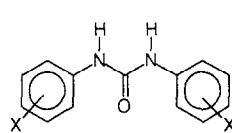
(9): X = 2-Cl
(10): X = 3-Cl
(11): X = 4-Cl
(22): X = 2-F
(23): X = 3-F
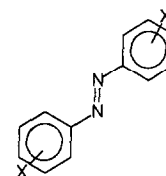(24): X = 4-F
(34): X = 2-CH3
(35): X = 3-CH3
(36): X = 4-CH3
(49): X = 2-OCH3
(50): X = 3-OCH3
(51): X = 4-OCH3
(60): X = 3-Br
(61): X = 4-Br

(12): X = 2-Cl
(13): X = 4-Cl
(25): X = 4-F
(37): X = 2-CH3
(38): X = 3-CH3
(39): X = 4-CH3
(52): X = 2-OCH3
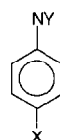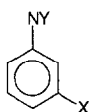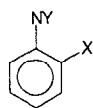(53): X = 3-OCH3
(54): X = 4-OCH3
(62): X = 3-Br
(63): X = 4-Br

Scheme 3.

Schemes 2 and 3 show starting materials and reaction products.

3. Experimental

Anilines were commercial grade reagents. All solvents were distilled before use. The catalyst N,N-bis(salicylidene)ethylenediaminocobalt(II)

(1): X = Cl; Y = H2
(4): X = Cl; Y = CO
(6): X = Cl; Y = HCOOCH3
(14): X = F; Y = H2
(17): X = F; Y = CO
(19): X = F; Y = HCOOCH3
(26): X = CH3; Y = H2
(29): X = CH3; Y = CO
(31): X = CH3; Y = HCOOCH3
(40): X = OCH3; Y = H2
(43): X = OCH3; Y = CO
(46): X = OCH3; Y = HCOOCH3

(2): X = Cl; Y = H2
(5): X = Cl; Y = CO
(7): X = Cl; Y = HCOOCH3
(15): X = F; Y = H2
(18): X = F; Y = CO
(20): X = F; Y = HCOOCH3
(27): X = CH3; Y = H2
(30): X = CH3; Y = CO
(32): X = CH3; Y = HCOOCH3
(41): X = OCH3; Y = H2
(44): X = OCH3; Y = CO
(47): X = OCH3; Y = HCOOCH3
(55): X = Br; Y = H2
(57): X = Br; Y = CO
(58): X = Br; Y = HCOOCH3

(3): X = Cl; Y = H2
(8): X = Cl; Y = HCOOCH3
(16): X = F; Y = H2
(21): X = F; Y = HCOOCH3
(28): X = CH3; Y = H2
(33): X = CH3; Y = HCOOCH3
(42): X = OCH3; Y = H2
(45): X = OCH3; Y = CO
(48): X = OCH3; Y = HCOOCH3
(56): X = Br; Y = H2
(59): X = Br; Y = HCOOCH3

Scheme 2.

hydrate (Cosalen) was a commercial product (Aldrich Inc.). Carbon monoxide and dioxygen were high purity grade. GC-MS analyses were performed with a Hewlett Packard 5971A instrument, (split/splitless injector, capillary column SPB-5, 30 m, 0.32 mm I.D.) Mass spectra were recorded on a VG 7070 EQ instrument operating in electron impact at 70 eV or in chemical ionization, ionizing gas isobutane.

Force field calculations were performed using Hyperchem 2.0, Hypercube.

3.1. Reaction procedure

A 5×10^{-2} M methanol solution of the substrate and the appropriate amount of catalyst to give a [substrate]/catalyst ratio = 10 was put in a glass liner, fitted in an autoclave, charged with dioxygen (2 bar) and carbon monoxide (10 bar) and heated at 60°C in a thermoregulated oil bath. After 48 h, the autoclave was allowed to cool to room temperature, and outgassed. After evaporation of the solvent under reduced pressure, the residue was chromatographed on silica gel Merck 0.05–0.2 mm ($R = 100$), using chloroform–ethyl acetate as the eluting mixture. The fractions were then analyzed by gas chromatography. Direct recovery of the ureas from the reaction medium was obtained by cooling the reaction mixture to 0°C. The resulting precipitate was filtered and recrystallized from methanol.

Acknowledgements

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